The Association between Time Spent Outdoors and Myopia Using a Novel Biomarker of Outdoor Light Exposure

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Purpose. We sought to determine whether conjunctival ultraviolet autofluorescence (UVAF), a biomarker of outdoor light exposure, is associated with myopia.

Methods. We performed a cross-sectional study on Norfolk Island and recruited individuals aged ≥15 years. Participants completed a sun-exposure questionnaire and underwent non-cycloplegic autorefraction. Conjunctival UVAF used a specially adapted electronic flash system fitted with UV-transmission filters (transmittance range 300–400 nm, peak 365 nm) as the excitation source. Temporal and nasal conjunctival UVAF was measured in both eyes using computerized photographic analysis with the sum referred to as "total UVAF."

Results. In 636 participants, prevalence of myopia decreased with an increasing quartile of total UVAF ($P_{trend} = 0.002$). Median total UVAF was lower in subjects with myopia (spherical equivalent [SE] ≤ −1.0 diopter [D]) than participants without myopia: 16.6 mm^2 versus 28.6 mm^2, $P = 0.001$. In the multivariable model that adjusted for age, sex, smoking, cataract, height and weight, UVAF was independently associated with myopia (SE ≤ −1.0 D): odds ratio (OR) for total UVAF (per 10 mm^2) was 0.81, 95% confidence interval (CI) 0.69 to 0.94, $P = 0.007$. UVAF was also significantly associated with myopia when analysis was restricted to subjects <50 years, and in moderate-severe myopia (SE ≤ −3.0 D). Prevalence of myopia decreased with increasing time outdoors ($P_{trend} = 0.03$), but time outdoors was not associated with myopia on multivariable analysis.

Conclusions. Study authors identified a protective association between increasing UVAF and myopia. The protective association of higher UVAF against myopia was stronger than that of increased levels of time spent outdoors as measured by this study's questionnaire. Future studies should investigate the association between UVAF and incident myopia, and its relationship to myopic progression. (*Invest Ophthalmol Vis Sci.* 2012;53:4363–4370) DOI:10.1167/iovs.11-8677

Myopia is the most common refractive error globally, with an estimated 1.44 billion people affected, equal to 22.6% of the world's population.[1] The prevalence of myopia has increased worldwide during the 20th century, and is now considered to have reached an epidemic level, especially in some populations including those from East Asia where prevalence estimates often exceed 80%.[2,3] Myopia carries a significant economic and social burden; the potential complications of severe myopia, including retinal detachment, glaucoma, myopic retinopathy, and myopic maculopathy, may lead to visual impairment and blindness.[4]

Myopic refractive error may be easily corrected with spectacles, contact lenses, or refractive surgery. Satisfactory correction of myopia can improve participation in daily living and visual functioning in people with myopia.[5] Results from randomized controlled trials have shown that myopic children receiving multifocal lenses or antimuscarinic topical medication such as pirenzepine gel, cyclopentolate eyedrops or atropine eyedrops show significantly less myopic progression than children receiving placebo.[6] However, use of many of these therapies is limited by side-effect profiles, and not all are commercially available. Further, multifocal lenses have produced only a statistical but not clinically significant slowing of progression, other than in the children who are also esophoric and have large accommodative lags.[6]

Although the precise cause of myopia is unknown, experimental, clinical, and epidemiological studies have shown that myopia is influenced by both genetic and environmental mechanisms.[7] Even though evidence for a genetic contribution to the pathogenesis of myopia is compelling,[8–11] rapid changes in the prevalence of myopia in many populations in the twentieth century[2] provide support for a major environmental contribution to myopia. Nonetheless, it remains unclear whether or not environmental risk factors for myopia act in isolation or are modified by genetic factors.[12]

Epidemiological studies have suggested that sustained schooling, study, reading, and other near-work activities are associated with axial elongation and myopia.[4,13] Increased accommodation, as occurs when performing near work, could mediate the association between myopia and schooling, but epidemiological evidence to support this is not strong[14] and the biological link between schooling and myopia remains unclear. One possibility is that children may have suboptimal accommodation during near work (accommodative lag),

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leading to hyperopic defocus of the retina that results in axial elongation.[15,16] This has been shown in animal studies of myopia[17] and is supported by clinical trials in humans.[18] Time spent outdoors is increasingly recognized as a protective factor for myopia development,[19] although it is possible that near work and time outdoors can act independently of each other. Epidemiological evidence for an inverse relationship between increasing time spent outdoors and myopia is derived from several recent cross-sectional[20–23] and prospective studies.[24,25]

The exact mechanism by which time spent outdoors decreases the risk of developing myopia and its progression is unknown. One of the major theories relates to an increased release of dopamine from the retina in response to bright light that has been demonstrated in animal models of myopia. Increased dopamine release has been shown to reduce axial elongation in chickens.[26] This postulated role of dopamine is supported by findings that a dopamine antagonist blocked the protective effect of bright light on axial elongation in another chicken model.[27] More recently in a primate model, high ambient lighting retarded development of form-deprivation myopia, supporting the earlier findings in chicken models, and suggesting that alteration of indoor light levels may be protective against myopia in humans.[28] Prepas hypothesized that myopia is attributed to increased exposure to artificial light, and that UV light is required to prevent myopia,[29] but no epidemiological evidence exists to support this theory; the protective effect of bright light has been replicated using UV-free light in animal models.[30,31]

There is a need to understand environmental and lifestyle determinants of myopia as identifying protective and harmful factors may pave the way for effective prevention and treatment strategies. For this study, authors used an objective measurement of ocular exposure to outdoor light, conjunctival UV autofluorescence (UVAF). [32,33] In response to UV radiation (especially UV-B and UV-C), the ocular surface may be altered via many cellular responses including inhibition of mitosis, nuclei fragmentation, eosinophilic staining, and loss of cellular adhesion,[34] as well as possible immunological changes to damaged epithelial or stem cells.[35,36]

The clinical correlates of acute or chronic ocular surface exposure to UV radiation are diverse. Photokeratoconjunctivitis (also known as "ultraviolet keratoconjunctivitis") may be induced acutely by exposure to direct sunlight, reflected light from snow or water, as well as artificial sources of UV radiation from tanning lights, arc welding, and lasers.[34] UV radiation is also linked to several other ocular surface disorders including ocular surface squamous neoplasia, climate droplet keratopathy, pterygium, and limbal stem cell deficiency.[37]

On Norfolk Island, there is an inverse, linear relationship between UVAF and increasing age ($P < 0.001$), and UVAF is higher in males.[33] Adjusted to the 2006 Norfolk Island census, the prevalence of myopia (spherical equivalent [SE] ≤ -1.0 diopter [D]) in the Norfolk Islanders—10.1% in subjects aged $\geq$15 years—is lower than that in the mainland Australian population.[38,39] Study authors wished to determine the relationship between myopic refractive error and time spent outdoors using both subjective and objective methods of measuring outdoors exposure.

Methods

Study Population and Recruitment

From 2007 to 2008, a cross-sectional study was conducted on Norfolk Island, an external territory of Australia located in the South Pacific Ocean. Norfolk Island is an ideal location in which to undertake ophthalmic epidemiological research because of its small population, inherent geographical and genetic isolation,[40] and history of research participation including a study in the early 21st century investigating the genetic determinants of cardiovascular disease.[41] An additional reason to study this island population is because the subtropical climate is relatively constant year round. The prevalence of blindness on Norfolk Island is low and most commonly due to age-related macular degeneration, amblyopia, and glaucoma.[42]

The full methodology of the Norfolk Island Eye Study (NIES) is described elsewhere.[43] In brief, all permanent residents of the Island aged $\geq$15 years were invited to participate by means of radio and newspaper advertisements, referral from healthcare providers, and word of mouth. Participants were also sent letters if they were involved in a previous study investigating the genetics of cardiovascular disease.[41] According to the most recent census estimate, 61.5% of permanent residents agreed to participate in the NIES. There were no specific exclusion criteria for NIES. The 636 subjects from the NIES (81.4% of 781 subjects) who had conjunctival UVAF photography performed constituted the baseline population for this study. The reason for a subject not having UVAF performed was that UVAF equipment was not available on all fieldwork visits to Norfolk Island.

Ethics Approval

The original cardiovascular disease study received ethics approval from the Griffith University, Human Research and Ethics Committee. This same committee, in addition to the Human Research and Ethics Committee at the Royal Victorian Eye and Ear Hospital in Melbourne, approved the NIES. All research was conducted in concordance with the Declaration of Helsinki and its tenets. Informed consent was obtained from all study participants for all parts of the ophthalmic questionnaire and clinical examination and to link this with the earlier cardiovascular and genetic research as well as ongoing genetic eye research. In addition, there was local community consultation with the hospital administration, local doctors, local optometrist, and visiting ophthalmologists to check that all concerns were met regarding the possible long-term impact of the study.

Questionnaire

At the time of the study examinations, participants filled out a sun-exposure questionnaire, which included questions pertaining to history of sun exposure and sun-protective strategies (e.g., use of sunscreen and wearing of protective hat and sunglasses). There were five response categories for sunglasses and hat use: never, seldom, ½ of the time, usually, and always. Subjects were questioned about their current time spent outdoors when they were awake: "In the summer, when not working at your job or at school, what part of the day do you spend outside?" There were four possible responses for this question: none, <¼ of day, approximately half, >¾ of day. The "none" and "<¼ day" categories were combined due to low numbers in the none category (1.5% of total). Self-reported diabetics and cigarette smokers were also determined by questionnaire.

Clinical Examination

Visual acuity was assessed using a logMAR chart at a distance of 6 meters. (Precision Vision, LaSalle, IL). Best-corrected visual acuity was recorded with spectacles, trial lenses, or pinhole. Refractive error was measured with a handheld autorefractometer (Nidek ARK-30; Nidek, Gamagori, Japan). Three measurements were taken from each eye and the final result was the mean of the three measurements. Refractive error readings used in the analysis were from predilated eyes. SE represented the sum of spherical errors and ½ cylindrical errors. There is no universally used cutoff for myopia; therefore, study authors employed two different but widely used classifications in the statistical analyses: SE ≤ -1.0 D and SE ≤ -0.5 D. Moderate-high myopia was defined as SE ≤ -3.0 D. Hyperopia was defined as either SE $\geq +0.5$ D or $\geq +1.0$ D. Emmetropia was classified as SE -0.49 to $+0.49$ D. Slit-lamp

biomicroscopy was also performed as part of a comprehensive ocular assessment.

Conjunctival UVAF Measurement

Conjunctival UVAF photos were taken using the camera system developed by Coroneo and colleagues.[32,44] Photographs were taken using both reflected visible light (control) and UV-induced fluorescence with the aid of two portable photographic systems. Each consisted of a height adjustable table equipped with subject headrest, camera positioning assembly, digital single-lens reflex camera, macro lens, and filtered electronic flash. Each eye was photographed at 0.94 magnification, with separate views of the nasal and temporal regions of both eyes. Colored low-voltage light emitting diodes (LED) were positioned on stands in the subject's visual field, at approximately 35 degrees to the camera–subject axis to aid fixation.

The UV-induced fluorescence photography was based on standard principles, using a specially adapted electronic flash system fitted with UV-transmission filters (transmittance range 300–400 nm, peak 365 nm) as the excitation source. Subject fluorescence was recorded with a digital camera (Nikon D100; Nikon, Melville, NY) and 105 mm f/2.8 lens (Micro Nikon; Nikon) fitted with infrared and UV barrier filters. Thus, the camera recorded only fluorescence. The operator was masked to refractive status prior to the subject being photographed. Images were saved in RGB format at the D100 settings of JPEG Fine (1:4 compression). Each photograph could be verified immediately after it was taken and reshot, if necessary, to obtain a better result. Criteria for requiring a repeat photography were decentration, blur from poor focus, or subject movement.

Following manual delineation of the region(s) of UVAF in the photographs, a graphics editing program (Adobe Photoshop CS4 Extended; Adobe Systems, Mountain View, CA) was used to estimate the area of UVAF with the resultant area expressed in mm^2. Four photos were analyzed per person (right nasal, left nasal, right temporal, left temporal). The sum of the area in the four photos was referred to as "total UVAF." The settings required for the computerized area measurement to correspond with the area in the eyes of participants were pixel length = 3008 (number of pixels per micron) and logical length = 2.4 cm. Intra- and interobserver reliability was high, as demonstrated by concordance correlation coefficients (CCCs) for total UVAF of 0.988 and 0.924, respectively.[45]

Statistical Analysis

Total UVAF was divided into quartiles. 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 two continuous variables were assessed with the Mann-Whitney *U* test. Trends across categories were assessed using Cuzick's nonparametric test for trend.[46]

Study authors used mean SE of both eyes for each individual for estimation of prevalence of myopia. Logistic regression was utilized to estimate the odds ratio (OR) and 95% confidence interval (95% CI) of refractive error. For the logistic regression analyses, study authors used the SE for each eye using sandwich variance estimates to model the paired data and allow for intra-individual correlation. Robust standard errors were generated.[47] Covariates that were statistically significant ($P < 0.05$) in univariable analyses were included in the multivariable models, in addition to age and sex. Study authors constructed separate multivariable models containing either total UVAF or time spent outdoors due to the expected collinearity between the two covariates. Total UVAF quartile was also assessed in a separate multivariable model to assess for a possible dose-response relationship. Study authors subsequently repeated the analysis by restricting the participants to those aged <50 years, to control for the hyperopic shift in individuals aged >50 years.[48] Interaction was evaluated with the likelihood ratio test, and results of interaction and other statistical analyses were considered significant at the $P < 0.05$ level. All *P*-values were two-tailed. Statistical analyses were undertaken using statistical software (Stata 10.1 for Macintosh; Stata Corp, College Station, TX).

Results

Baseline Characteristics Including Results of UV Exposure Questionnaire

Of the 636 subjects included in this arm of the NIES, 361 (56.8%) were female and the mean age of subjects was 54.1 ± 16.2 years (range 15–89 years). The majority (78.6%) of subjects were aged ≥40 years, and 17.5% were aged ≥70 years. There were 354 (55.7%) current or previous cigarette smokers. Self-reported history of diabetes was reported in 4.4% of respondents.

Of the 636 subjects, 595 (93.6%) had completed the UV exposure questionnaire. Two hundred and twenty-six subjects (35.5%) spent less than ¼ of an average day outside, 236 (37.1%) spent approximately ½ their day outside, and 133 subjects (20.9%) spent ¾ or more of their day outside. Approximately half (49.5%) either wore their hat outside usually or always while 85 (13.4%) never wore it outside. Similarly, 49.7% wore sunglasses usually or always when outside, and 19.0% never wore sunglasses outside.

Hat use outdoors was different between sexes ($P < 0.001$) and age categories ($P = 0.034$). Specifically, hat use was more common in males (59.3% of males versus 52.0% of females wore hats usually or always when outdoors), and fewer males never wore hats (10.2% vs. 16.5%). Hat use tended to increase with increasing age. In those aged <40 years, 44.5% wore hats usually or always when outdoors, 47.0% aged 40 to 49 years, 50.7% in subjects aged 50 to 59 years, 58.8% in those aged 60 to 69 years, and 54.1% in those aged 70 years and over.

Sunglasses use outdoors was also significantly different between sexes ($P = 0.030$) and different age categories ($P < 0.001$). Sunglasses use was highest amongst the youngest participants. In subjects below 50 years, 61.4% wore sunglasses always or usually when outdoors, decreasing to 45.6% in subjects aged 50 to 59 years, 45.4% aged between 60 to 69 years and 37.0% in subjects aged 70 years and over. Sunglasses use when outdoors was more common in females (54.9% wearing sunglasses usually or always versus 44.2% in males), and fewer females never wore sunglasses (15.8% vs. 24.3%).

Time Spent Outdoors, UVAF, and Myopia

Median UVAF was lower in subjects with myopia (SE ≤ −1.0 D), 16.6 mm^2 vs. 28.6 mm^2, $P = 0.001$, and was also lower using the SE ≤ −0.5 D definition, 24.5 mm^2 vs. 28.6 mm^2, $P = 0.012$. Baseline characteristics of participants with myopia are presented in Table 1. Prevalence of myopia (SE ≤ −1.0 D) decreased with increasing time spent outdoors ($P_{trend} = 0.03$), and with increased quartile of UVAF ($P_{trend} = 0.002$).

Prevalence of myopic refractive error (SE ≤ −1.0 D) significantly decreased across the UVAF quartiles (Table 2). The prevalence of subjects with hyperopia (SE ≥ 1.0 D) was higher in the first and second UVAF quartile compared with the third and fourth quartiles. Study authors repeated these analyses using different definitions of myopia and hyperopia. There was a statistically significant trend of decreasing prevalence of myopia (SE ≤ −0.5 D) across UVAF quartiles ($P_{trend} = 0.011$), but not with hyperopia (SE ≥ 0.5 D; $P_{trend} = 0.255$) or emmetropia (SE −0.49 to +0.49 D; $P_{trend} = 0.439$).

Study authors performed a univariable logistic regression analysis (Table 3).

Table 1. Demographic, UV Exposure, and Conjunctival UVAF Characteristics of Subjects with Myopia in the NIES

	Myopia (SE ≤ −0.5 D)				Myopia (SE ≤ −1.0 D)			
Category	***N***	**Prevalence (%)**	***P***	P_{trend}	***N***	**Prevalence (%)**	***P***	P_{trend}
N (with UVAF data)	91	14.3			47	7.4		
Sex			0.06	–			0.05	–
Female	60	16.6			33	9.1		
Male	31	11.3			14	5.1		
Age			0.49	0.09			0.14	0.54
<40	25	19.2			15	11.5		
40–49	13	11.2			5	4.3		
50–59	21	14.2			13	8.8		
60–69	19	14.5			12	9.2		
70+	13	11.7			2	1.8		
UVAF mm²			0.01	0.01			0.01	0.002
First quartile (≤14.4)	35	22.0			21	13.2		
Second quartile (14.5–28.0)	18	11.3			10	6.3		
Third quartile (28.1–47.7)	21	13.2			10	6.3		
Fourth quartile (≥47.8)	17	10.8			6	3.8		
UVAF mm²			0.001	–			0.001	–
Lowest 25% (≤14.4)	35	22.0			21	13.2		
Remaining 75% (≥14.5)	56	11.7			26	5.5		
Proportion of day spent outdoors			0.71	0.41			0.08	0.03
<¼ of day	36	15.9			23	10.2		
∼½ day	34	14.4			14	5.9		
>¾ day	17	12.8			6	4.5		
Use of hats			0.27	0.82			0.48	0.94
Never	13	15.3			7	8.2		
Seldom	22	16.2			10	7.4		
½ the time	6	7.2			3	3.6		
Usually	33	17.0			19	9.8		
Always	16	12.9			8	6.5		
Use of sunglasses		0.40	0.40	0.36			0.76	0.27
Never	18	14.9			7	5.8		
Seldom	5	11.4			9	6.8		
½ the time	5	8.8			3	5.3		
Usually	25	17.6			13	9.2		
Always	28	16.1			15	8.6		

Numbers of subjects with myopia may not equal 91 (SE ≤ −0.5 D) or 47 (SE ≤ −1.0 D) due to missing data in the time spent outdoors, hat use, or sunglasses use categories.

UVAF quartile was associated with an OR of myopia of 0.76, 95% CI = 0.66–0.96, $P_{trend} = 0.015$ (SE ≤ −0.5 D); and OR of myopia 0.68 (95% CI = 0.54–0.86), $P_{trend} = 0.001$ (SE ≤ −1.0 D). There was a statistically significant trend for decreasing time spent outdoors and myopia ($P_{trend} = 0.032$) when using the SE ≤ −1.0 D definition of myopia but not the SE ≤ −0.5 D definition ($P_{trend} = 0.112$).

In age and sex-adjusted and multivariable models, UVAF as a continuous variable was significantly associated with myopia (Table 4). There was also evidence of a dose-response relationship, with increasing quartile of UVAF being associated with reduced odds of myopia in both models, although confidence intervals were wide. However, time spent outdoors was not significantly associated with myopia when adjusted for age, sex, and additional covariates in the multivariable model.

Subjects with myopia (SE ≤ −0.5 D) had an increased odds of being in the bottom quartile of UVAF than the top three quartiles compared with subjects without myopia: OR 2.04, 95% CI = 1.35–3.10, $P = 0.001$. The association was slightly attenuated following adjustment for age, sex, smoking, cataract, height, and weight: OR 1.85, 95% CI = 1.12 to 3.04, $P = 0.015$. Subjects with myopia (SE ≤ −1.0 D) were also more likely to be in the bottom quartile of UVAF than those without myopia: OR 2.27, 95% CI = 1.37 to 3.77, $P = 0.002$. The association was marginally weaker following adjustment for the same covariates, using the SE ≤ −1.0 D definition: OR 2.19, 95% CI = 1.19 to 4.02, $P = 0.012$.

There were no significant interactions between UVAF and age ($P_{interaction} = 0.213$ [SE ≤ −0.5 D] and $P_{interaction} = 0.115$ [SE ≤ −1.0 D]) or sex ($P_{interaction} = 0.090$; $P_{interaction} = 0.082$). The

Table 2. Relationships between Quartiles of Total UVAF and Refractive Error in the NIES

Refractive Error	**Lowest Quartile (≤14.4 mm²), *N* (%)**	**Second Quartile (14.5–28.0 mm²), *N* (%)**	**Third Quartile (28.1–47.7 mm²), *N* (%)**	**Highest Quartile (≥47.8 mm²), *N* (%)**	P_{trend}
Hyperopia (SE ≥ 1.0 D)	65 (27.6)	66 (28.1)	50 (21.3)	54 (23.0)	0.080
SE > −1.0 to <+1.0 D	73 (20.6)	84 (23.7)	99 (27.9)	98 (27.9)	0.001
Myopia (SE ≤ −1.0 D)	21 (44.7)	10 (21.3)	10 (21.3)	6 (12.8)	0.002

Table 3. Univariable Logistic Regression Analysis of Associations with Myopia in the NIES

	Myopia (SE ≤ −0.5 D)			Myopia (SE ≤ −1.0 D)		
Category	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Sex						
Female	1			1		
Male	0.57	0.38–0.86	0.007	0.55	0.32–0.92	0.023
Age						
Per 10 years	0.97	0.87–1.09	0.647	0.95	0.82–1.11	0.544
UVAF						
Per 10-mm² increase, total UVAF	0.90	0.83–0.99	0.027	0.82	0.72–0.92	0.001
UVAF						
First quartile	1			1		
Second quartile	0.46	0.27–0.79	0.005	0.55	0.29–1.03	0.062
Third quartile	0.52	0.30–0.88	0.017	0.48	0.25–0.94	0.031
Fourth quartile	0.49	0.29–0.83	0.008	0.29	0.14–0.64	0.001
Proportion of day outdoors						
<¼ of day	1			1		
∼½ day	0.82	0.52–1.29	0.402	0.67	0.38–1.18	0.165
>¾ day	0.70	0.41–1.20	0.199	0.54	0.27–1.06	0.072
Use of hats						
Never	1			1		
Seldom	1.49	0.70–3.17	0.295	1.55	0.51–4.76	0.442
½ the time	1.52	0.68–3.38	0.304	1.51	0.47–4.89	0.492
Usually	1.83	0.88–3.79	0.104	2.27	0.78–6.54	0.130
Always	1.86	0.94–3.69	0.075	2.59	0.94–7.17	0.067
Use of sunglasses						
Never	1			1		
Seldom	1.05	0.50–2.20	0.894	1.71	0.55–5.32	0.351
½ the time	0.97	0.44–2.14	0.939	1.31	0.39–4.38	0.663
Usually	0.96	0.45–2.07	0.916	1.60	0.50–5.09	0.427
Always	1.28	0.61–2.69	0.517	1.54	0.49–4.87	0.462

interaction between time spent outdoors and age approached statistical significance ($P_{interaction} = 0.056$; $P_{interaction} = 0.131$), although the interaction between time outdoors and sex was not ($P_{interaction} = 0.534$; $P_{interaction} = 0.777$).

Study authors performed several sensitivity analyses. Firstly, authors investigated the severity of myopia. There were 13 participants (2.0%) with moderate-high myopia. Median total UVAF was lower in participants with moderate-high myopia (SE ≤ −3.0 D), 16.1 mm² vs. 28.3mm², $P = 0.018$. Following adjustment for age, sex, cataract, height, weight, and smoking, each 10-mm² increase in UVAF was associated with a reduced odds of moderate-high myopia: OR 0.76, 95% CI = 0.60 to 0.96, $P = 0.020$. Study authors also investigated the association between UVAF and myopia in individuals aged <50 years. Following adjustment for age, sex, smoking, height, weight and cataract, the OR of myopia (SE ≤ −1.0) for every 10 mm² increase in UVAF was 0.65, 95% CI = 0.50–0.85, $P = 0.001$. Using the SE ≤ –0.5 definition of myopia, the OR was 0.89, 95% CI = 0.65–1.09, $P = 0.132$. As UV radiation (especially UV-B) is associated with cataract,[49] study authors performed a sensitivity analysis excluding people with cataract (any eye). Following adjustment for age, sex, height, weight, and

Table 4. Multivariable Logistic Regression Analysis of the Association between Time Spent Outdoors, Conjunctival UVAF, and Myopia in the NIES

	Myopia (SE ≤ −0.5 D)						Myopia (SE ≤ −1.0 D)					
	Age and Sex Adjusted			Multivariable Model			Age and Sex Adjusted			Multivariable Model		
	OR	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
UVAF												
Per 10 mm²	0.90	0.82–0.98	0.020	0.88	0.80–0.97	0.027	0.81	0.71–0.93	0.003	0.81	0.69–0.94	0.007
UVAF												
First quartile	1			1			1			1		
Second quartile	0.44	0.26–0.77	0.003	0.51	0.27–0.97	0.045	0.53	0.28–0.91	0.045	0.63	0.28–1.41	0.257
Third quartile	0.52	0.29–0.91	0.022	0.62	0.28–1.40	0.269	0.46	0.23–0.91	0.025	0.61	0.20–1.93	0.405
Fourth quartile	0.52	0.30–0.91	0.022	0.61	0.17–1.16	0.442	0.29	0.13–0.67	0.004	0.29	0.03–2.61	0.269
Time spent outdoors												
∼<¼ day	1			1			1			1		
∼½ day	0.89	0.56–1.42	0.638	0.71	0.41–1.22	0.215	0.73	0.41–1.30	0.285	0.56	0.27–1.13	0.108
∼>¾ day	0.90	0.51–1.60	0.720	1.08	0.57–2.00	0.827	0.69	0.33–1.47	0.342	0.93	0.43–2.02	0.849

Multivariable model adjusted for all age (continuous), sex, smoking, cataract, height, and weight.

smoking, total UVAF remained significantly associated with myopia. The OR of myopia (SE ≤ -1.0 D) per 10 mm^2 UVAF was 0.83 (95% CI, 0.68–0.99), $P = 0.047$. For myopia (SE ≤ -0.5 D), the OR was 0.97 (95% CI, 0.95–0.99), $P = 0.021$.

Time Spent Outdoors, UVAF, and Hyperopia or Emmetropia

There were no statistically significant findings for either time spent outdoors or UVAF and these refractive groups. The OR for hyperopia (SE ≥ 0.5 D) per 10 mm^2 of UVAF was 1.03 (95% CI, 0.97–1.09), $P = 0.303$; and following adjustment for age and sex was 1.05 (95% CI, 0.98–1.12), $P = 0.137$. For hyperopia (SE ≥ 1.0), the OR per 10 mm^2 of UVAF was 0.97 (0.92–1.02), $P = 0.268$; and the association was less protective following age and sex adjustment: OR = 1.01 (95% CI, 0.91–1.08), $P = 0.675$. Time spent outdoors was not significantly associated with hyperopia: SE ≥ 0.5 D ($P = 0.654$), or SE ≥ 1.0 D ($P = 0.390$).

The OR for emmetropia (SE –0.49–0.49 D) per 10 mm^2 of UVAF was 1.02 (95% CI, 0.97–1.09), $P = 0.414$ and 0.99 (95% CI, 0.97–1.01), $P = 0.818$ following age and sex adjustment. Time spent outdoors was not associated with emmetropia ($P = 0.711$).

Sun Protective Strategies and UVAF

There was no significant trend in median UVAF across groups of hat use when outdoors ($P_{trend} = 0.462$), neither was there a significant trend in median UVAF across groups of sunglasses use outdoors ($P_{trend} = 0.458$). Following adjustment for age and sex, neither hats ($P = 0.452$) nor sunglasses use ($P = 0.085$) was independently associated with UVAF. There were no significant interactions between time spent outdoors and hat use (SE ≤ -0.5 D and SE ≤ -1.0 D; $P_{interaction} = 0.876$; $P_{interaction} = 0.220$, respectively) or sunglasses use ($P_{interaction} = 0.205$; $P_{interaction} = 0.405$). Similarly, there were no significant interactions between UVAF and hat use ($P_{interaction} = 0.979$; $P_{interaction} = 0.903$) or sunglasses use ($P_{interaction} = 0.468$; $P_{interaction} = 0.750$).

Discussion

In this genetically and geographically isolated population, study authors demonstrated a protective association between area of conjunctival UVAF and prevalent myopia. This protective association remained significant following adjustment for several covariates that were significantly associated with myopia in this population. Study findings extend previous epidemiological research using questionnaire-based assessment of time spent outdoors.[20–24] The direction of association between increasing UVAF and myopia also appears to extend to younger adults, and in subjects with increased severity of myopic refractive error.

UVAF is unlikely to be involved in the causal pathway of myopia, but represents a valid biomarker of subacute (weeks to months) exposure to light outdoors. Degree of UVAF is strongly correlated with time spent outdoors in both sexes, and in both winter and summer.[45] This is supported by findings that UVAF is highest in males of younger age,[33] who generally report spending the most time outdoors on Norfolk Island. It is currently unknown whether or not UVAF can be modified by other factors, including poor UV protective mechanisms and/or a predisposition (genetic or otherwise) to develop UVAF.

Given that no statistically significant association was observed between sunglasses or hat use and degree of UVAF, study findings do not directly support a role of UV radiation in myopia. However, there are several other explanations for this lack of association, including the possibility that study questionnaire methods were inadequate, and because study authors investigated prevalent and not incident myopia. The assumption that current or recent environmental exposures, such as time spent outdoors, are consistent with previous levels may be incorrect in this study. Throughout one's lifespan, there are many possible lifestyle changes that may modify an individual's time spent outdoors, such as educational practices and level, vocation, geographical/climatic factors, and health. Subjects who wear spectacles and/or contact lenses to correct myopic refractive error may have some physical protection against the development of UVAF. UV-blocking contact lenses can provide a safe and effective protection of the cornea, limbus, and crystalline lens when wearing sunglasses or hats is undesirable or unsuitable.[50] As ocular exposure to UV radiation is likely to be highly correlated to time spent outdoors, there is a need to be aware of the many ocular and systemic disorders that are associated with excessive UV radiation, including potentially blinding disorders such as cataract, and various ocular malignancies including squamous cell carcinoma and melanoma.[51]

The association between UVAF and myopia was stronger than that observed between the current study's subjective assessments of time spent outdoors and myopia, and may reflect the inherent problems with the current study's questionnaire-based methods of assessing time spent outdoors. Recall bias would have been unlikely as participants were asked current outdoors exposure, and subjects were interviewed prior to measurement of refraction thus minimizing interviewer bias. It must be acknowledged that he validity and reliability of this question to measure time spent outdoors has not been previously evaluated. Moreover, as time spent outdoors in this study was classified into broad categories, this would have reduced the power of study authors to detect any associations, especially with a relatively small sample size and low myopia prevalence. Despite a statistically significant trend for a protective association of increasing time spent outdoors and myopia, the multivariable model was not statistically significant.

In residents of Norfolk Island, myopia is associated with lower age, and ocular biometric characteristics including longer axial length, shallower anterior chamber depth, and increasing corneal curvature.[39] Study authors showed that corneal shape (central curvature and peripheral shape factor) determines, in part, the intensity of the limbal focus.[52] UVAF detects only a subset of wavelengths in the UV spectrum: transmittance range 300 to 400 nm. There is limited evidence to support a UV hypothesis of myopia; however, it is difficult to separate the role of UV light from that of other components of outdoor light in epidemiological studies. In outdoor environments, exposure to UV light and bright light are likely to be highly correlated, and higher UVAF measurements will probably also reflect higher exposure to bright light outdoors. Efforts to disentangle bright light from UV light have shown that exposure to bright light is protective of myopia in animal models which the use of UV-free light.[27,30] An alternate hypothesis is that light intensity is typically higher outdoors than indoors, and pupils tend to be more constricted outdoors, resulting in a larger depth of field and reduced image blur.[23] This is underscored by a consistently lower prevalence of myopia in rural environments where light intensities are generally higher and optical field depth is greater.[2]

UVAF correlates strongly with the presence of pterygium,[53] an ocular surface disorder strongly associated with UV exposure, but additional study is required to determine if UVAF is also associated with other ophthalmic diseases that are associated with excess UV exposure.[51] Elsewhere, it has been shown the pterygia are less common in myopes.[54] In residents

of Norfolk Island, the prevalence of myopia (SE ≤ -1.0 D) in phakic individuals with bilateral pterygium was 7.6%, which is lower than people without pterygium (10.1%).[36] No known ophthalmic disorders are associated with insufficient UV radiation, although the systemic relationship with vitamin D deficiency, leading to rickets, osteomalacia and osteoporosis, is well established.[51] Despite being highly reliable and correlating strongly with time spent outdoors,[45] it remains unclear what the UVAF specifically represents, and the timeframe over which the UVAF develops. Further work is therefore required to characterize the natural history and precise pathophysiological changes that represent UVAF.

There are several limitations to this study. Study results are only cross-sectional and information relating to time spent outdoors (and other possible risk factors in the study questionnaire) and UVAF was only measured at one point in time. Prospective studies are required to elucidate the natural history of UVAF and its relationship with the incidence of myopia and other refractive errors. Evidence from prospective studies has shown that time spent outdoors is protective of developing myopia,[24] and time spent outdoors is inversely related to myopia progression.[55] Moreover, study authors did not collect data on several potential confounders of the relationship between UVAF and myopia, including education level, occupation, or socioeconomic status, as these factors are related both to myopia and time outdoors.[56] The current study is also limited by the wide range and older age of study participants, as the majority of cases of myopia are determined in childhood, and the risk of incident myopia is highest in this period.[2] There is also a limited robustness to study findings, especially in the sensitivity analyses, given the relatively small sample size and low prevalence of myopia, indicating that few subjects drive the protective effect of UVAF and prevalent myopia in this study. As study data on refraction were gathered before pupil dilation in subjects, it is possible that the prevalence of myopia is overestimated and hyperopia underestimated.[57] However, most of the current study population (61.6%) were aged over 50 years, and in this age-band, cycloplegic autorefraction is associated with a myopic shift and consequently an overestimation of myopia prevalence.[58]

In conclusion, study authors revealed a protective association of UVAF—an objective marker of ocular outdoors light exposure and time spent outdoors—with myopia in this cross-sectional study. This study objectively supports the hypothesis that exposure to light outdoors is protective against myopia. Further evidence is required from prospective studies to further characterize this relationship between UVAF and incident myopia, and to assess the role of UVAF in myopic progression.

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