Received: 14 July 2021 | Accepted: 17 September 2021 | Published online: 22 October 2021

DOI: 10.1111/opo.12905

OPO THE COLLEGE OF OPTOMETRISTS

ORIGINAL ARTICLE

Associations of 12-year sleep behaviour trajectories from childhood to adolescence with myopia and ocular biometry during young adulthood

Nicholas Stafford-Bell[1,2] | **Joanne McVeigh**[3,4] | **Gareth Lingham**[1] | **Leon Straker**[3] | **Peter R Eastwood**[5] | **Seyhan Yazar**[6] | **David A Mackey**[1,7,8] | **Samantha Sze-Yee Lee**[1]

[1]Centre for Ophthalmology and Visual Sciences (incorporating the Lions Eye Institute), University of Western Australia, Perth, Western Australia, Australia

[2]Fiona Stanley Hospital, Murdoch, Western Australia, Australia

[3]Curtin School of Allied Health, Curtin University, Perth, Western Australia, Australia

[4]Movement Physiology Laboratory, School of Physiology, University of Witwatersrand, Johannesburg, South Africa

[5]College of Medicine and Public Health, Flinders Health and Medical Research Institute, Flinders University, Adelaide, South Australia, Australia

[6]Garvan-Weizmann Centre for Cellular Genomics, Garvan Institute of Medical Research, Darlinghurst, New South Wales, Australia

[7]School of Medicine, Menzies Research Institute Tasmania, University of Tasmania, Hobart, Tasmania, Australia

[8]Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, Melbourne, Victoria, Australia

Correspondence
Samantha Sze-Yee Lee, Centre for Ophthalmology and Visual Sciences (incorporating the Lions Eye Institute), University of Western Australia, Perth, Western Australia, Australia.
Email: samantha.sy.lee29@gmail.com

Funding information
University of Western Australia; Curtin University of Technology; National Health and Medical Research Council, Grant/Award Number: 003209, 1021105, 323200 and 353514; University of Notre Dame Australia; Edith Cowan University; Murdoch University; Women and Infants Research Foundation; Australian Foundation for the Prevention of Blindness; Telethon Kids Institute; Lions Eye Institute (AU); Ophthalmic Research Institute of Australia; BrightFocus Foundation; Alcon Research Institute; Raine Medical Research Foundation

Abstract

Purpose: Cross-sectional studies have variably reported that poor sleep quality may be associated with myopia in children. Longitudinal data, collected over the ages when myopia develops and progresses, could provide new insights into the sleep-myopia paradigm. This study tested the hypothesis that 12-year trajectories of sleep behaviour from childhood to adolescence is associated with myopia during young adulthood.

Methods: At the 5-, 8-, 10-, 14- and 17-year follow-ups of the longitudinal Raine Study, which has been following a cohort since their birth in 1989–1992, participants' parents/guardians completed the Child Behaviour Checklist questionnaire (CBCL), which collected information on their child's sleep behaviour and quality. The CBCL includes six questions measuring sleep behaviour, which parents rated as 0 = not true, 1 = somewhat/sometimes true, or 2 = very/often true. Scores were summed at each follow-up to form a composite "sleep behaviour score". Latent Class Growth Analysis (LCGA) was used to classify participants according to their 12-year trajectory of sleep behaviour. At the 20-year follow-up, an eye examination was performed which included cycloplegic autorefraction and axial length measurement.

Results: The LCGA identified three clusters of participants based on their trajectory of sleep behaviour: those with minimal' (43.6% of the total Raine Study sample), 'declining' (48.9%), or 'persistent' (7.5%) sleep problems. A total of 1194 participants had ophthalmic data and longitudinal sleep data available for analysis (47.2% female, 85.6% Caucasian). No significant differences were observed in regards to age, sex, ethnicity or ocular parameters between trajectory groups. Unadjusted and fully adjusted analyses demonstrated that sleep problem behaviour was not significantly associated with changes in refractive error, axial length or corneal radius.

Conclusions: Our findings do not support the hypothesis that there is an association between sleep behaviour and myopia. Future longitudinal studies should explore sleep trajectory data pre- and post-myopia diagnosis to confirm our results.

KEYWORDS
myopia, sleep behaviour, sleep problems, sleep quality, The Raine Study

INTRODUCTION

Myopia is the most common ocular disorder worldwide with an anticipated rise in global prevalence from 22.9% in the year 2000 to 49.8% by the year 2050.[1] Of concern are the complications of myopic axial elongation, including sight-threatening conditions such as primary open-angle glaucoma, retinal detachment and myopic macular atrophy.[2] While the aetiology remains unclear, there are well-established links with both genetic and environmental factors, including parental myopia, increased education and reduced time outdoors.[1–3]

The protective effect of increased outdoor time on myopia has been confirmed in numerous studies[4–11] including meta-analyses.[12,13] While the mechanism underlying this relationship is unclear, animal models[14–17] suggest dopamine up-regulation from sunlight exposure controls axial elongation. Dopamine has a role in regulating wakefulness and perception, and its levels fluctuate in a day-night circadian/sleep pattern. This is such that dopamine levels are highest during daylight hours, decreasing through the day and lowest during sleep.[18]

Axial length and choroidal thickness, which are both associated with refraction,[19–21] vary in a diurnal manner, in part, mediated by light input to photosensitive retinal ganglion cells.[22–24] Light exposure upregulates retinal dopamine while downregulating melatonin, thus creating diurnal variations.[22–24] A review by Stone *et al*.[22] suggests a potential link between sleep and axial elongation, given that dopamine has a circadian rhythm aligning with the sleep-wake cycle. It is thus possible that perturbations of circadian rhythms or sleep derangement could influence retinal emmetropisation in children.[22,25–28]

Supporting such an association between disrupted circadian rhythms and myopia, a recent study found significant delays in sleep and salivary dim-light melatonin onset, as well as shorter sleep duration in myopes relative to non-myopes.[29] Several studies have reported an association between myopia and reduced sleep duration or sleep disorders. For instance, Ayaki *et al*.[30] reported that children and teenagers aged 10 to 19 years with high myopia (≤ −6 D) had significantly shorter sleep duration, later bedtime and poorer scores on the Pittsburgh Sleep Quality Index than mild myopes or emmetropes of similar age. The authors proposed that this relationship may be due to distress at night time caused by poor unaided vision in myopes, or there may be intrinsic biochemical changes in the eye which may affect the sleep cycle, especially in this age group when myopia evolves and accelerates.[30] Consistent with this hypothesis, this trend of deranged sleep in high myopes compared to those with mild- or no myopia was not seen in adults over 20 years old.[30] In a cross-sectional study of over 3000 Korean children (12 to 19 years old), Jee *et al*.[31] found each additional hour of sleep was associated with a 0.1 D increase in spherical equivalence (less myopia). Conversely, Zhou *et al*.'s cross-sectional study[32] did not find an association between sleep duration or disturbances with myopia in Chinese children.

In most previous studies,[24–26] sleep behaviour or quality have been assessed at a single time-point. Given the marked changes in sleep quantity and quality that occur over the lifespan,[33,34] single measurements may not represent the sleep quality over the years prior to and during myopia development, and therefore obscure any relationship between sleep and myopia. Arguing against this is a recent study by Wei *et al*.[35] who found no relationship between sleep duration over a 4-year period and myopia progression or axial length in early childhood. However, this study used quantitative sleep duration which failed to consider sleep quality and assumed no variations in inter-individual sleep duration needs.[33] It is possible that trajectories or trends of sleep quality or behaviour over time, especially longer periods of time that include the ages when myopia evolves and accelerates, may provide new insights into the potential relationships between sleep and myopia. The current study aimed to fill this gap in knowledge by

Key points

- Findings from several publications on the relationship between sleep quality or quantity and myopia have been conflicting with no clear consensus.
- The current study assessed the relationship between long-term sleep quality from 5 to 17 years of age and myopia at age 20 years in a community-based cohort.
- There is no significant association between longitudinal sleep quality and myopia, concluding that poor or good sleep is unlikely to affect risk of myopia.

exploring the relationship between a 12-year trajectory of sleep behaviour from childhood to adolescence and myopia in young adulthood.

MATERIALS AND METHODS

Participants

Participants were recruited as part of the Raine Study, which is a longitudinal study that has followed a cohort since their prenatal periods and birth between 1989 and 1992. The study originally included 2900 pregnant women (termed "Gen1") recruited between 16- and 20-weeks gestation from the King Edward Memorial Hospital in Perth, Western Australia. From these women, 2868 children were born which comprise the original cohort (Gen2). This original cohort has since been undergoing health and medical assessments, including an eye examination at the Gen2 20-year follow-up. The complete methodology and recruitment of the cohort have been described previously.[36] All participants received a full explanation of the nature of the study and provided informed consent before participation. The study was conducted in accordance with the tenets of the Declaration of Helsinki, and ethical approval for each follow-up was obtained from the University of Western Australia's Human Research Ethics Committee. All participants or their parents/guardians signed an informed consent form prior to each follow-up.

Sleep data and sleep behaviour trajectories

At the Gen2 5-, 8-, 10-, 14- and 17-year follow-ups (conducted between 1994 and 2007), parents or guardians completed the Child Behaviour Checklist questionnaire (CBCL).[37] The CBCL includes six measurements of sleep disturbance, each rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true): 'trouble getting to sleeping', 'nightmares', 'overtired without good reason', 'sleeps less than most kids', 'talks or walks in sleep' and 'sleeps more than most kids during day and/or night'. At each follow-up, the scores from the six questions were summed ranging from 0 to 12, with higher scores indicating worse sleep behaviours.[38] While the CBCL-derived sleep composite is not a standard sleep scale, it is strongly correlated with validated measures such as the Children's Sleep Habits Questionnaire (CSHQ) and with sleep disorder diagnoses.[39]

The sleep trajectory of a given individual was derived from their five CBCL-derived sleep composite scores (range 0–12) using Latent Class Growth Analysis (LCGA). Trajectory modelling is a statistical technique used to identify unseen or latent subgroups within a population based on a set of response variables at different time points,[40] and its use is becoming increasingly common in eye research.[41–43] For example, the Avon Longitudinal Study of Parents and Children[42] modelled the trajectory of height and weight growth during early childhood, and found associations between these growth trajectories and ocular biometry. While traditional longitudinal statistics, such as repeated-measures analysis of variance (ANOVA) or multiple regression analyse average change between time points and inter-subject variance, growth modelling examines overall trends and takes into consideration all time points as well as inter- and intra-subject variability to create population-based trends.[44]

The LCGA is able to identify meaningful homogeneous subpopulations within the larger heterogeneous population[45] and differentiate classes which may be defined by different developmental trajectories.[46] Participants are allocated based on a 'group assignment probability', which represents the accuracy of the participant belonging to the assigned trajectory. As there are no definitive criteria for the optimal number of classes, the judgement as to the optimum solution is based on a combination of statistical criteria, model parsimony and interpretability.[47] The sleep behaviour trajectory of the current cohort of participants and the method of modelling have been described previously.[43] In brief, Stata v13.1 (stata.com) was used to run the LCGAs and to plot all participants' sleep trajectories over the 12-year study period. Participants with a minimum of three sleep behaviour data points out of the five follow-ups were included in the trajectory modelling. The LCGA identified three discernible classes of sleep behaviour trajectory based on participants' pattern of sleep behaviours over the 12-year time span (year-5 to year-17): those with 'minimal sleep problems' (43.6% of the Raine Study Gen2 participants); 'declining sleep problems' (48.9%) or 'persistent problematic sleep' (7.5%).[48]

Ophthalmic examination

The ophthalmic examination was conducted at the Lions Eye Institute, Perth, Australia, at the Gen2 20-year follow-up in 2010 to 2012.[49] Assessments included measurements of cycloplegic autorefraction and autokeratometry (Nidek ARK-510A; Nidek, nidek.com), axial length (IOLMaster version 5; Carl Zeiss Meditec, zeiss.com) and conjunctival ultraviolet autofluorescence (CUVAF) area (Nikon D100 digital camera with a 105 mm 147 f/2.8 micro Nikon lens, nikon.com). CUVAF is an objective measure of ocular sun exposure. As in dermatology, where areas of actinic damage on the skin fluoresces under ultraviolet light,[50] a similar phenomenon occurs on the conjunctiva which can be captured with a camera system.[51] The area of conjunctival fluorescence with the ultraviolet light filters can then be digitally measured. As measures of such "actinic" damage are cumulative, CUVAF is a validated objective measure of cumulative ocular sun exposure.[52] Complete CUVAF methodology was described previously by Huynh *et al.*[53]

Cycloplegic autorefraction was performed at least 20 min after instillation of 1% tropicamide and 2.5%

phenylephrine eye drops. As per Flitcroft and colleagues,[54] myopia was defined as a spherical equivalent ≤−0.5 dioptres (D) in either eye, and subclassified as low (−0.5 D to −3.00 D), moderate (≤−3.00 D to −6.00 D) or high (≤−6.00 D). Emmetropia was defined as a spherical equivalent of within ±0.5 D, while hyperopia is ≥+0.5 D.

Participants additionally completed a self-administered questionnaire as part of the 20-year ophthalmic assessment. The questionnaire collected information regarding highest level of education (primary school, secondary school, university, other/Technical and Further Education (TAFE), as well as family history of myopia.

Statistical analysis

Statistical analyses were conducted in R software version 3.6.3 (R Foundation for Statistical Programming, r-project.org), with level of significance set at $p < 0.05$. The sociodemographic makeup was compared across sleep trajectory class using Chi-square test or Fisher exact test for categorical variables and one-way ANOVA or the Kruskal-Wallis test for continuous variables, depending on the normality of the data. Continuous normal data were expressed as mean ± standard deviation, while continuous non-parametric data was expressed as median and interquartile range.

The association between sleep trajectory and myopia or high myopia was explored using logistic regression, adjusting for potential confounders of age, sex, parental myopia and level of education. We additionally corrected for time spent outdoors by including CUVAF area in multivariate analyses. All other analyses involving continuous eye data as the outcome measure were examined using generalised estimating equations (GEEs). This is an appropriate statistical method given it accounts for missing data, non-parametric data and adjustment for covariates. Importantly, an exchangeable correlation structure can be implemented within GEE models to account for the within-subject correlation between two eyes.[55,56]

RESULTS

Study participant characteristics

Of 1344 participants who attended the ophthalmic examination, 1194 had sleep trajectory data and were thus included in the analysis. There was no significant difference in age or sex between those included or excluded from the analysis ($p > 0.05$). However, there was a significantly lower proportion of participants of "other or mixed" ethnicities, and higher proportion of Caucasian participants included in the analysis, compared to those excluded (other/mixed: 9.9% vs. 16.7%; Caucasians: 85.6% vs. 79.1%; $p = 0.004$).

The characteristics of participants included in the analysis are presented in *Table 1*. The mean age of this cohort was 20.0 ± 0.5 years and 48.7% were female. Caucasians comprised 86.4% of the study sample. The overall prevalence of myopia in this cohort was 25.4% ($n = 303$), including 1.5%

TABLE 1 Participant demographics and study variables by sleep trajectory

		Sleep trajectory			
	All ($n = 1194$)	**Minimal ($n = 567$)**	**Declining ($n = 612$)**	**Persistent ($n = 83$)**	***p*-Value[a]**
Female sex (n, %)[b]	581 (48.7%)	274 (48.3%)	306 (50.0%)	40 (48.2%)	0.84
Parent myopia (no. participants with ≥1 parent with myopia)[b]	274 (22.9%)	135 (23.8%)	129 (21.1%)	16 (19.3%)	0.67
Highest level of education (n, %)[b,c]					
Primary	17 (1.4%)	6 (1.1%)	11 (1.8%)	1 (1.2%)	0.54
Secondary	714 (59.8%)	342 (60.3%)	344 (56.2%)	43 (51.8%)	
Tertiary	62 (5.2%)	31 (5.5%)	34 (5.6%)	1 (1.2%)	
Other	201 (16.8%)	89 (15.7%)	103 (16.8%)	15 (18.1%)	
Ethnicity (n, %)[b]					
Caucasian	1032 (86.4%)	484 (85.4%)	532 (86.9%)	72 (86.7%)	0.88
East Asian	36 (3.0%)	16 (2.8%)	10 (1.6%)	1 (1.2%)	
South Asian	15 (1.3%)	7 (1.2%)	7 (1.1%)	1 (1.2%)	
Other/mixed	121 (10.1%)	60 (10.6%)	63 (10.3%)	9 (10.8%)	
CUVAF area (mm^2; mean ± 1 SD)[d]	48.3 ± 34.2	46.5 ± 33.5	50.6 ± 35.5	43.1 ± 33.8	0.13

Abbreviation: CUVAF, conjunctival ultraviolet autofluorescence.

[a]*p*-Value for difference between groups.

[b]Group difference analysed using Chi-square test.

[c]Does not add up to 100% due to some non-responses.

[d]Analysed using generalised estimating equations with an exchangeable correlation structure implemented.

TABLE 2 Ocular measures by sleep trajectory

		Sleep trajectory		
	All (*n* = 1194)	**Minimal (*n* = 567)**	**Declining (*n* = 612)**	**Persistent (*n* = 83)**
Non-myopes (*n*, %)[a]	873 (73.1%)	414 (73.0%)	464 (75.8%)	63 (75.9%)
Any myopia (*n*, %)[a]	321 (26.9%)	153 (27.0%)	148 (24.2%)	20 (24.1%)
High myopia (*n*, %)[b]	18 (1.5%)	9 (1.6%)	7 (1.1%)	2 (2.4%)
Spherical equivalent (D; median [IQR])[c]	+0.25 (−0.38 to +0.63)	+0.25 (−0.38 to +0.63)	+0.25 (−0.25 to +0.63)	+0.25 (−0.38 to +0.59)
Axial length (mm; mean ± 1 SD)[c]	23.6 ± 0.9	23.6 ± 1.0	23.5 ± 0.9	23.7 ± 1.0
Corneal radius (mm; mean ± 1 SD)[c]	7.73 ± 0.25	7.74 ± 0.25	7.73 ± 0.26	7.73 ± 0.28

Abbreviations: IQR, interquartile range; SD, standard deviation.

[a]Group difference analysed using Chi-square test.

[b]Analysed using Fisher Exact test.

[c]Analysed using generalised estimating equations with an exchangeable correlation structure implemented.

TABLE 3 Logistic regression associations between myopia and study variables

	Odds Ratio (95% CI)	**Wald χ^2**
Sleep trajectory (ref = Minimal)		
Declining	0.87 (0.57 to 1.17)	−0.9
Persistent	0.85 (0.20 to 1.50)	−0.5
Gender (ref = Female)	1.10 (0.79 to 1.40)	0.6
Parent myopia (no. participants with ≥1 parent with myopia) (ref = None)	2.19 (1.88 to 2.50)**	4.9
Education (ref = Primary)		
Secondary	1.35 (0.06 to 2.63)	0.5
Tertiary	1.34 (−0.06 to 2.74)	0.4
Other	1.41 (−0.17 to 2.45)	0.2
Ethnicity (ref = Caucasian)		
East Asian	2.75 (1.86 to 3.63)	2.2
South Asian	2.60 (1.47 to 3.74)	1.7
Other or Mixed	1.23 (0.76 to 1.69)	0.9
CUVAF	0.99 (0.99 to 1.00)*	−3.9

Note: *$p < 0.05$; **$p < 0.01$.

Abbreviations: CI, confidence interval; CUVAF, conjunctival ultraviolet autofluorescence.

(*n* = 18) with high myopia. No significant differences were observed in regards to age, sex, or ethnicity between trajectory groups ($p > 0.05$).

There was no significant association between sleep trajectory and the proportion of those with myopia or high myopia ($p \geq 0.36$; *Table 2*). Logistical regression comparing myopia to the study variables did not report any novel significant associations (*Table 3*), as was the case with high myopia when compared to study variables. Likewise, the GEE models did not reveal significant sleep group difference in spherical equivalence, axial length or corneal radius (*Tables 4* and *5*), with or without corrections for sex, ethnicity, education, CUVAF area and parental myopia.

DISCUSSION

Literature to date has presented variable findings regarding sleep quality and its associations with myopia. Moreover, previous studies[30–32,57,58] have failed to fully capture sleep quality information during the pre-myopic period or have explored sleep quality at a period prior to myopic stabilisation. The current longitudinal sleep data captured both the pre-myopic period and peak age of diagnosis that occurs at approximately 6 to 10 years of age,[59–61] with eye examination performed during young adulthood, which is after the mean age of myopia stabilisation of 15 years.[62] Despite collecting data in a large cohort over the age range considered to be the period of vulnerability for myopia, the current study did not find any relationship between problematic sleep in childhood and adolescence and myopia or ocular parameter perturbance when assessed in young adulthood.

Previous reviews and meta-analyses[11,22] have highlighted the significant overlap in regulation between circadian rhythm and eye growth with respect to the common pathway of light exposure. In particular, animal models propose dopamine as a common regulator,[14–17] including studies demonstrating circadian gene knock-out to be influential for the development of myopia.[16,17] However, our study found neither refractive error nor ocular parameters varied significantly between longitudinal sleep trajectories. One recent study[35] examined 4-year longitudinal changes in myopia and axial length by sleep duration and also found no significant relationship. Other explorations of sleep quality and myopia have revealed conflicting results.[24–26, 42, 43] Notably, most of these studies assessed sleep quality or duration at a single time-point (with the exception of Wei *et al.*[35] who used average sleep time over 4 years) and are thus unable to conclude any direction of temporal relationship between sleep and myopia. Recently, a cross-sectional study by Xu *et al.*[63] found longer sleep duration in adult myopes (60+ years old). It was hypothesised that this demographic slept for longer to compensate for poorer sleep quality owing to myopia-related

TABLE 4 Association between sleep trajectory and spherical equivalent

	Unadjusted			Fully-adjusted		
	Estimate (95% CI)	**Wald χ^2**	***p*-Value**	**Estimate (95% CI)**	**Wald χ^2**	***p*-Value**
Sleep trajectory (ref = Minimal)						
Declining	−0.12 (−0.35 to 0.10)	1.1	0.30	0.13 (−0.10 to 0.37)	1.3	0.26
Persistent	0.02 (−0.36 to 0.40)	0.0	0.93	0.03 (−0.35 to 0.42)	0.0	0.86
Gender (ref = Female)	–	–	–	0.06 (−0.15 to 0.27)	0.3	0.59
Parent myopia (no. participants with ≥1 parent with myopia) (ref = None)	–	–	–	−0.69 (−1.00 to −0.39)	20.2	<0.001**
Education (ref = Primary)						
Secondary	–	–	–	−0.17 (−0.47 to 0.13)	1.2	0.27
Tertiary	–	–	–	−0.06 (−0.59 to 0.46)	0.1	0.81
Other	–	–	–	−0.22 (−0.62 to 0.17)	1.2	0.27
Ethnicity (ref = Caucasian)						
East Asian	–	–	–	−1.43 (−2.24 to −0.62)	12.1	<0.001**
South Asian	–	–	–	−0.42 (−0.99 to 0.15)	2.0	0.15
Other or Mixed	–	–	–	−0.66 (−1.08 to −0.25)	9.8	0.002**
CUVAF	–	–	–	0.05 (0.05 to 0.06)	14.0	<0.001**

Note: *$p < 0.05$; **$p < 0.01$.

Abbreviations: CI, confidence interval; CUVAF, conjunctival ultraviolet autofluorescence.

TABLE 5 Association between sleep trajectory and axial length

	Unadjusted			Fully-Adjusted		
	Estimate (95% CI)	**Wald χ^2**	***p* Value**	**Estimate (95% CI)**	**Wald χ^2**	***p* Value**
Sleep trajectory (ref = Minimal)						
Declining	−0.1 (−0.2 to 0.1)	1.3	0.26	−0.1 (−0.2 to 0.0)	2.2	0.14
Persistent	0.1 (−0.2 to 0.4)	0.4	0.54	0.0 (−0.3 to 0.3)	0.2	0.70
Gender (ref = Female)	–	–	–	0.5 (0.4 to 0.6)	54.2	<0.001**
Parent myopia (no. participants with ≥1 parent with myopia) (ref = None)	–	–	–	0.3 (0.1 to 0.5)	10.5	0.001**
Education (ref = Primary)						
Secondary	–	–	–	0.3 (−0.1 to 0.6)	2.4	0.12
Tertiary	–	–	–	0.4 (−0.0 to 0.8)	3.4	0.07
Other	–	–	–	0.2 (−0.2 to 0.6)	1.3	0.26
Ethnicity (ref = Caucasian)						
East Asian	–	–	–	0.8 (0.2 to 1.4)	6.0	0.02*
South Asian	–	–	–	−0.2 (−0.6 to 0.3)	0.4	0.54
Other or Mixed	–	–	–	0.3 (0.1 to 0.6)	8.7	0.003**
CUVAF	–	–	–	−0.0 (−0.0 to 0.0)	0.5	0.46

Note: *$p < 0.05$; **$p < 0.01$.

Abbreviations: CI, confidence interval; CUVAF, conjunctival ultraviolet autofluorescence.

complications such as cataracts or impaired activities of daily living. Given this age is well beyond myopia onset, it may suggest myopia or its related complications may be a factor for poor sleep rather than sleep disturbance resulting in myopia. With these considerations alongside our data, it is likely that the benefits of myopic-prevention derived from outdoor exposure are unique and the same beneficial pathways may not be achieved through other circadian-related pathways such as sleep quality.

Physiological evidence may support a relationship between sleep and myopia, and therefore the potential for sleep disturbance to contribute to emmetropisation has

been proposed. However, our findings, supported by some less powered studies,[32,35] suggest this direction of relationship does not exist, or more specifically, that deranged sleep in younger years does not pre-empt the onset of myopia when tested in early adulthood. Studies suggesting that sleep disturbance occurs in myopia may be identifying myopes who sleep poorly because of various factors. For example, those with intense educational or study habits (a known risk factor for myopia) may work late into the night under ambient light and have poorer sleep hygiene, causing reduced sleep latency or duration.[64] This scenario may be misinterpreted as myopia resulting in poor sleep or vice versa, depending on when the data were collected. Another possible reason for the previously observed links between sleep and myopia could be related to the confounding effects of reduced outdoor time in such studious individuals.[63] Such examples would create a correlation between sleep and myopia, without true causation.

It should be noted that the sleep data in the current study was collected before the widespread use of smart mobile devices, which can easily be used in bed. With the increasing popularity of such handheld devices, especially in children, future studies could explore how the use of such devices affect sleep behaviour and if this may be associated with myopia development or severity. Our current findings thus serve as important baseline data from the pre-device era, to which these studies could compare.

The results expressed herein should be interpreted in context of this study's limitations. First, parent-reported subjective sleep data is an imperfect measure, especially during the children's teenage years. Moreover, given our single time-point of eye examination, the age of first myopia onset is not known for certain. Therefore, sleep behaviours pre- and post-myopia diagnosis cannot be established, and sleep behaviours as predisposing myopia or vice versa cannot be discriminated. An approach to address this limitation may be to record sleep scores combined with regular eye examinations, which enables the assessment of whether pre-myopic sleep patterns predispose myopia and how myopia may affect subsequent sleep. Future studies may also make use of modern objective sleep measures to assess both sleep quality and sleep quantity in the sample study. Measures such as actigraphy would serve a purpose in this setting but was not widely available at the time of study design or data collection of sleep quality (~1998 to 2007).

This observational longitudinal study contributes significantly to the circadian-myopia literature by using sleep trajectory data and fully capturing both the pre-myopic period and the period of maximal myopia progression. The longitudinal sleep data analysed by LCGA and presented here, combined with a substantial sample size, are both features novel to this field. In particular, sleep trajectories did not correlate significantly with refraction, axial length or corneal radius. Ocular biometry and refraction, as well as the established benefits of outdoor exposure for myopia prevention, are unlikely to be subject to sleep quality. Future studies may consider comparing longitudinal sleep trajectory data pre- and post-myopia diagnosis to further assess the circadian-myopia paradigm.

ACKNOWLEDGEMENTS

We would like to acknowledge Raine Study participants and their families and thank the Raine Study and Lions Eye Institute research staff for cohort coordination and data collection. We further acknowledge the Australian National Health and Medical Research Council (NHMRC) for their long-term contribution to the Raine Study in the past 30 years. The Raine Study Gen2 14- and Gen2 17-year follow-up- were funded by the NHMRC (grant IDs 003209 and 353514, respectively). The activity data collection at these follow-ups were supported by the NHMRC (grant no. 323200). The eye data collection of the Gen2 20-year follow-up of the Raine Study was funded by the NHMRC (grant no. 1021105), Ophthalmic Research Institute of Australia (ORIA), Alcon Research Institute, Lions Eye Institute, the BrightFocus Foundation, and the Australian Foundation for the Prevention of Blindness. The core management of the Raine Study is funded by The University of Western Australia, Curtin University, Telethon Kids Institute, Women and Infants Research Foundation, Edith Cowan University, Murdoch University, The University of Notre Dame Australia and the Raine Medical Research Foundation. SY supported by a NHMRC Early Career Fellowship. DAM is supported by a NHMRC Practitioner Fellowship. The funding organisations had no role in the design or conduct of this research.

CONFLICT OF INTEREST

None of the authors has any conflicts of interest or proprietary interest in any of the materials mentioned in this article.

AUTHOR CONTRIBUTIONS

Nicholas Antony Stafford-Bell: Data curation (supporting); Formal analysis (lead); Writing-original draft (lead). **Joanne McVeigh:** Formal analysis (supporting); Methodology (equal); Writing-review & editing (supporting). **Gareth Lingham:** Data curation (supporting); Writing-review & editing (supporting). **Leon Straker:** Funding acquisition (equal); Writing-review & editing (supporting). **Peter Eastwood:** Methodology (supporting); Writing-review & editing (supporting). **Seyhan Yazar:** Data curation (lead); Writing-review & editing (supporting). **David A Mackey:** Conceptualization (lead); Data curation (equal); Funding acquisition (lead); Resources (equal); Supervision (equal); Writing-review & editing (equal). **Samantha Sze-Yee Lee:** Data curation (supporting); Formal analysis (equal); Methodology (equal); Project administration (supporting); Supervision (lead); Visualization (supporting); Writing-review & editing (lead).

ORCID

Nicholas Stafford-Bell https://orcid.org/0000-0002-5354-3581
Joanne McVeigh https://orcid.org/0000-0002-2446-3814

Gareth Lingham https://orcid.org/0000-0002-8957-0733
Leon Straker https://orcid.org/0000-0002-7786-4128
Peter R Eastwood https://orcid.org/0000-0002-4490-4138
Seyhan Yazar https://orcid.org/0000-0003-0994-6196
David A Mackey https://orcid.org/0000-0001-7914-4709
Samantha Sze-Yee Lee https://orcid.org/0000-0001-6635-1098

REFERENCES

1. Holden BA, Fricke TR, Wilson DA, *et al*. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology* 2016;123:1036–1042.
2. Wu PC, Huang HM, Yu HJ, Fang PC, Chen CT. Epidemiology of myopia. *Asia Pac J Ophthalmol* 2016;5:386–393.
3. Pan CW, Ramamurthy D, Saw SM. Worldwide prevalence and risk factors for myopia. *Ophthalmic Physiol Opt* 2012;32:3–16.
4. He M, Xiang F, Zeng Y, *et al*. Effect of time spent outdoors at school on the development of myopia among children in China a randomized clinical trial. *JAMA* 2015;314:1142–1148.
5. Wu PC, Tsai CL, Wu HL, Yang YH, Kuo HK. Outdoor activity during class recess reduces myopia onset and progression in school children. *Ophthalmology* 2013;120:1080–1085.
6. Dirani M, Tong L, Gazzard G, *et al*. Outdoor activity and myopia in Singapore teenage children. *Br J Ophthalmol* 2009;93:997–1000.
7. Guo Y, Liu LJ, Xu L, *et al*. Outdoor activity and myopia among primary students in rural and urban regions of Beijing. *Ophthalmology* 2013;120:277–283.
8. Guggenheim JA, Northstone K, McMahon G, *et al*. Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. *Invest Ophthalmol Vis Sci* 2012;53:2856–2865.
9. French AN, Morgan IG, Mitchell P, Rose KA. Risk factors for incident myopia in Australian schoolchildren: the Sydney adolescent vascular and eye study. *Ophthalmology* 2013;120:2100–2108.
10. Rose KA, Morgan IG, Ip J, *et al*. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology* 2008;115:1279–1285.
11. Lingham G, Mackey DA, Lucas R, Yazar S. How does spending time outdoors protect against myopia? A review. *Br J Ophthalmol* 2019;104:593–599.
12. Cao K, Wan Y, Yusufu M, Wang N. Significance of outdoor time for myopia prevention: a systematic review and meta-analysis based on randomized controlled trials. *Ophthalmic Res* 2020;63:97–105.
13. Xiong S, Sankaridurg P, Naduvilath T, *et al*. Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. *Acta Ophthalmol* 2017;95:551–566.
14. Cohen Y, Belkin M, Yehezkel O, Solomon AS, Polat U. Dependency between light intensity and refractive development under light-dark cycles. *Exp Eye Res* 2011;92:40–46.
15. Cohen Y, Peleg E, Belkin M, Polat U, Solomon AS. Ambient illuminance, retinal dopamine release and refractive development in chicks. *Exp Eye Res* 2012;103:33–40.
16. Ashby RS, Schaeffel F. The effect of bright light on lens compensation in chicks. *Invest Ophthalmol Vis Sci* 2010;51:5247–5253.
17. Ashby R, Ohlendorf A, Schaeffel F. The effect of ambient illuminance on the development of deprivation myopia in chicks. *Invest Ophthalmol Vis Sci* 2009;50:5348–5354.
18. Radwan B, Liu H, Chaudhury D. The role of dopamine in mood disorders and the associated changes in circadian rhythms and sleep-wake cycle. *Brain Res* 2019;1713:42–51.
19. Fontaine M, Gaucher D, Sauer A, Speeg-Schatz C. Choroidal thickness and ametropia in children: a longitudinal study. *Eur J Ophthalmol* 2017;27:730–734.
20. Nickla DL, Wallman J. The multifunctional choroid. *Prog Retin Eye Res* 2010;29:144–168.
21. Nickla DL, Totonelly K. Choroidal thickness predicts ocular growth in normal chicks but not in eyes with experimentally altered growth. *Clin Exp Optom* 2015;98:564–570.
22. Stone RA, Pardue MT, Iuvone PM, Khurana TS. Pharmacology of myopia and potential role for intrinsic retinal circadian rhythms. *Exp Eye Res* 2013;114:35–47.
23. Viney TJ, Balint K, Hillier D, *et al*. Local retinal circuits of melanopsin-containing ganglion cells identified by transsynaptic viral tracing. *Curr Biol* 2007;17:981–988.
24. Besharse JC, McMahon DG. The retina and other light-sensitive ocular clocks. *J Biol Rhythms* 2016;31:223–243.
25. Kearney S, O'Donoghue L, Pourshahidi LK, Cobice D, Saunders KJ. Myopes have significantly higher serum melatonin concentrations than non-myopes. *Ophthalmic Physiol Opt* 2017;37:557–567.
26. Green CB, Besharse JC. Retinal circadian clocks and control of retinal physiology. *J Biol Rhythms* 2004;19:91–102.
27. Nowak JZ, Zurawska E, Zawilska J. Melatonin and its generating system in vertebrate retina: circadian rhythm, effect of environmental lighting and interaction with dopamine. *Neurochem Int* 1989;14:397–406.
28. Tosini G, Pozdeyev N, Sakamoto K, Iuvone PM. The circadian clock system in the mammalian retina. *BioEssays* 2008;30:624–633.
29. Chakraborty R, Micic G, Thorley L, *et al*. Myopia, or near-sightedness, is associated with delayed melatonin circadian timing and lower melatonin output in young adult humans. *Sleep* 2021;44:zsaa208. doi.org/10.1093/sleep/zsaa208
30. Ayaki M, Torii H, Tsubota K, Negishi K. Decreased sleep quality in high myopia children. *Sci Rep* 2016;6:33902. doi.org/10.1038/srep33902
31. Jee D, Morgan IG, Kim EC. Inverse relationship between sleep duration and myopia. *Acta Ophthalmol* 2016;94:e204–e210.
32. Zhou Z, Morgan IG, Chen Q, *et al*. Disordered sleep and myopia risk among chinese children. *PLoS One* 2015;10:e0121796. doi.org/10.1371/journal.pone.0121796
33. Matricciani L, Blunden S, Rigney G, Williams MT, Olds TS. Children's sleep needs: is there sufficient evidence to recommend optimal sleep for children? *Sleep* 2013;16:203–211.
34. Chaput JP, Dutil C, Sampasa-Kanyinga H. Sleeping hours: what is the ideal number and how does age impact this? *Nat Sci Sleep* 2018;10:421–430.
35. Wei SF, Li SM, Liu L, *et al*. Sleep duration, bedtime, and myopia progression in a 4-year follow-up of Chinese children: the Anyang childhood eye study. *Invest Ophthalmol Vis Sci* 2020;61:ARVO E-Abstract 37.
36. Straker L, Mountain J, Jacques A, *et al*. Cohort profile: the Western Australian Pregnancy Cohort (RAINE) study-generation 2. *Int J Epidemiol* 2017;46:1384J–1385J.
37. Achenbach TM. Manual for the child behavior checklist/4–18 and 1991 profiles. Burlington, VT: University of Vermont Department of Psychiatry; 1991.
38. Wang B, Isensee C, Becker A, *et al*. Developmental trajectories of sleep problems from childhood to adolescence both predict and are predicted by emotional and behavioral problems. *Front Psychol* 2016;7:1874. doi.org/10.3389/fpsyg.2016.01874
39. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep* 2000;23:1043–1051.
40. Nagin DS. Group-based trajectory modeling: an overview. *Ann Nutr Metab* 2014;65:205–210.
41. Newman-Casey PA, Blachley T, Lee PP, *et al*. Patterns of glaucoma medication adherence over four years of follow-up. *Ophthalmology* 2015;122:2010–2021.
42. Northstone K, Guggenheim JA, Howe LD, *et al*. Body stature growth trajectories during childhood and the development of myopia. *Ophthalmology* 2013;120:1064–1073.
43. Lee SSY, Beales DJ, Chen FK, *et al*. Associations between seven-year C-reactive protein trajectory or pack-years smoked with choroidal or retinal thicknesses in young adults. *Sci Rep* 2021;11:6147. doi.org/10.1038/s41598-021-85626-3

44. Duncan TE, Duncan SC. The ABC's of LGM: an introductory guide to latent variable growth curve modeling. *Soc Personal Psychol Compass* 2009;3:979–991.
45. Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. *Annu Rev Clin Psychol* 2010;6:109–138.
46. Cole VT, Apud JA, Weinberger DR, Dickinson D. Using latent class growth analysis to form trajectories of premorbid adjustment in schizophrenia. *J Abnorm Psychol* 2012;121:388–395.
47. Collins L, Lanza S. Latent class and latent transition analysis: with applications in the social behavioural and health sciences. Hoboken, NJ: John Wiley & Sons Inc; 2010.
48. McVeigh JA, Smith A, Howie EK, *et al*. Developmental trajectories of sleep during childhood and adolescence are related to health in young adulthood. *Acta Paediatr* 2021;110:2435–2444.
49. Yazar S, Forward H, Mcknight CM, *et al*. Raine eye health study: design, methodology and baseline prevalence of ophthalmic disease in a birth-cohort study of young adults. *Ophthalmic Genet* 2013;34:199–208.
50. Asawanonda P, Taylor CR. Wood's light in dermatology. *Int J Dermatol* 1999;38:801–807.
51. Ooi JL, Sharma NS, Papalkar D, *et al*. Ultraviolet fluorescence photography to detect early sun damage in the eyes of school-aged children. *Am J Ophthalmol* 2006;141:294–298.
52. Sherwin JC, McKnight CM, Hewitt AW, *et al*. Reliability and validity of conjunctival ultraviolet autofluorescence measurement. *Br J Ophthalmol* 2012;96:801–805.
53. Huynh E, Bukowska DM, Yazar S, *et al*. Quantification of sun-related changes in the eye in conjunctival ultraviolet autofluorescence images. *J Med Imaging* 2016;3:034001. doi.org/10.1117/1.JMI.3.3.034001
54. Flitcroft DI, He M, Jonas JB, *et al*. IMI – defining and classifying myopia: a proposed set of standards for clinical and epidemiologic studies. *Invest Ophthalmol Vis Sci* 2019;60:M20–M30.
55. Ying GS, Maguire MG, Glynn R, Rosner B. Tutorial on biostatistics: linear regression analysis of continuous correlated eye data. *Ophthalmic Epidemiol* 2017;24:130–140.
56. Glynn RJ, Rosner B. Regression methods when the eye is the unit of analysis. *Ophthalmic Epidemiol* 2012;19:159–165.
57. Xu S, Wan Y, Xu Z, *et al*. Association between time spent on physical exercise, sleep, homework and suspected myopia among students. *Zhonghua Liuxingbingxue Zazhi* 2016;37:183–186.
58. Pan CW, Liu JH, Wu RK, Zhong H, Li J. Disordered sleep and myopia among adolescents: a propensity score matching analysis. *Ophthalmic Epidemiol* 2019;26:155–160.
59. Wajuihian SO, Mashige KP. Gender and age distribution of refractive errors in an optometric clinical population. *J Optom* 2021. doi.org/10.1016/j.optom.2020.09.002
60. Verkicharla PK, Kammari P, Das AV. Myopia progression varies with age and severity of myopia. *PLoS One* 2020;15:e0241759. doi.org/10.1371/journal.pone.0241759
61. Wong K, Dahlmann-Noor A. Myopia and its progression in children in London, UK: a retrospective evaluation. *J Optom* 2020;13:146–154.
62. Hardy R, Hillis A, Mutti D, *et al*. Myopia stabilization and associated factors among participants in the correction of myopia evaluation trial (COMET). *Invest Ophthalmol Vis Sci* 2013;54:7871–7884.
63. Xu C, Pan C, Zhao C, *et al*. Prevalence and risk factors for myopia in older adult east Chinese population. *BMC Ophthalmol* 2017;17:191. doi.org/10.1186/s12886-017-0574-4
64. Alsaggaf MA, Wali SO, Merdad RA, Merdad LA. Sleep quantity, quality, and insomnia symptoms of medical students during clinical years: relationship with stress and academic performance. *Saudi Med J* 2016;37:173–182.

How to cite this article: Stafford-Bell N, McVeigh J, Lingham G, *et al*. Associations of 12-year sleep behaviour trajectories from childhood to adolescence with myopia and ocular biometry during young adulthood. *Ophthalmic Physiol Opt* 2022;42:19–27. doi: 10.1111/opo.12905