

Sunshine and Nightshade to prevent myopia

David A Mackey

Lions Eye Institute, University of Western Australia



Outdoors and Atropine to prevent myopia

David A Mackey

Lions Eye Institute, University of Western Australia



Disclosures

- Funding NHMRC, Telethon, Australian Vision Research
- Consultant/Advisor:
 - Novartis
 - Health Advances
 - Editas
 - Lakshimi
- (all unrelated to myopia)
- “Could you patent the sun?” Jonas Salk



THE MYOPIA BOOM

SHORT-SIGHTEDNESS IS REACHING EPIDEMIC PROPORTIONS. SOME SCIENTISTS THINK THEY HAVE FOUND A REASON WHY.

BY ELIE DOLGIN

The southern city of Guangzhou has long held the largest eye hospital in China. But about five years ago, it became clear that the Zhongshan Ophthalmic Center needed to expand. More and more children were arriving with the blurry distance vision caused by myopia, and with so many needing eye tests and glasses, the hospital was bursting at the seams. So the centre began adding new testing rooms — and to make space, it relocated some of its doctors and researchers to a local shopping mall. Now during the summer and winter school holidays, when most diagnoses are made, “thousands and thousands of children” pour in every day, says ophthalmologist Nathan Congdon, who was one of those uprooted. “You literally can’t walk through the halls because of all the children.”

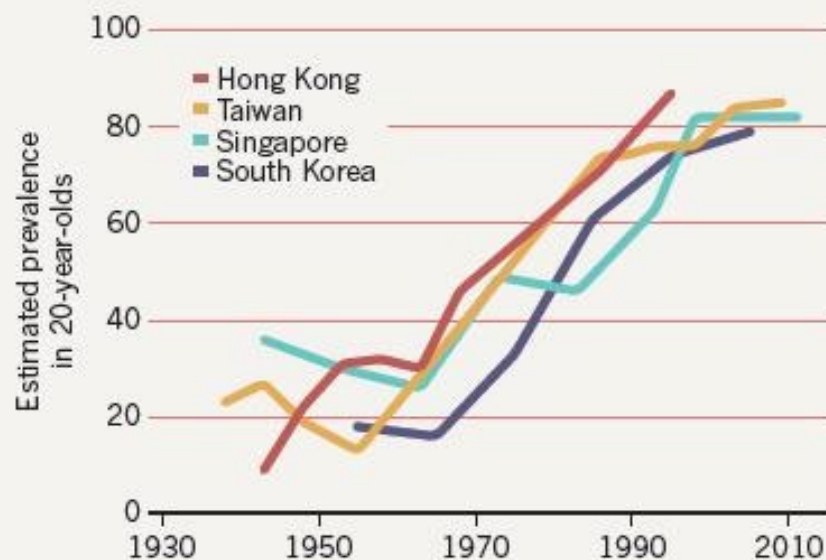
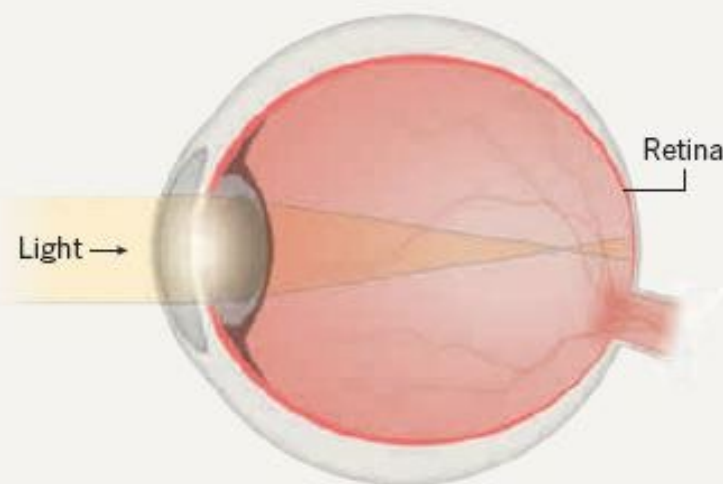
East Asia has been gripped by an unprecedented rise in myopia, also known as short-sightedness. Sixty years ago, 10–20% of the Chinese population was short-sighted. Today, up to 90% of teenagers and young adults are. In Seoul, a whopping 96.5% of 19-year-old men are short-sighted.

Other parts of the world have also seen a dramatic increase in the condition, which now affects around half of young adults in the United States and Europe — double the prevalence of half a century ago. By some estimates, one-third of the world’s population — 2.5 billion people — could be affected by short-sightedness by the end of this decade. “We are going down the path of having a myopia epidemic,” says

Glasses have become the rule, not the exception, in Chinese universities.

THE MARCH OF MYOPIA

East Asian countries have seen a steep rise in short-sightedness over the past 50 years. The condition is caused by a slightly elongated eyeball, which means that light is focused just in front of the retina instead of on it.

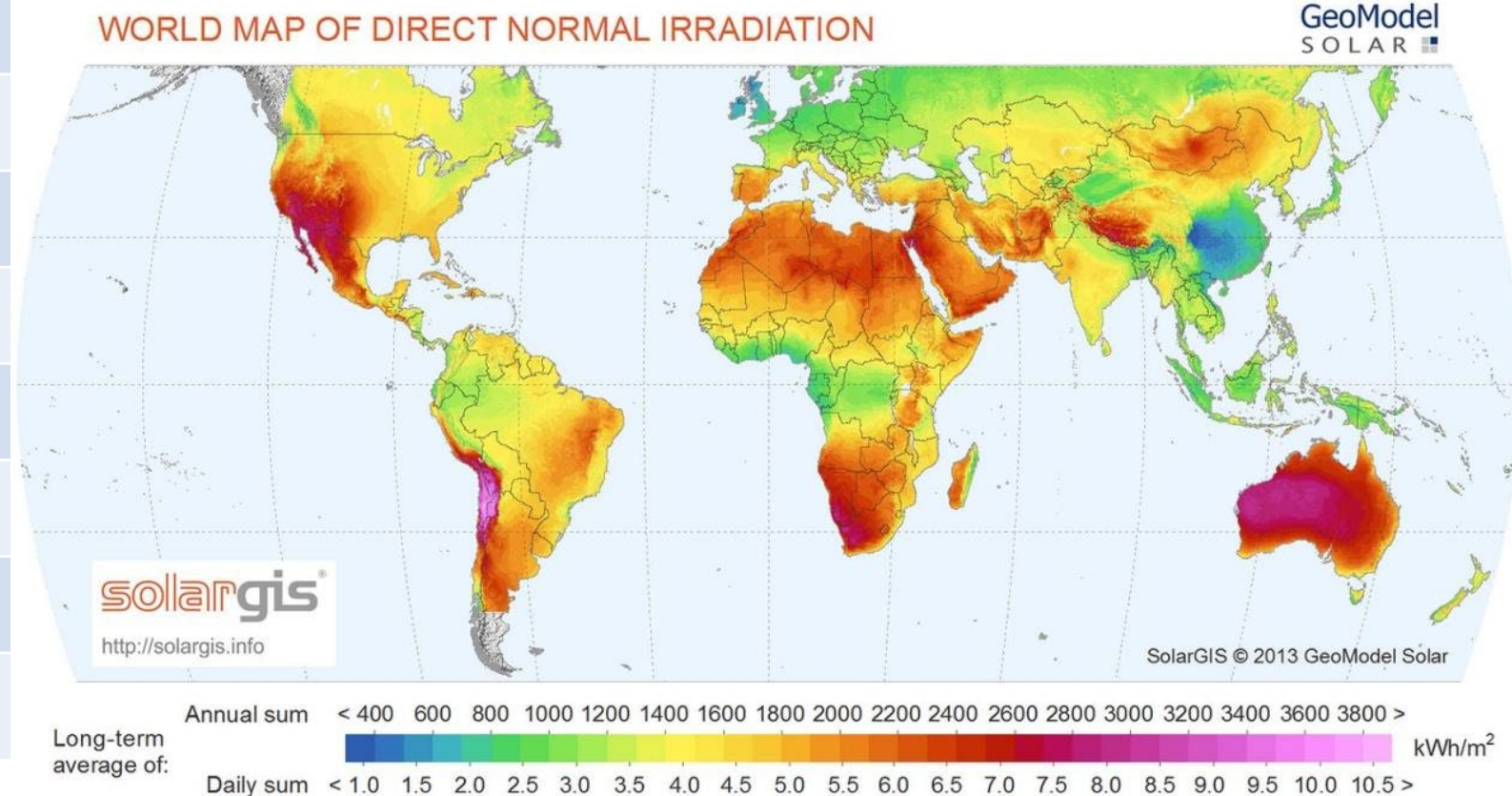




Skin Cancer in Australia is Highest in the World

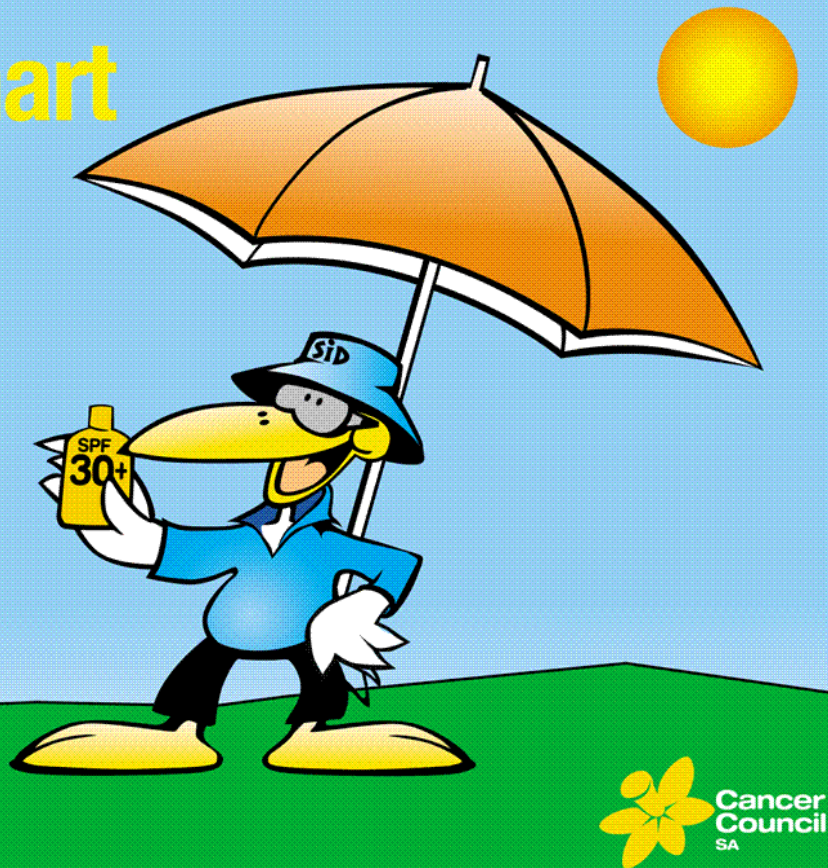


Country	Melanoma incidence per 100,000
Australia	88.7
New Zealand	80.9
Norway	44.5
Sweden	39.5
Switzerland	39.5
Denmark	37.5
United States	37.4
Austria	31.7
Iceland	29.1
Netherlands	28.5



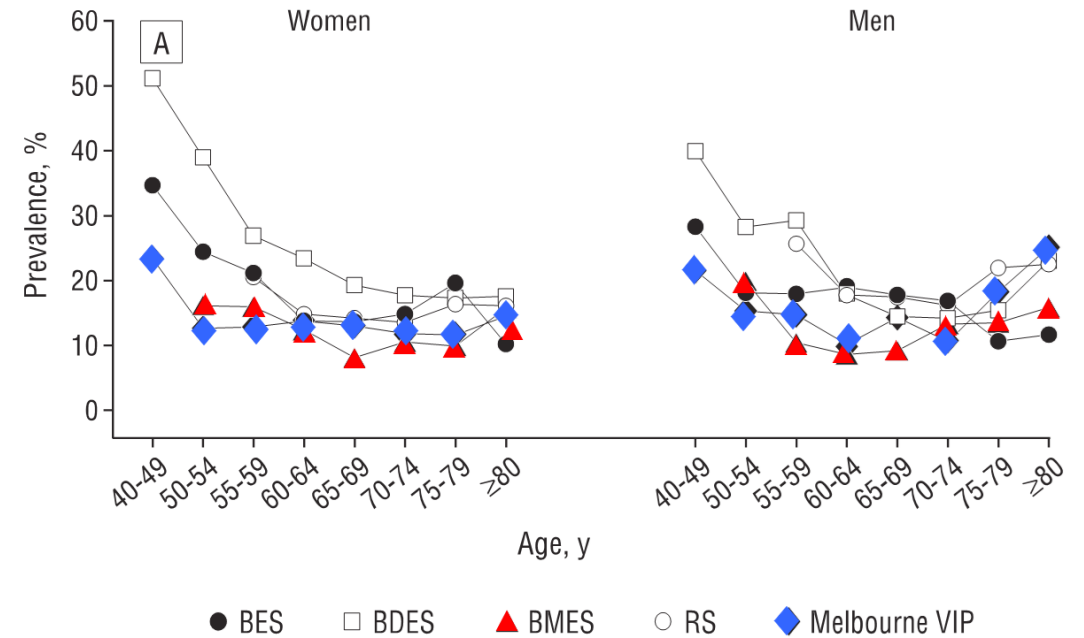
Be SunSmart

Slip!
Slop!
Slap!
Seek!
Slide!



Prevalence of myopia of -1.0 diopter or less

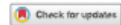
Kempen JH et al Arch Ophthalmol 2004



Kempen 2004

Australia and New Zealand have the highest rates of skin cancer in the world
But some of the lowest rates of myopia

We spend a lot of time outside



Has the Sun Protection Campaign in Australia Reduced the Need for Pterygium Surgery Nationally?

Louis J. Stevenson^{a,b}, David A. Mackey^a, Gareth Lingham^a, Alex Burton^a, Holly Brown^a, Emily Huynh^a, Irene J. Tan^a, Maria Franchina^a, Paul G. Sanfilippo^c, and Seyhan Yazar^a

^aLions Eye Institute, Centre for Ophthalmology and Visual Science, University of Western Australia, Nedlands, Western Australia; ^bFaculty of Medicine and Health, University of Sydney, Camperdown, New South Wales, New South Wales, Australia; ^cCentre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, Australia

ABSTRACT

Background: The Slip! Slap! Slap! Sunsmart safety campaign was an Australian initiative implemented in the 1980s. To assess this campaign's effect on pterygium, we examined the rate of pterygium surgery across Australia and described the prevalence and associations of pterygium in Perth, Australia's sunniest capital city.

Methods: The rate of pterygium surgery was examined using Australian Medicare data. A cross-sectional analysis of the Generation 1 (Gen1) cohort of the Raine Study was performed to investigate the prevalence of pterygium in Perth. We investigated the association between pterygium and conjunctival ultraviolet autofluorescence (CUVAF) area, an objective biomarker of sun exposure, and demographics and health variables derived from a detailed questionnaire.

Results: Between 1994 and 2017, the rate of Medicare funded pterygium surgery in Western Australia fell 11%, well below the national average decline of 47%. Of the 1049 Gen1 Raine Study participants, 994 (571 females; mean age 56.7 years, range = 40.9–81.7) were included in the analysis. The lifetime prevalence of pterygium was 8.4% (n = 83). A higher prevalence of pterygium was associated with outdoor occupation (p-trend = 0.007), male sex (p-trend 0.01) and increasing CUVAF area (p-value <0.001).

Conclusions: The effect of Australia's Slip! Slap! Slap! Sunsmart safety campaign on pterygium been mixed. Since 1994, the rate of private pterygium surgery has declined significantly in all Australian states except Western Australia. Perth, Western Australia, has the highest pterygium prevalence of any mainland-Australian cohort. Higher CUVAF area, male sex, and outdoor occupation were associated with an increased risk of pterygium.

ARTICLE HISTORY

Received 20 February 2020
Revised 29 June 2020
Accepted 9 July 2020

KEYWORDS

Epidemiology; ultraviolet radiation; Raine study; pterygium

Raine Gen 1 8.4% Pterygium

Introduction

Pterygium is a wing-shaped fibrovascular growth of the bulbar conjunctiva that extends across the limbus onto the cornea.¹ Visual impairment can result from direct occlusion of the visual axis or astigmatism induced by corneal deformation.² The pathophysiological changes leading to pterygium development are incompletely understood; however, ultraviolet radiation (UV) exposure has been identified as the single most important risk factor.^{3–6} Reflecting this relationship, pterygium is also strongly associated with malignancy. Ocular surface squamous neoplasia, including squamous cell carcinoma, occurs simultaneously in 10% of cases,⁷ and the presence of pterygium is associated with a 24% increase in the lifetime risk of cutaneous melanoma.⁸ Pterygium imposes a significant public health burden, with pterygium excision being the second most commonly performed ophthalmic surgical procedure after cataract surgery.⁴

Sun-related disease is highly prevalent in Australia, which has the world's highest incidence of melanoma.⁹ The Slip! Slap! Slap! Sunsmart safety campaign was an Australian public health initiative in the early 1980s that sought to encourage people to protect themselves from the harmful effects of ultraviolet radiation. This campaign initially featured a television advertisement with a seagull wearing a t-shirt, 'Slap' on some sunscreen. In 2005, this message was expanded to include 'Slide' on some sunglasses. It now stipulates that clothes must cover the body as possible, sunglasses should have a wide brim and be broad brimmed and cover the face.

Rate of private pterygium surgery in Australia between 1994 and 2017

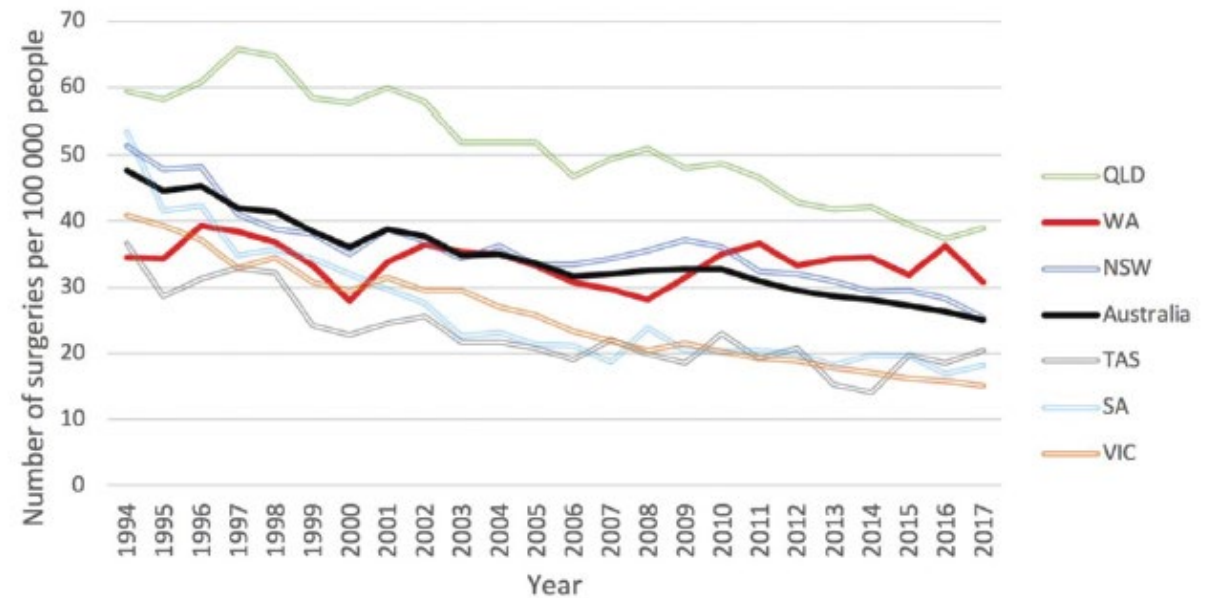
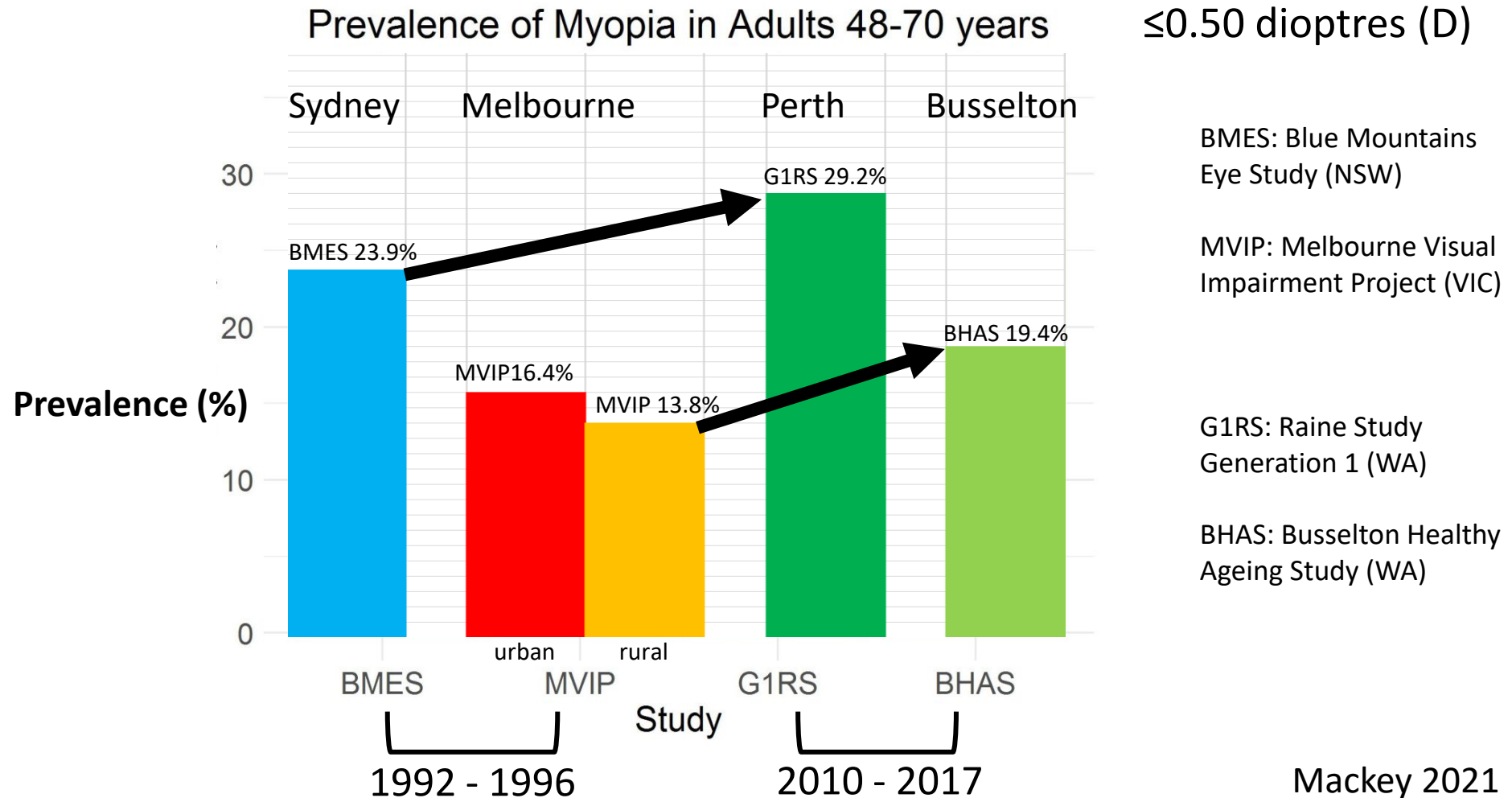


Table 3. Summary of the prevalence of pterygium in Australia.

Author	Study	Year of publication	Age mean	Latitude (degrees south)	Males	Females	Overall
Sherwin <i>et al.</i> ¹⁹	Norfolk Island Eye Study	2013	54.1	29 (Norfolk Island)	15.0%	7.7%	10.9%
Landers <i>et al.</i> ³⁰	Central Australian Ocular Health Study	2011	48.4	26–20 (South Australian/Northern Territory border – Tanami)	No significant difference		7.8%
Panchapakesan <i>et al.</i> ³¹	Blue Mountains Eye Study	1998	Not reported	33 (Blue Mountains)	11.0%	4.5%	7.3%
			All participants >49 years.				
McCarty <i>et al.</i> ³²	Melbourne Visual Impairment Project	2000	60.6	37 (Melbourne)	4.6%	1.8%	2.83%
Moran and Hollows ³	National Trachoma and Eye Health Program	1984	Not reported	Variable – study sites distributed across entirety of Australia	2.7%	2.3%	2.5%
	Indigenous cohort				3.5%	3.3%	3.4%
	Non-indigenous cohort				1.5%	0.65%	1.1%
McKnight <i>et al.</i> ³³	The Raine Study (Gen 2)	2015	20.0	31 (Perth)	2.0%	0.3%	1.2%

Australian Rates of Myopia over time

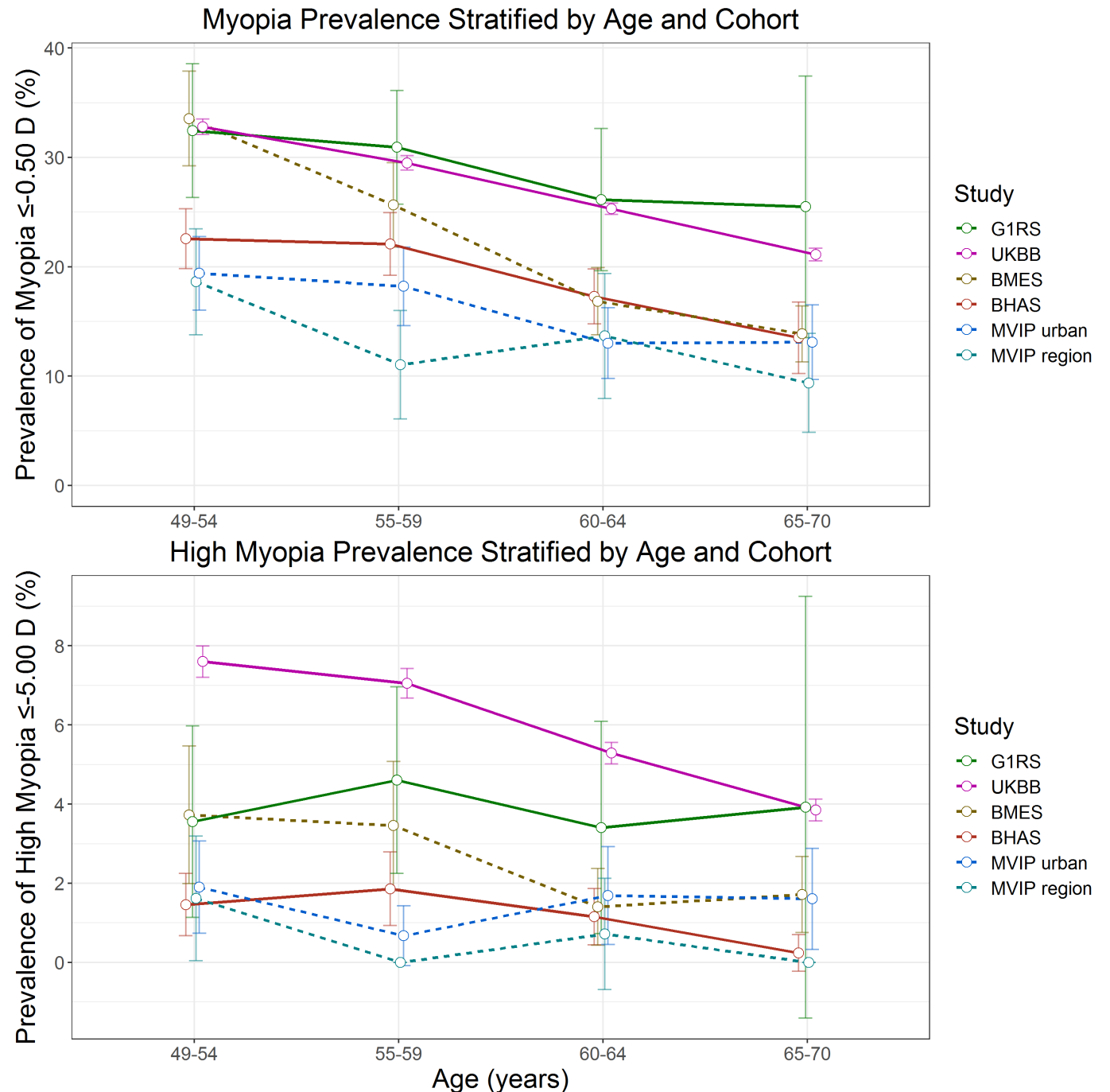
Older adults



- Comparison of middle-aged adults in four Australian studies and UK Biobank

• DEPENDS ON AGE & MYOPIA LEVEL

- Mackey DA et al. 2021
Change in the prevalence of myopia in Australian middle-aged adults across 20 years.



Younger adults

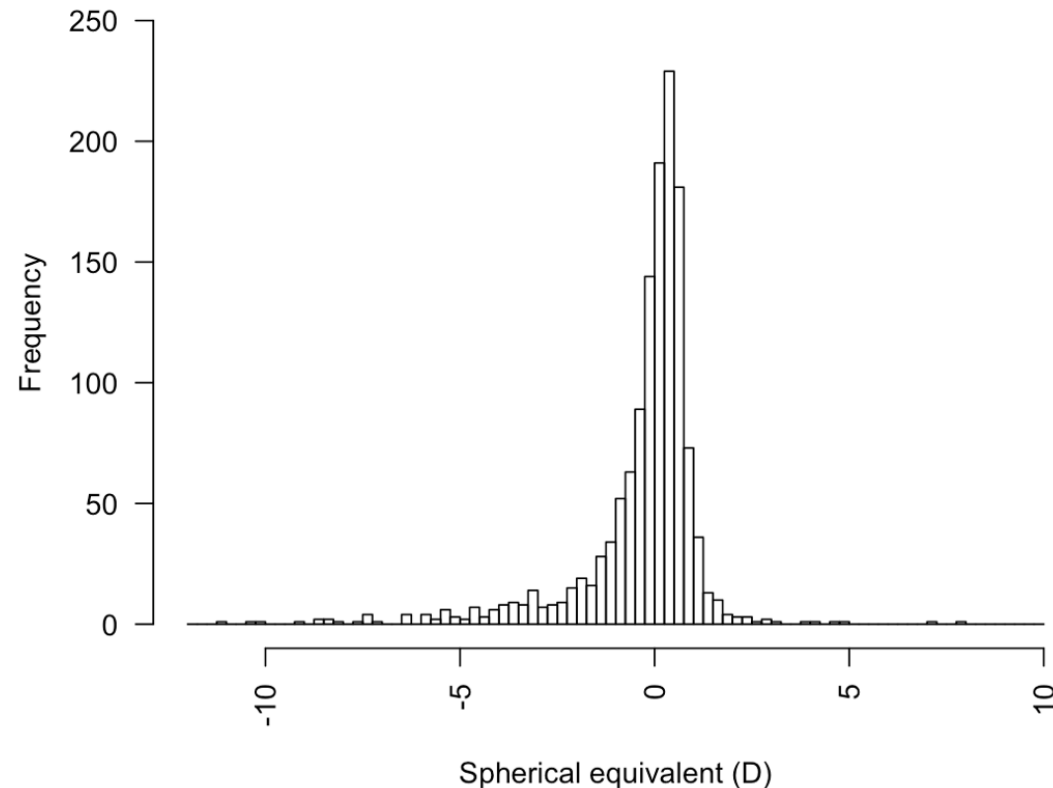
Myopia in Raine Generation 2 age 20 years (2010-2012) n=1,344

Histogram of se_min

SphE ≤ -0.50 in **any eye** (-0.50 inclusive)

25.8%

Histogram of se_min



Young Adult onset Myopia

Research

JAMA Ophthalmology | Original Investigation

Incidence and Progression of Myopia in Early Adulthood

Samantha Sze-Yee Lee, PhD; Gareth Lingham, PhD; Paul G. Sanfilippo, PhD; Christopher J. Hammond, MD; Seang-Mei Saw, MBBS, PhD; Jeremy A. Guggenheim, PhD; Seyhan Yazar, PhD; David A. Mackey, MD

[Multimedia](#)
[Supplemental content](#)

IMPORTANCE Myopia incidence and progression has been described extensively in children. However, few data exist regarding myopia incidence and progression in early adulthood.

OBJECTIVE To describe the 8-year incidence of myopia and change in ocular biometry in young adults and their association with the known risk factors for childhood myopia.

DESIGN, SETTING, AND PARTICIPANTS The Raine Study is a prospective single-center cohort study. Baseline and follow-up eye assessments were conducted from January 2010 to August 2012 and from March 2018 to March 2020. The data were analyzed from June to July 2021. A total of 1328 participants attended the baseline assessment, and 813 participants attended the follow-up assessment. Refractive information from both visits was available for 701 participants. Participants with keratoconus, previous corneal surgery, or recent orthokeratology wear were excluded.

EXPOSURES Participants' eyes were examined at ages 20 years (baseline) and 28 years.

MAIN OUTCOMES AND MEASURES Incidence of myopia and high myopia; change in spherical equivalent (SE) and axial length (AL).

RESULTS A total of 516 (261 male [50.6%]) and 698 (349 male [50.0%]) participants without myopia or high myopia at baseline, respectively, were included in the incidences analyses, while 691 participants (339 male [49%]) were included in the progression analysis. The 8-year myopia and high myopia incidence were 14.0% (95% CI, 11.5%-17.4%) and 0.7% (95% CI, 0.3%-1.2%), respectively. A myopic shift (of 0.50 diopters [D] or greater in at least 1 eye) occurred in 261 participants (37.8%). Statistical significance was found in longitudinal changes in SE (-0.04 D per year; $P < .001$), AL (0.02 mm per year; $P < .001$), and lens thickness (0.02 mm per year; $P < .001$). Incident myopia was associated with self-reported East Asian vs White race (odds ratio [OR], 6.13; 95% CI, 1.06-35.25; $P = .04$), female vs male sex (OR, 1.81; 95% CI, 1.02-3.22; $P = .04$), smaller conjunctival ultraviolet autofluorescence area (per 10-mm^2 decrease, indicating less sun exposure: OR, 9.86; 95% CI, 9.76-9.97; $P < .0009$), and parental myopia (per parent: OR, 1.57; 95% CI, 1.03-2.38; $P = < .05$). Rates of myopia progression and axial elongation were faster in female participants (estimate: SE, 0.02 D per year; 95% CI, 0.01 - 0.02 and AL, 0.007 mm per year, 95% CI, 0.00 - 0.01 ; $P \leq .001$) and those with parental myopia (estimate per parent: SE, 0.01 D per year; 95% CI, 0.00 - 0.02 and AL, 95% CI, 0.002 - 0.008 ; $P \leq .001$). Education level was not associated with myopia incidence or progression.

CONCLUSIONS AND RELEVANCE These findings suggest myopia progression continues for more than one-third of adults during the third decade of life, albeit at lower rates than during childhood. The protective effects of time outdoors against myopia may continue into young adulthood.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Samantha Sze-Yee Lee, PhD, Lions Eye Institute, 2 Verdun St, Nedlands, WA 6009, Australia (samantha.szelee29@gmail.com).

JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2021.5067
Published online January 6, 2022.

- The Raine Study
20 years -> 28 years
- Myopia progression in 1/3 during third decade
- 8-year incidence= 14.0%

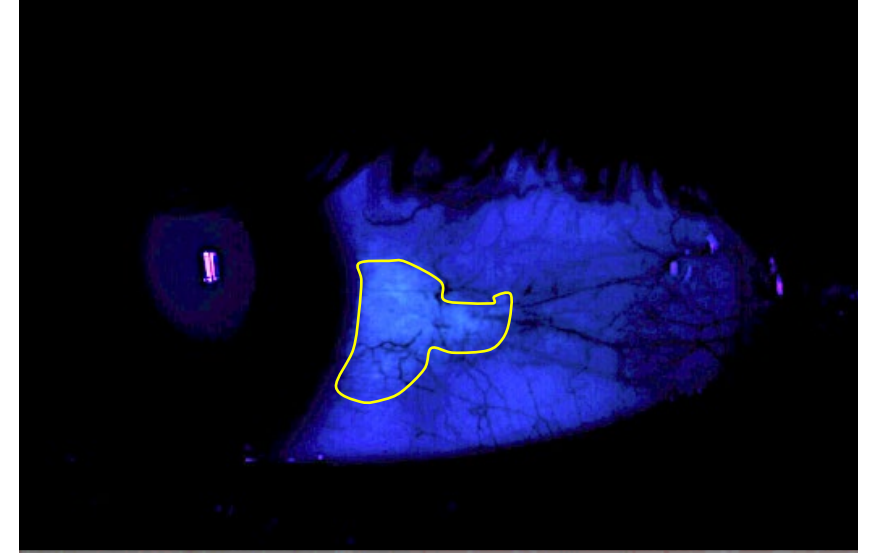
Measures in Raine Study



Cycloplegic Autorefraction
& ocular biometry

Myopia:

Spherical equiv $\leq -0.05D$ in
either eye¹



Conjunctival UV autofluorescence
(CUVAF; ocular sun exposure)

Self-report:

- Highest level of education
- Years in formal education
- Parental myopia

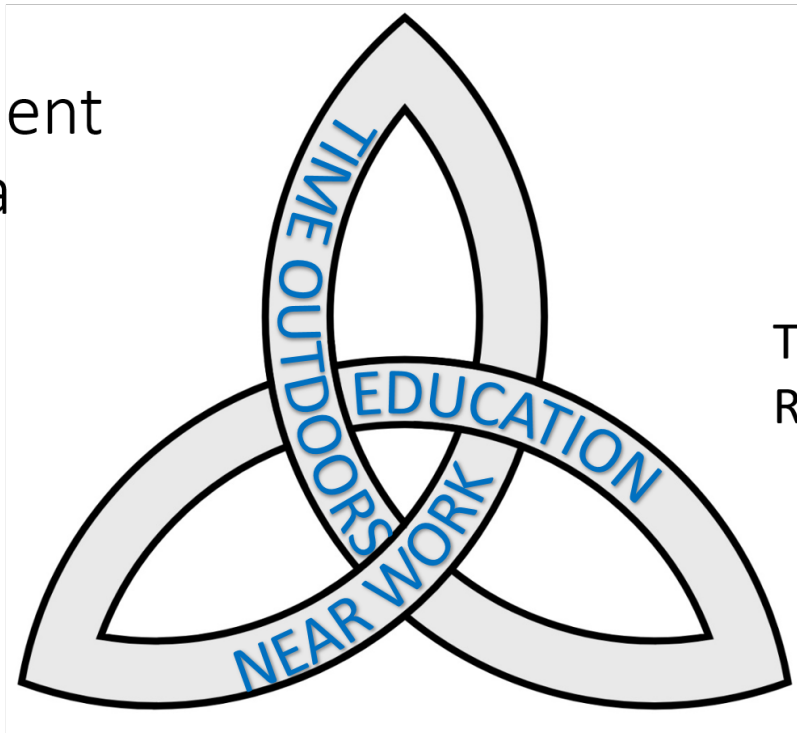
Risk Factors for Myopia incidence in young adults

Associations:

- Women OR= 1.8 [95%CI= 1.0 to 3.2] vs men
- East Asian ethnicity OR= 6.1 [95%CI= 1.1 to 35.3] vs Caucasians
- Parental myopia OR= 1.6 [95%CI= 1.0 to 2.4] per parent
- Less sun exposure OR= 9.9 [95%CI= 9.8 to 10.0] per 10mm² decrease in CUVAF area

Untangling the Risk factors for Myopia

Environment
& Myopia



Three Intertwined
Risk Factors

Increased Time Outdoors Prevents Myopia

Outdoor Activity Reduces the Prevalence of Myopia in Children

Kathryn A. Rose, PhD,¹ Ian G. Morgan, BSc, PhD,² Jenny Ip, MBBS,³ Annette Kifley, MBBS, MAppStat,³ Son Huynh, MBBS, MMed (ClinEpi),⁴ Wayne Smith, BMed, PhD,⁴ Paul Mitchell, MD, PhD⁵

Objective: To assess the relationship of near, midworking distance, and outdoor activities with prevalence of myopia in school-aged children.

Design: Cross-sectional study of 2 age samples from 51 Sydney schools, selected using a random cluster design.

Participants: One thousand seven hundred sixty-five 6-year-olds (year 1) and 2367 12-year-olds (year 7) participated in the Sydney Myopia Study from 2003 to 2005.

Methods: Children had a comprehensive eye examination, including cycloplegic refraction. Parents and children completed detailed questionnaires on activity.

Main Outcome Measures: Myopia prevalence and mean spherical equivalent (SE) in relation to patterns of near, midworking distance, and outdoor activities. Myopia was defined as SE refraction ≤ -0.5 diopters (D).

Results: Higher levels of outdoor activity (sport and leisure activities) were associated with more hyperopic refractions and lower myopia prevalence in the 12-year-old students. Students who combined high levels of near work with low levels of outdoor activity had the least hyperopic mean refraction (+0.27 D; 95% confidence interval [CI], 0.02–0.52), whereas students who combined low levels of near work with high levels of outdoor activity had the most hyperopic mean refraction (+0.56 D; 95% CI, 0.38–0.75). Significant protective associations with increased outdoor activity were seen for the lowest ($P = 0.04$) and middle ($P = 0.02$) tertiles of near-work activity. The lowest odds ratios for myopia, after adjusting for confounders, were found in groups reporting the highest levels of outdoor activity. There were no associations between indoor sport and myopia. No consistent associations between refraction and measures of activity were seen in the 6-year-old sample.

Conclusions: Higher levels of total time spent outdoors, rather than sport per se, were associated with less myopia and a more hyperopic mean refraction, after adjusting for near work, parental myopia, and ethnicity. *Ophthalmology* 2008;115:1279–1285 © 2008 by the American Academy of Ophthalmology.

Myopia is an eye condition that poses significant costs for optical correction and costs due to associated cataract^{1–3} and glaucoma^{4–6} in the longer term. In the latter part of the 20th century in highly urbanized East Asian regions,^{7–9} the prevalence of myopia has increased dramatically and, in some highly educated groups, now exceeds 80%.^{10–12} In parallel with the increase in overall myopia, there has been a rise in the prevalence of high myopia (≤ -6 diopters [D]),¹³ which is associated with increased levels of visual impairment and blindness,¹⁴ primarily due to chorioretinal degeneration and retinal detachment. Furthermore, myopia is appearing with greater prevalence in young children,^{13,15} which places

these children at greater risk of developing high myopia, with its associated complications.

Due to these trends in the prevalence of myopia, there has been a research focus on factors that could increase the risk of myopia. It is well established that the prevalence of myopia in children is greater if their parents are myopic.^{16–21} East Asian ethnicity has also been proposed as a possible risk factor. Although these 2 factors could indicate a genetic contribution, myopia is generally believed to have a multifactorial etiology, and the rapid rise in prevalent myopia suggests that rapidly changing environmental factors are predominant in determining the current patterns of myopia.²²

The Sydney Myopia Study is supported by the National Health & Medical Research Council, Canberra, Australia (grant no. 253732), and Westmead Millennium Institute, University of Sydney, Sydney, Australia. Dr Morgan's contribution was supported by the Australian Research Council, Canberra, Australia (grant no. COE561903). The sponsors and funding organizations had no role in the design or conduct of the research. No conflicting relationship exists for any author.

Correspondence and reprint requests to Dr Kathryn Rose, Discipline of Applied Vision Sciences, Faculty of Health Sciences, University of Sydney, PO Box 170, Lidcombe, NSW Australia, 1515. E-mail: k.rose@usyd.edu.au

Originally received: September 4, 2007.

Final revision: November 14, 2007.

Accepted: December 14, 2007.

Available online: February 21, 2008.

Manuscript no. 2007-1147.

¹ School of Applied Vision Sciences, Faculty of Health Sciences, University of Sydney, Sydney, Australia.

² ARC Centre of Excellence in Vision Science and Research School of Biological Sciences, Australian National University, Canberra, Australia.

³ Department of Ophthalmology (Centre for Vision Research, Westmead Hospital) and Westmead Millennium Institute, Sydney, Australia.

⁴ Centre for Clinical Epidemiology and Biostatistics, University of Newcastle, Newcastle, Australia.

© 2008 by the American Academy of Ophthalmology
Published by Elsevier Inc.

ISSN 0161-6420/08/05-0000-00 \$12.00
doi:10.1016/j.ophtha.2007.12.019

How does spending time outdoors protect against myopia? A review

Gareth Lingham ●,¹ David A Mackey ●,¹ Robyn Lucas ●,^{1,2} Seyhan Yazar ●,^{1,3}

► Additional material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bjophthalmol-2019-314675>).

¹Centre for Ophthalmology and Visual Science, Lions Eye Institute, University of Western Australia, Perth, Western Australia, Australia

²National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Canberra, Australian Capital Territory, Australia

³Single Cell and Computational Genomics, Garvan Institute of Medical Research, Sydney, New South Wales, Australia

ABSTRACT

Myopia is an increasingly common condition that is associated with significant costs to individuals and society. Moreover, myopia is associated with increased risk of glaucoma, retinal detachment and myopic maculopathy, which in turn can lead to blindness. It is now well established that spending more time outdoors during childhood lowers the risk of developing myopia and may delay progression of myopia. There has been great interest in further exploring this relationship and exploiting it as a public health intervention aimed at preventing myopia in children. However, spending more time outdoors can have detrimental effects, such as increased risk of melanoma, cataract and pterygium. Understanding how spending more time outdoors prevents myopia could advance development of more targeted interventions for myopia. We reviewed the evidence for and against eight facets of spending time

possibly progression in children and adolescents.^{4–6} Spending more time outdoors may reduce the risk of myopia by a number of pathways (figure 1). Identifying the factors behind this relationship might allow interventions to be targeted, thereby avoiding potentially detrimental effects associated with spending time outdoors, such as sunburn and an increased risk of skin cancers.⁷ The means by which spending time outdoors might lower myopia risk have been briefly discussed in broader reviews, as well as comprehensively in reviews on individual elements (online supplementary table 1). However, the rapid expansion of studies warrants an updated and focused review comparing the evidence for different causal factors linking time spent outdoors and myopia. We conducted a comprehensive narrative review of eight leading hypotheses on how time spent outdoors prevents myopia. The online

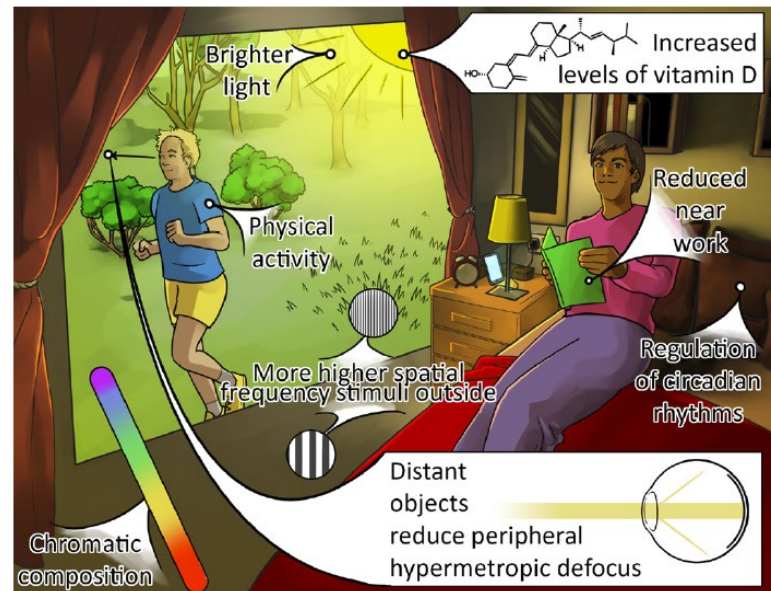


Figure 1 Spending more time outdoors may reduce risk of myopia via multiple means.

Clinical and Epidemiologic Research

Myopia Is Associated With Lower Vitamin D Status in Young Adults

Seyhan Yazar,¹ Alex W. Hewitt,^{1,2} Lucinda J. Black,³ Charlotte M. McKnight,¹ Jenny A. Mountain,³ Justin C. Sherwin,⁴ Wendy H. Oddy,³ Minas T. Coroneo,⁵ Robyn M. Lucas,^{5,6} and David A. Mackey¹

¹Centre for Ophthalmology and Vision Science, University of Western Australia and the Lions Eye Institute, Perth, Western Australia, Australia

²Centre for Eye Research Australia, Melbourne University, Melbourne, Victoria, Australia

³TR

⁴TR

⁵TR

⁶TR

⁷TR

⁸TR

⁹TR

¹⁰TR

¹¹TR

¹²TR

¹³TR

¹⁴TR

¹⁵TR

¹⁶TR

¹⁷TR

¹⁸TR

¹⁹TR

²⁰TR

²¹TR

²²TR

²³TR

²⁴TR

²⁵TR

²⁶TR

²⁷TR

²⁸TR

²⁹TR

³⁰TR

³¹TR

³²TR

³³TR

³⁴TR

³⁵TR

³⁶TR

³⁷TR

³⁸TR

³⁹TR

⁴⁰TR

⁴¹TR

⁴²TR

⁴³TR

⁴⁴TR

⁴⁵TR

⁴⁶TR

⁴⁷TR

⁴⁸TR

⁴⁹TR

⁵⁰TR

⁵¹TR

⁵²TR

⁵³TR

⁵⁴TR

⁵⁵TR

⁵⁶TR

⁵⁷TR

⁵⁸TR

⁵⁹TR

⁶⁰TR

⁶¹TR

⁶²TR

⁶³TR

⁶⁴TR

⁶⁵TR

⁶⁶TR

⁶⁷TR

⁶⁸TR

⁶⁹TR

⁷⁰TR

⁷¹TR

⁷²TR

⁷³TR

⁷⁴TR

⁷⁵TR

⁷⁶TR

⁷⁷TR

⁷⁸TR

⁷⁹TR

⁸⁰TR

⁸¹TR

⁸²TR

⁸³TR

⁸⁴TR

⁸⁵TR

⁸⁶TR

⁸⁷TR

⁸⁸TR

⁸⁹TR

⁹⁰TR

⁹¹TR

⁹²TR

⁹³TR

⁹⁴TR

⁹⁵TR

⁹⁶TR

⁹⁷TR

⁹⁸TR

⁹⁹TR

¹⁰⁰TR

¹⁰¹TR

¹⁰²TR

¹⁰³TR

¹⁰⁴TR

¹⁰⁵TR

¹⁰⁶TR

¹⁰⁷TR

¹⁰⁸TR

¹⁰⁹TR

¹¹⁰TR

¹¹¹TR

¹¹²TR

¹¹³TR

¹¹⁴TR

¹¹⁵TR

¹¹⁶TR

¹¹⁷TR

¹¹⁸TR

¹¹⁹TR

¹²⁰TR

¹²¹TR

¹²²TR

¹²³TR

¹²⁴TR

¹²⁵TR

¹²⁶TR

¹²⁷TR

¹²⁸TR

¹²⁹TR

¹³⁰TR

¹³¹TR

¹³²TR

¹³³TR

¹³⁴TR

¹³⁵TR

¹³⁶TR

¹³⁷TR

¹³⁸TR

¹³⁹TR

¹⁴⁰TR

¹⁴¹TR

¹⁴²TR

¹⁴³TR

¹⁴⁴TR

¹⁴⁵TR

¹⁴⁶TR

¹⁴⁷TR

¹⁴⁸TR

¹⁴⁹TR

¹⁵⁰TR

¹⁵¹TR

¹⁵²TR

¹⁵³TR

¹⁵⁴TR

¹⁵⁵TR

¹⁵⁶TR

¹⁵⁷TR

¹⁵⁸TR

¹⁵⁹TR

¹⁶⁰TR

¹⁶¹TR

¹⁶²TR

¹⁶³TR

¹⁶⁴TR

¹⁶⁵TR

¹⁶⁶TR

¹⁶⁷TR

¹⁶⁸TR

¹⁶⁹TR

¹⁷⁰TR

¹⁷¹TR

¹⁷²TR

¹⁷³TR

¹⁷⁴TR

¹⁷⁵TR

¹⁷⁶TR

¹⁷⁷TR

¹⁷⁸TR

¹⁷⁹TR

¹⁸⁰TR

¹⁸¹TR

¹⁸²TR

¹⁸³TR

¹⁸⁴TR

¹⁸⁵TR

¹⁸⁶TR

¹⁸⁷TR

¹⁸⁸TR

¹⁸⁹TR

¹⁹⁰TR

¹⁹¹TR

¹⁹²TR

¹⁹³TR

¹⁹⁴TR

¹⁹⁵TR

¹⁹⁶TR

¹⁹⁷TR

¹⁹⁸TR

¹⁹⁹TR

²⁰⁰TR

²⁰¹TR

²⁰²TR

²⁰³TR

²⁰⁴TR

²⁰⁵TR

²⁰⁶TR

²⁰⁷TR

²⁰⁸TR

²⁰⁹TR



GPS UV
monitors

Markers of outdoor activity

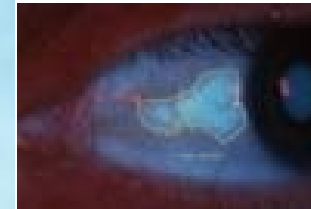
Skin Cancer
(BCC SCC
Melanoma)

Vitamin D Level

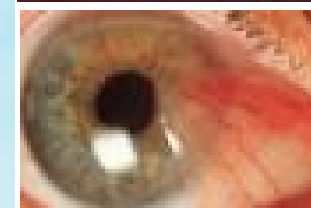
Bone Density



Conjunctival
Auto-fluorescence



Pterygium



Total Body
or
Arm Mole Counts

Dorsal Hand
Skin Wrinkling

Students
and Fellows
Wanted in Perth!

**Myopia and skin cancer are inversely correlated:
results of the Busselton Healthy Ageing Study.
Franchina M et al. Med J Aust. 2014;200:521-2.**



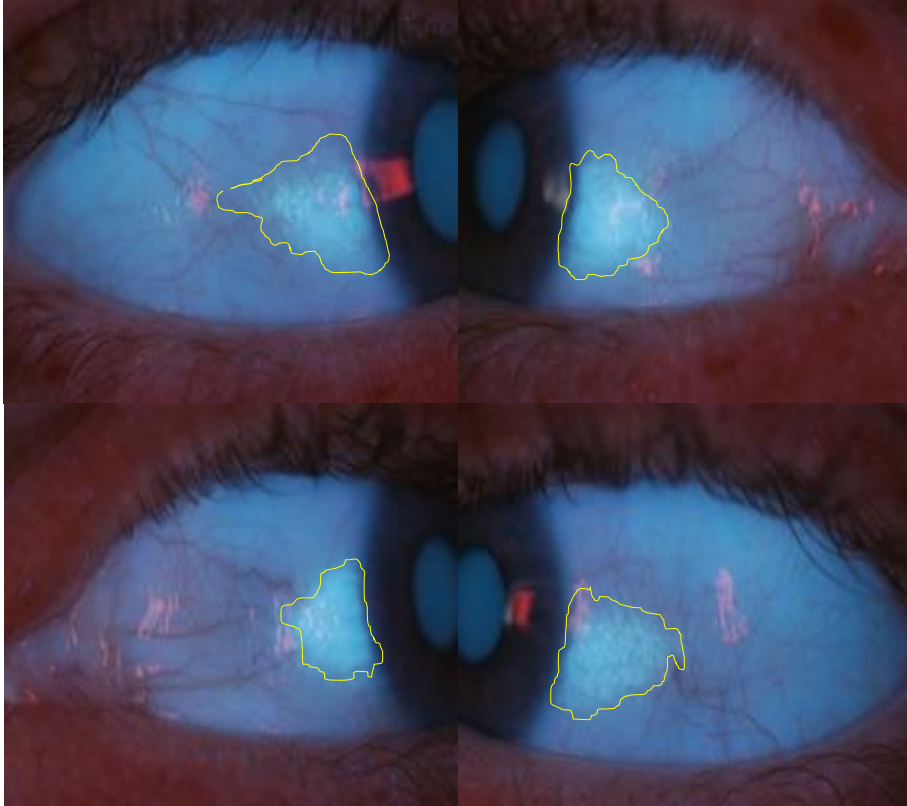
143/1,861 participants (7.7%) with a previous history of either cutaneous melanoma, squamous cell carcinoma or basal cell carcinoma

	Controls	Skin cancer history [#]	p-value
Age in years (Range)	56.2 (45.7 -66.4)	57.0 (45.5-65.7)	0.117*
Gender (%Male)	958 (53.8%)	74 (50.1%)	0.473**
Known ocular pathology			
<i>Diabetes-related</i>	32 (1.8%)	2 (1.4%)	1.000 [†]
<i>Macular degeneration</i>	42 (2.4%)	1 (0.7%)	0.251 [†]
<i>Glaucoma</i>	39 (2.2%)	3 (2.1%)	1.000 [†]
<i>Cataract</i>	97 (5.4%)	4 (2.7%)	0.242 [†]
<i>Eye injury/trauma</i>	32 (1.8%)	1 (0.7%)	0.509 [†]
<i>Other</i>	62 (3.5%)	8 (5.5%)	0.243 [†]
Myopia (mean SE both eyes $\leq$ -0.50D)	391 (21.9%)	17 (11.6%)	0.003**

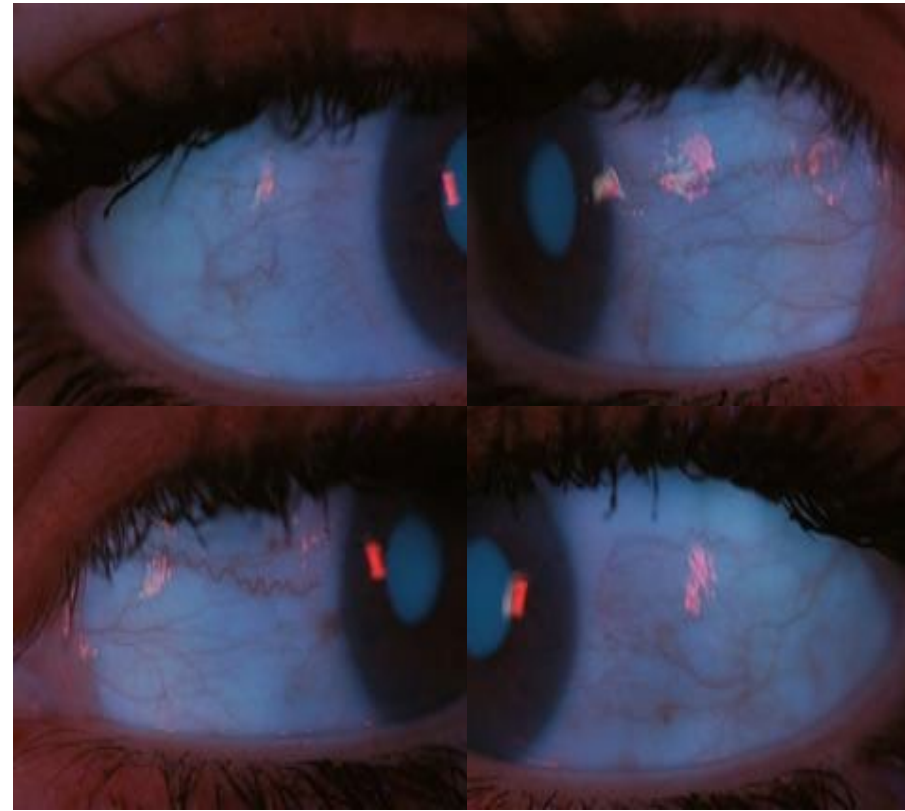
[#]Includes cutaneous melanoma, SCC, BCC.

Conjunctival Ultraviolet Autofluorescence (CUVAF)

A marker of long term ocular sun exposure in region where Pterygia form



← CUVAF evident in all four quadrants



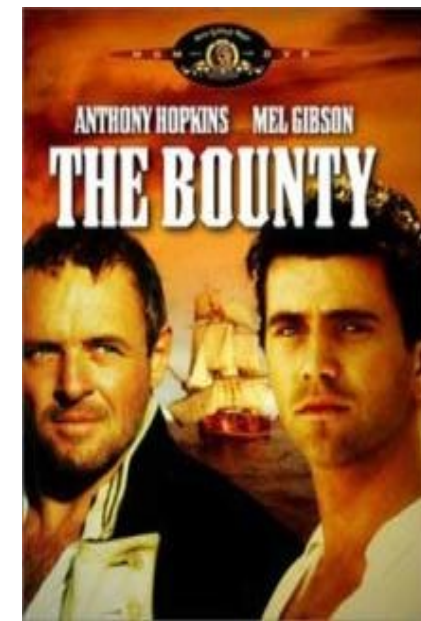
No CUVAF evident →





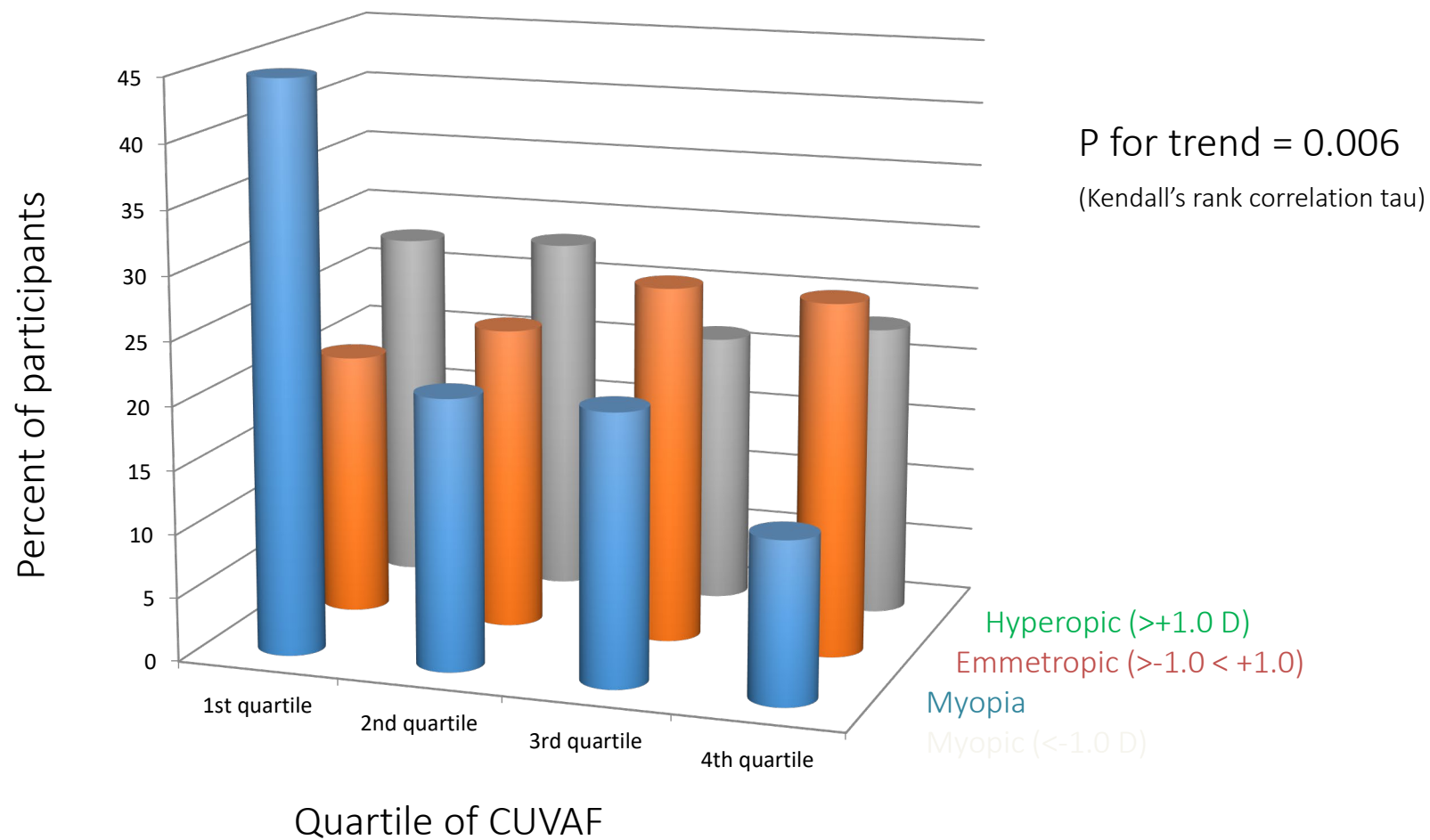
Norfolk Island Eye Study

- The Norfolk Island Eye Study (NIES): rationale, methodology and distribution of ocular biometry. Mackey DA et al. Twin Res Hum Genet. 2011;14:42-52.
- The association between pterygium and conjunctival ultraviolet autofluorescence: the Norfolk Island Eye Study. Sherwin JC et al. Acta Ophthalmol. 2013;91:363-70.
- The association between time spent outdoors and myopia using a novel biomarker of outdoor light exposure. Sherwin JC et al. Invest Ophthalmol Vis Sci. 2012;53:4363-70



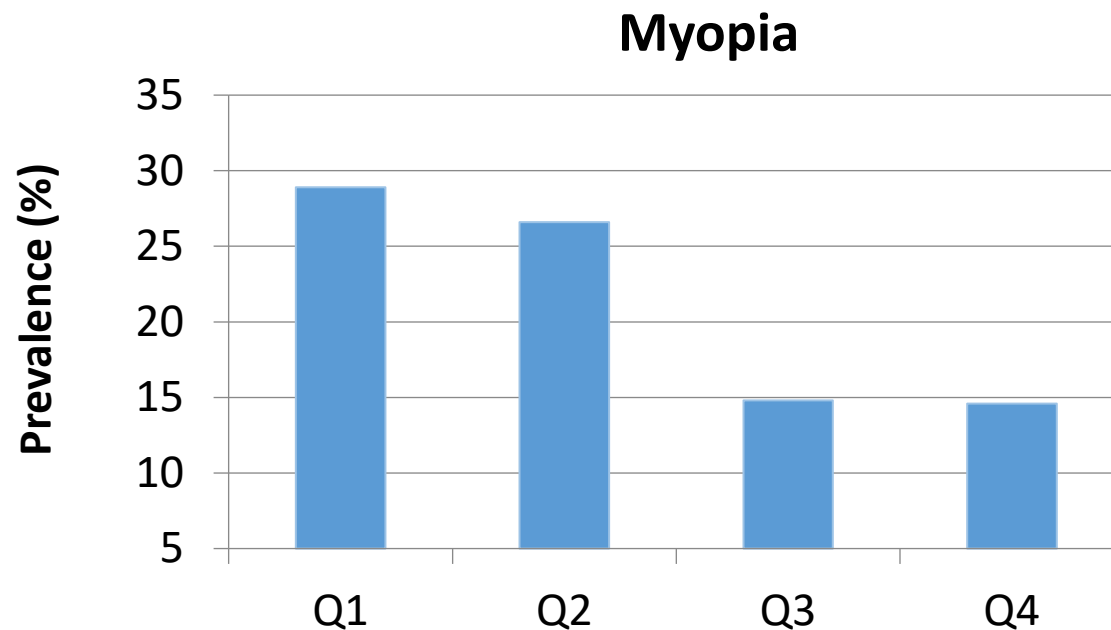


Relationships between quartiles of total CUVAF and refractive error

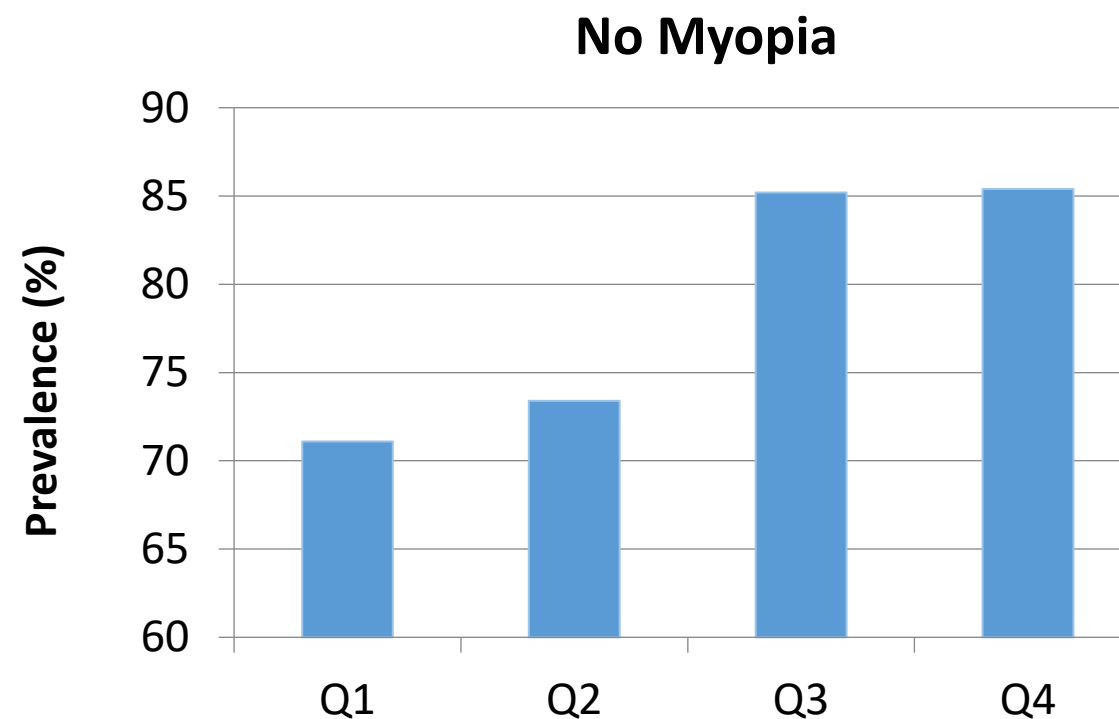


Conjunctival UV
Autofluorescence
(CUVAF) and
Myopia
in the Raine
Study @ age 20
years

McKnight 2014

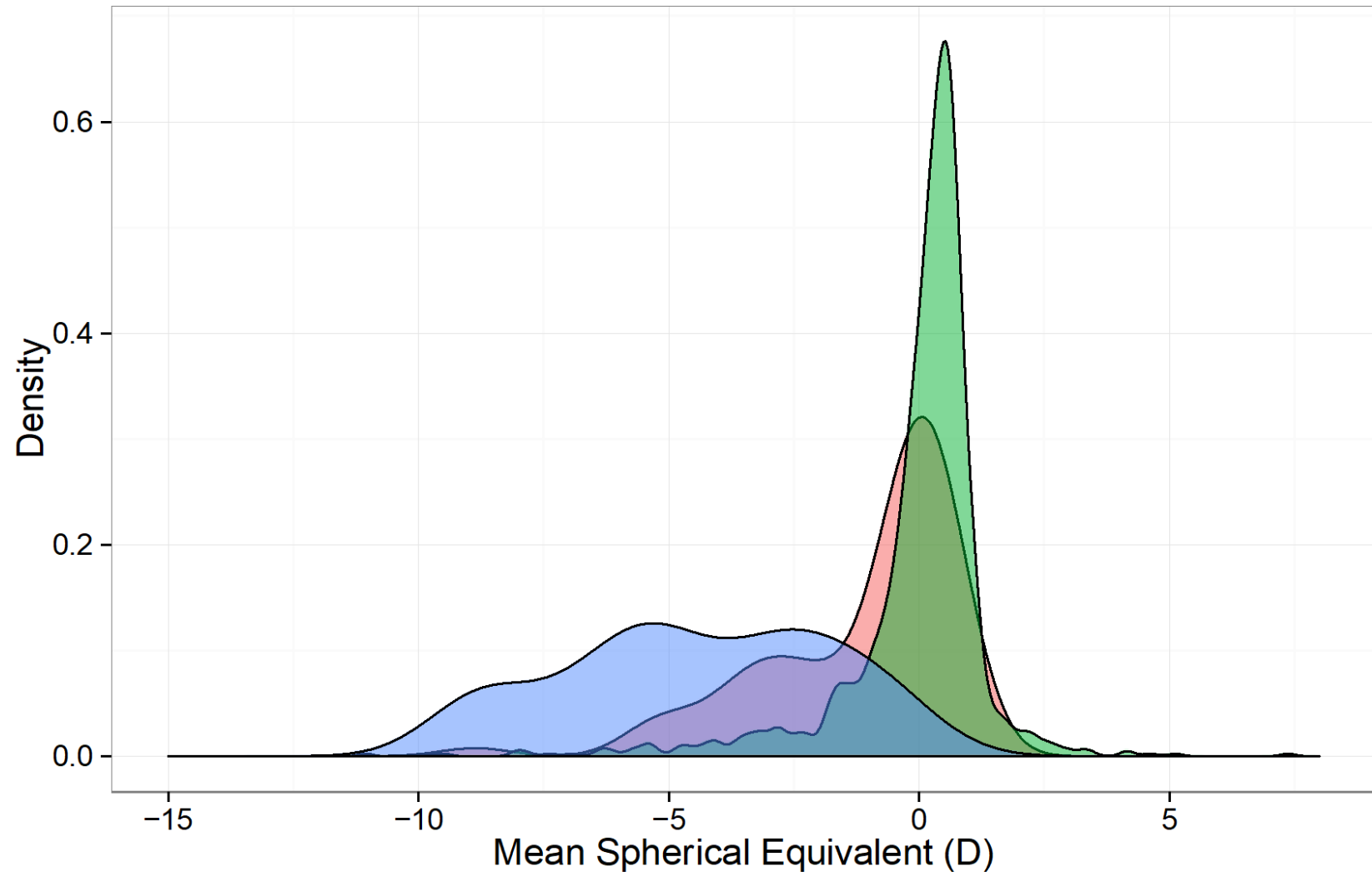


Quartiles
of CUVAF



Raine cohort compared with 74 Chinese Medical Students doing a term @ UWA

Refractive
Error

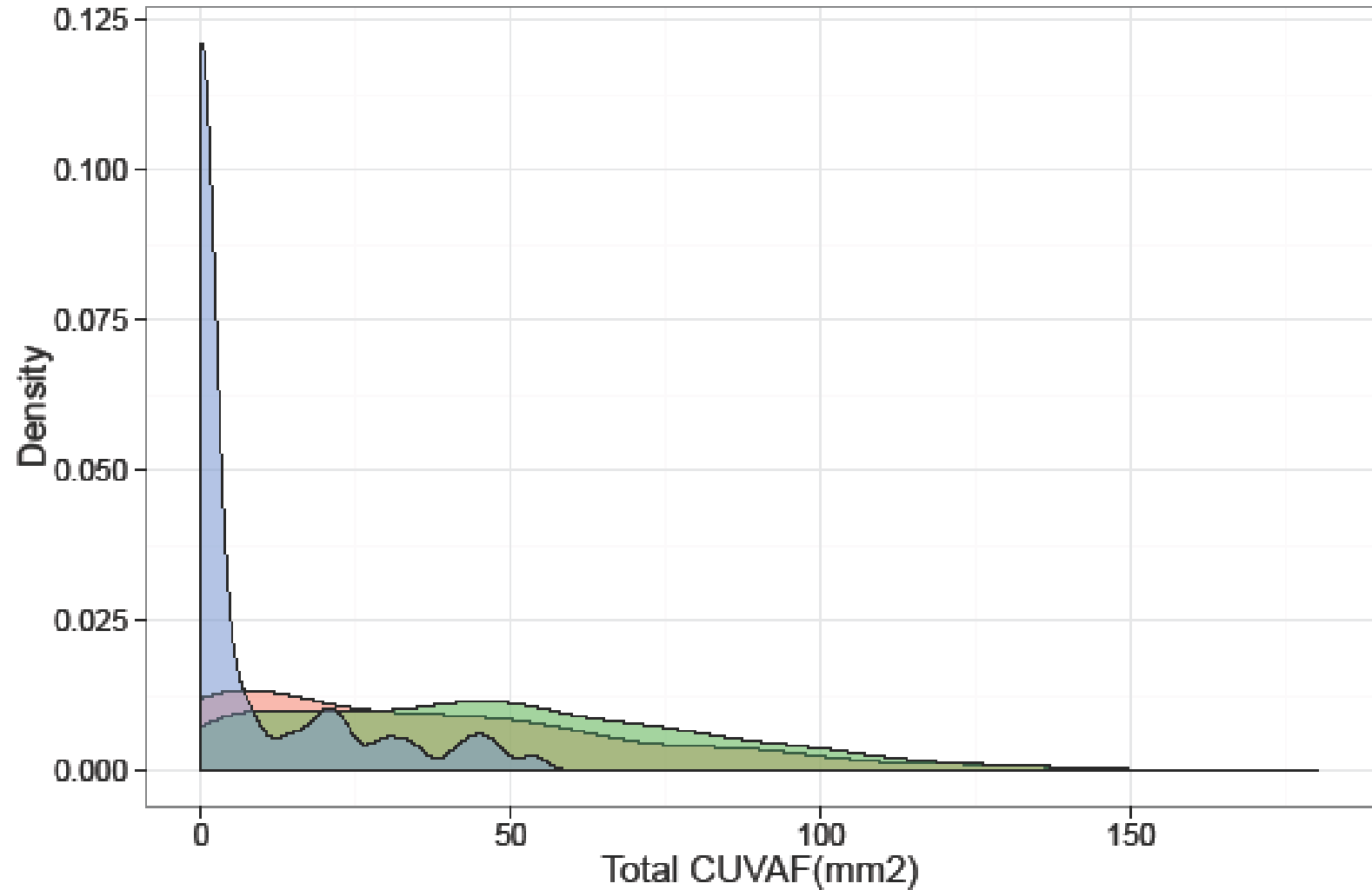


Ethnicity  Australian Asians  Australian Caucasians  Overseas Asian Medical Students



Raine cohort compared with 74 Chinese Medical Students doing a term @ UWA

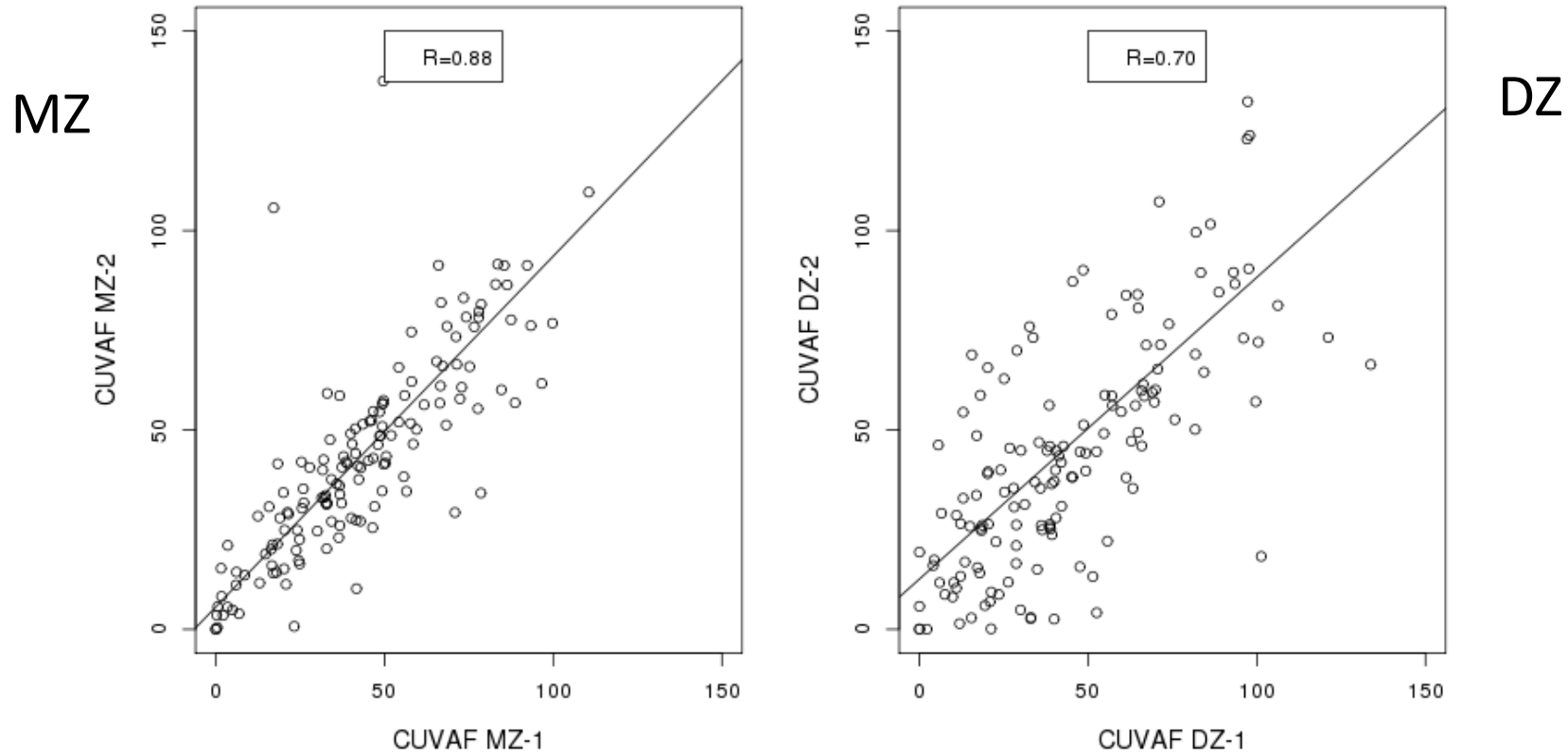
CUVAF



Ethnicity  Australian Asians  Australian Caucasians  Overseas Asian Medical Students



Genetic and environmental factors in conjunctival UV autofluorescence.
Yazar S et al. JAMA Ophthalmol. 2015;133:406-12.



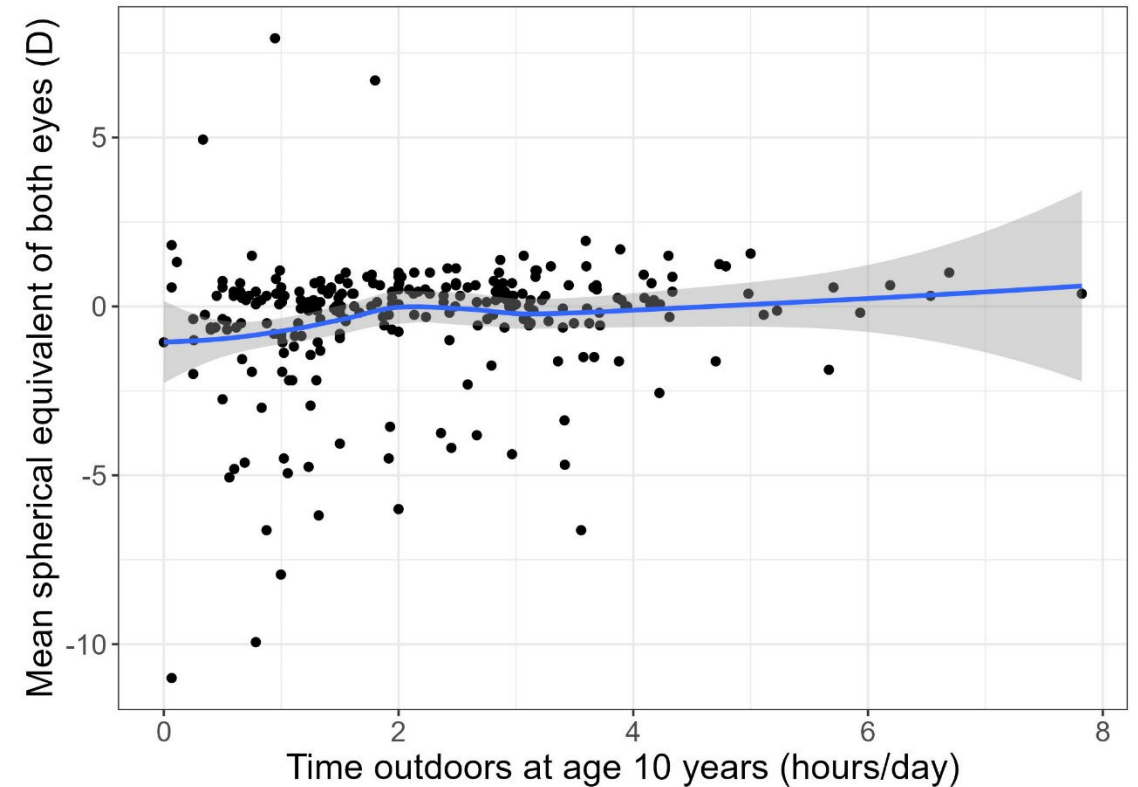
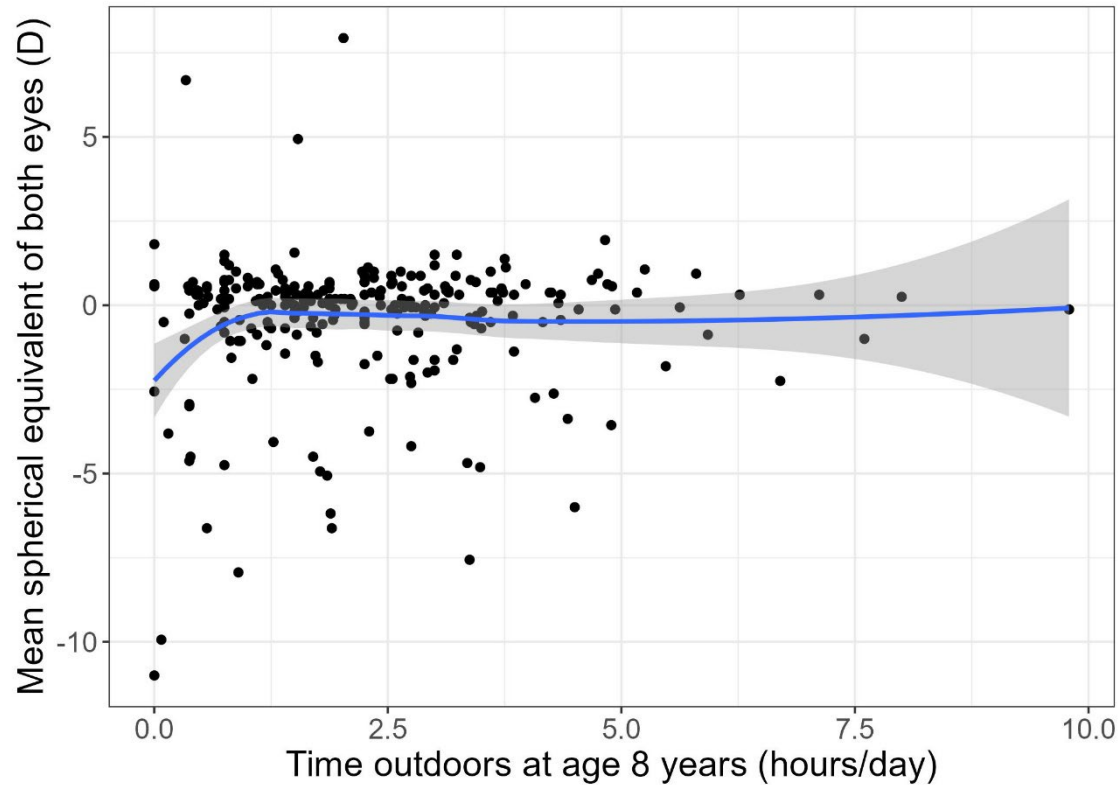
Additive genetic = **37%** (95% CI, 22%-50%) of the variation in CUVAF
Common environment = **50%** (95% CI, 29%-71%)

Effect of latitude in distribution of CUVAF

- Brisbane twins (closer to the equator @27°S)
= 45.2mm²
- Tasmania twins (southern regions @42° S)
= 28.7 mm² (p<0.001)
- after adjusting for age and sex

Age and amount of time outdoors that protects

Prospective data from Kidskin study and adult refraction



Changes in Refractive Error During Young Adulthood: The Effects of Longitudinal Screen Time, Ocular Sun Exposure, and Genetic Predisposition

Samantha Sze-Yee Lee¹, Gareth Lingham², Carol A. Wang^{3,4},
Santiago Diaz Torres^{5,6}, Craig E. Pennell^{3,4,7}, Pirro G. Hysi^{8,9},
Christopher J. Hammond^{8,9}, Puya Gharahkhani^{5,6,10}, Rosie Clark¹¹,
Jeremy A. Guggenheim¹¹ and David A. Mackey^{1,12,13}

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

²Centre for Eye Research Ireland, School of Physics, Clinical and Optometric Sciences, Technological University Dublin, Dublin, Ireland

³School of Medicine and Public Health, College of Health, Medicine and Wellbeing, The University of Newcastle, Callaghan, New South Wales, Australia

⁴Hunter Medical Research Institute, New Lambton Heights, New South Wales, Australia

⁵QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

⁶Faculty of Medicine, The University of Queensland, Brisbane, Queensland, Australia

⁷John Hunter Hospital, Department of Obstetrics and Gynaecology, Newcastle, New South Wales, Australia

⁸King's College London, Section of Ophthalmology, School of Life Course Sciences, London, United Kingdom

⁹King's College London, Department of Twin Research and Genetic Epidemiology, London, United Kingdom

¹⁰School of Biomedical Sciences, Queensland University of Technology, Brisbane, Queensland, Australia

¹¹School of Optometry & Vision Sciences, Cardiff University, Cardiff, United Kingdom

¹²Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, East Melbourne, Victoria, Australia

¹³School of Medicine, Menzies Research Institute Tasmania, University of Tasmania, Hobart, Tasmania, Australia

Correspondence: Samantha S. Y. Lee, Lions Eye Institute, 2 Verdun St., Nedlands, Western Australia 6009, Australia; samantha.sy.lee29@gmail.com.

Received: June 2, 2023

Accepted: October 23, 2023

Published: November 20, 2023

Citation: Lee SSY, Lingham G, Wang CA, et al. Changes in refractive error during young adulthood: The effects of longitudinal screen time, ocular sun exposure, and genetic predisposition. *Invest Ophthalmol Vis Sci.* 2023;64(14):28. <https://doi.org/10.1167/iov.64.14.28>

PURPOSE. Changes in refractive error during young adulthood is common yet risk factors at this age are largely unexplored. This study explored risk factors for these changes, including gene-environmental interactions.

METHODS. Spherical equivalent refraction (SER) and axial length (AL) for 624 community-based adults were measured at 20 (baseline) and 28 years old. Participants were genotyped and their polygenic scores (PGS) for refractive error calculated. Self-reported screen time (computer, television, and mobile devices) from 20 to 28 years old were collected prospectively and longitudinal trajectories were generated. Past sun exposure was quantified using conjunctival ultraviolet autofluorescence (CUVAF) area.

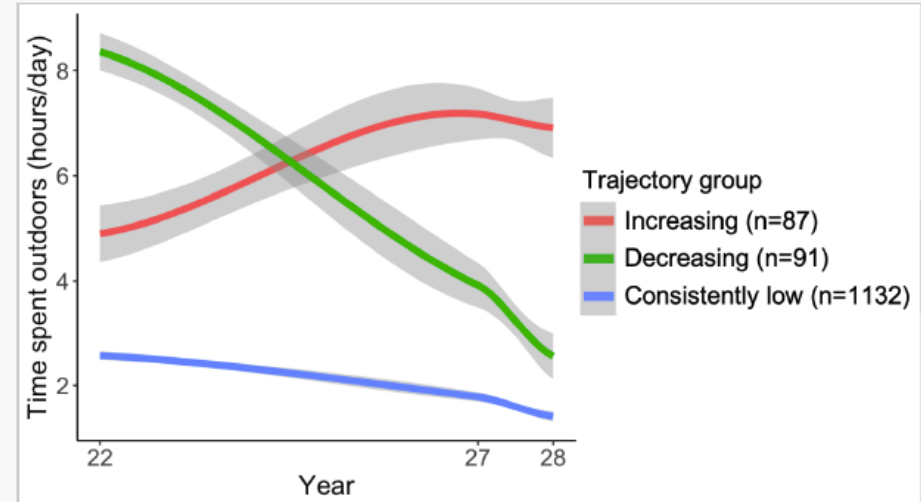
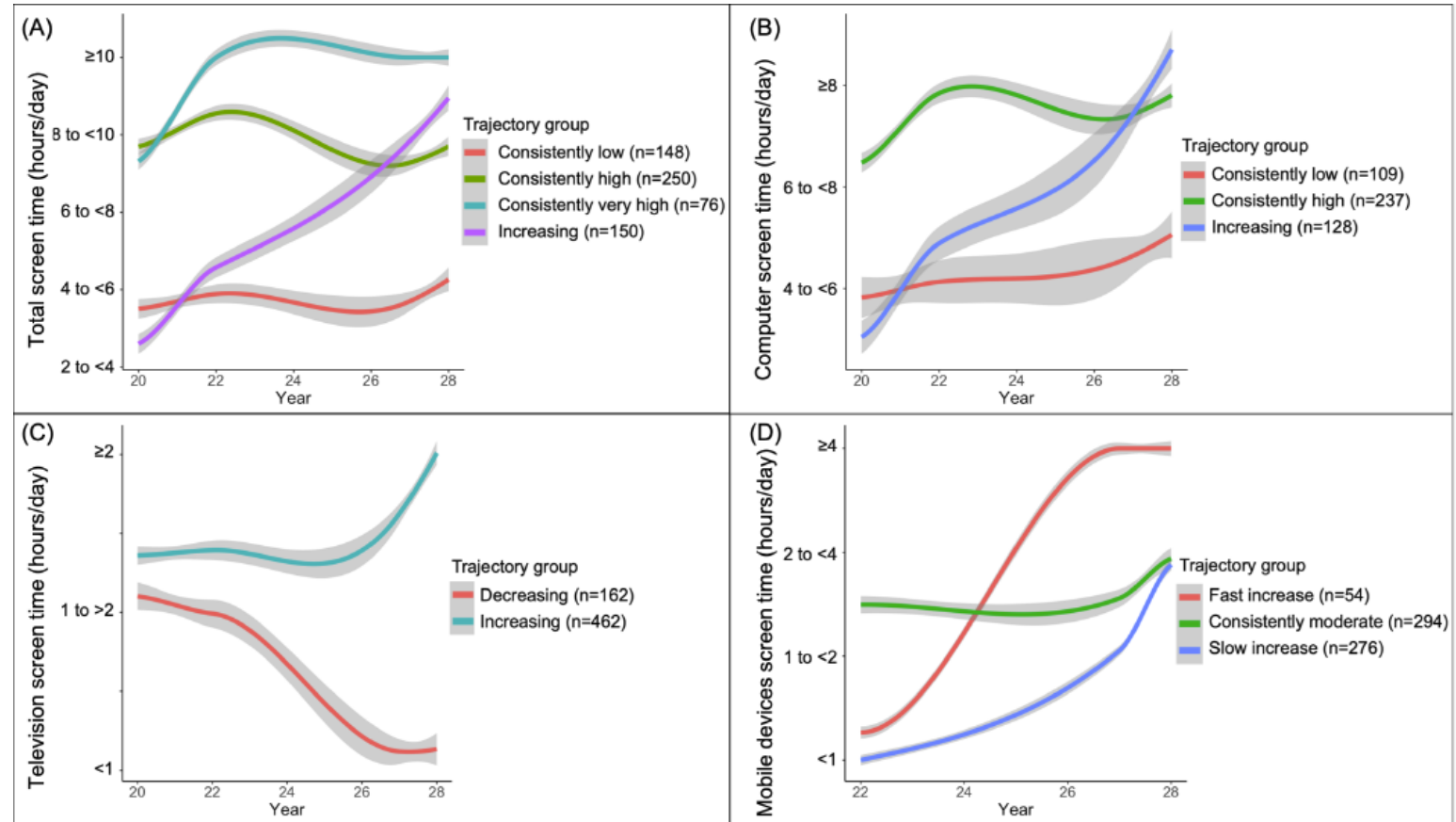
RESULTS. Median change in SER and AL were -0.023 diopters (D)/year (interquartile range [IQR] = -0.062 to -0.008) and $+0.01$ mm/year (IQR = 0.000 to 0.026), respectively. Sex, baseline myopia, parental myopia, screen time, CUVAF, and PGS were significantly associated with myopic shift. Collectively, these factors accounted for approximately 20% of the variance in refractive error change, with screen time, CUVAF, and PGS each explaining approximately 1% of the variance. Four trajectories for total screen time were found: "consistently low" ($n = 148$), "consistently high" ($n = 250$), "consistently very high" ($n = 76$), and "increasing" ($n = 150$). Myopic shift was faster in those with "consistently high" or "consistently very high" screen time compared to "consistently-low" ($P \leq 0.031$). For each z-score increase in PGS, changes in SER and AL increased by -0.005 D/year and 0.002 mm/year ($P \leq 0.045$). Of the three types of screen time, only computer time was associated with myopic shift ($P \leq 0.040$). There was no two- or three-way interaction effect between PGS, CUVAF, or screen time ($P \geq 0.26$).

CONCLUSIONS. Higher total or computer screen time, less sun exposure, and genetic predisposition are each independently associated with greater myopic shifts during young adulthood. Given that these factors explained only a small amount of the variance, there are likely other factors driving refractive error change during young adulthood.

Keywords: genetics, myopia, polygenic score (PGS), screen time, the Raine Study, young adults

Near Work Screen time and Myopia

- A) Total
- B) Computer
- C) Television
- D) Mobile device



Four trajectories for total screen time were found in young adults 20-28 years:

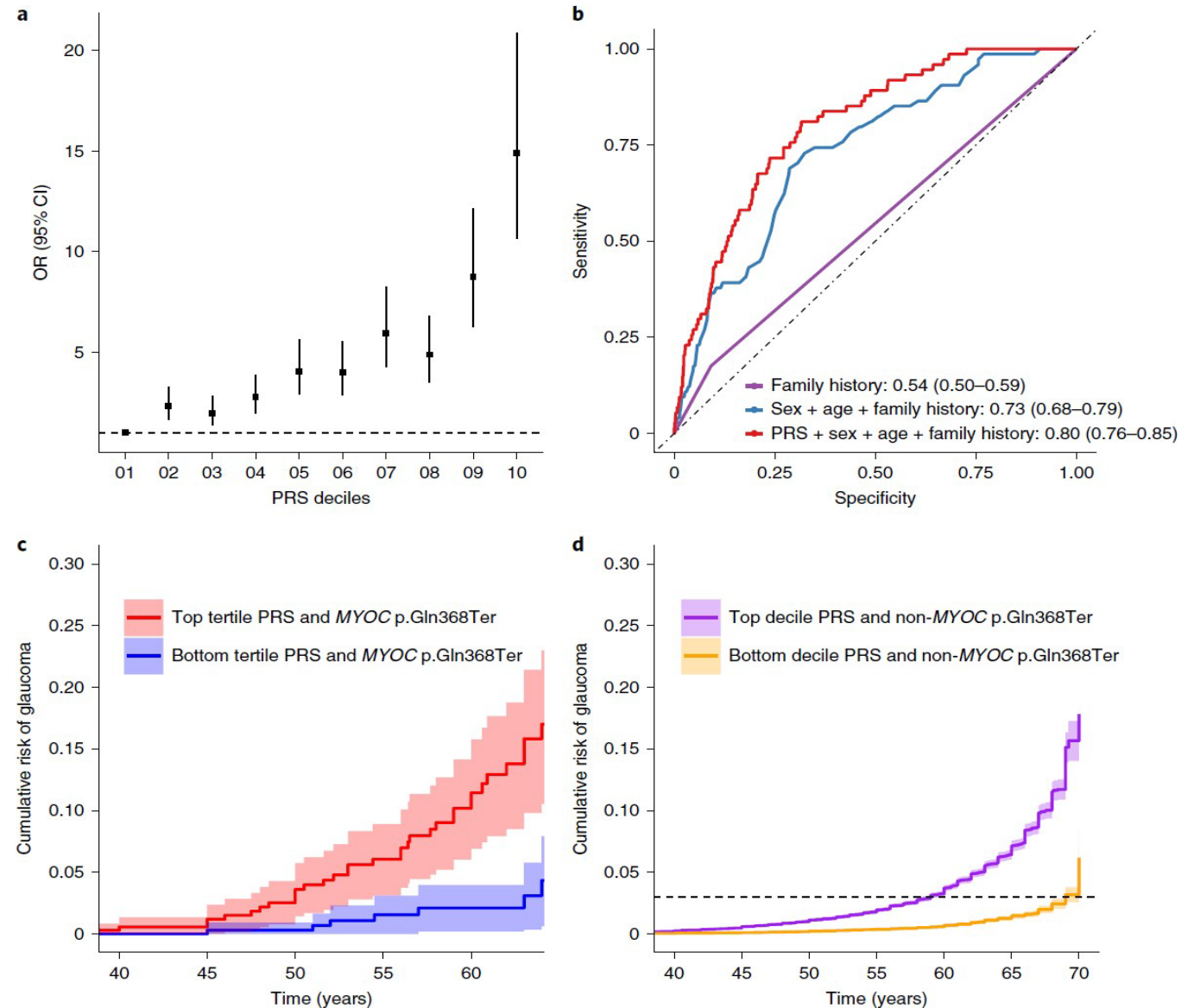
- “consistently-low” (n=148)
 - “consistently-high” (n=250)
 - “consistently-very high” (n=76)
 - “increasing” (n=150)
-
- Myopia progression was faster in those with “consistently-high” or “consistently-very-high” screen time compared to “consistently-low” ($p \leq 0.031$)
 - Only computer time was associated with myopia progression ($p \leq 0.040$)

Applying Polygenic Risk Scores

Already used in

- Primary Open Angle Glaucoma

- Craig et al 2020



A new polygenic score for refractive error improves detection of children at risk of high myopia but not the prediction of those at risk of myopic macular degeneration



Rosie Clark,^a Samantha Sze-Yee Lee,^b Ran Du,^{c,d} Yining Wang,^e Sander C. M. Knapik,^{f,g} Jason Chang,^{h,i} Yu Huang,^j Michael L. Hunter,^k Chen Jiang,^l J. Willem L. Tideman,^{m,n} Ronald B. Melle,^o Caroline C. W. Klaver,^{p,q,r,s} David A. Mackey,^{t,u,v} Cathy Williams,^w Hélène Choquet,^x Kyoko Ohno-Matsui,^{y,z} and Jeremy A. Guggenheim,^{aa,*} on behalf of the CREAM Consortium and on behalf of the UK Biobank Eye and Vision Consortium

^aSchool of Optometry & Vision Sciences, Cardiff University, Maindy Road, Cardiff, CF24 4HQ, UK

^bUniversity of Western Australia, Centre for Ophthalmology and Visual Science (incorporating the Lions Eye Institute), Perth, Western Australia, Australia

^cDepartment of Ophthalmology and Visual Science, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo, 1138510, Japan

^dDepartment of Ophthalmology, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, 100045, China

^eDepartment of Ophthalmology, Erasmus University Medical Center, Rotterdam, the Netherlands

^fDepartment of Epidemiology, Erasmus University Medical Center, Rotterdam, the Netherlands

^gGeneration R Study Group, Erasmus University Medical Center, Rotterdam, the Netherlands

^hDepartment of Optometry, School of Allied Health, University of Western Australia, Perth, Australia

ⁱDepartment of Ophthalmology, Guangdong Eye Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, 510080, China

^jBusselton Health Study Centre, Busselton Population Medical Research Institute, Busselton, Western Australia

^kSchool of Population and Global Health, University of Western Australia, Perth, Western Australia

^lDivision of Research, Kaiser Permanente Northern California, Oakland, CA, USA

^mDepartment of Ophthalmology, Martini Hospital, Groningen, the Netherlands

ⁿDepartment of Ophthalmology Kaiser Permanente Northern California, Redwood City, CA, USA

^oInstitute of Molecular and Clinical Ophthalmology, Basel, Switzerland

^pDepartment of Ophthalmology, Radboud University Medical Center, Nijmegen, the Netherlands

^qCentre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, East Melbourne, Victoria, Australia

^rSchool of Medicine, Menzies Research Institute Tasmania, University of Tasmania, Hobart, Tasmania, Australia

^sCentre for Academic Child Health, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, BS81NU, UK

Summary

Background High myopia (HM), defined as a spherical equivalent refractive error (SER) ≤ -6.00 diopters (D), is a leading cause of sight impairment, through myopic macular degeneration (MMD). We aimed to derive an improved polygenic score (PGS) for predicting children at risk of HM and to test if a PGS is predictive of MMD after accounting for SER.

Methods The PGS was derived from genome-wide association studies in participants of UK Biobank, CREAM Consortium, and Genetic Epidemiology Research on Adult Health and Aging. MMD severity was quantified by a deep learning algorithm. Prediction of HM was quantified as the area under the receiver operating curve (AUROC). Prediction of severe MMD was assessed by logistic regression.

Findings In independent samples of European, African, South Asian and East Asian ancestry, the PGS explained 19% (95% confidence interval 17–21%), 2% (1–3%), 8% (7–10%) and 6% (3–9%) of the variation in SER, respectively. The AUROC for HM in these samples was 0.78 (0.75–0.81), 0.58 (0.53–0.64), 0.71 (0.69–0.74) and 0.67 (0.62–0.72), respectively. The PGS was not associated with the risk of MMD after accounting for SER: OR = 1.07 (0.92–1.24).

Interpretation Performance of the PGS approached the level required for clinical utility in Europeans but not in other ancestries. A PGS for refractive error was not predictive of MMD risk once SER was accounted for.

*Corresponding author. School of Optometry & Vision Sciences, Cardiff University, Cardiff, UK.

Email address: guggenheimj1@cardiff.ac.uk (J.A. Guggenheim).

[†]Joint senior authors.

Polygenic Risk Scores (PRS)

- Performance of the PRS approached the level required for clinical utility in Europeans but not in other ancestries
- A PRS for refractive error was not predictive of Myopic Maculopathy risk once spherical equivalent was accounted for

eBioMedicine
2023;9: 104551
Published Online 11 April
2023
<https://doi.org/10.1016/j.ebiom.2023.104551>

Prevention is Better than Cure



Time Outdoors in Reducing Myopia

A School-Based Cluster Randomized Trial with Objective Monitoring of Outdoor Time and Light Intensity

Xiangui He, PhD,^{1,2} Padmaja Sankaridurg, PhD,^{3,4} Jingjing Wang, PhD,¹ Jun Chen, PhD,¹ Thomas Naduvilath, PhD,^{3,4} Mingguang He, PhD,^{5,6} Zhuoting Zhu, PhD,⁵ Wayne Li, MD,^{3,4} Ian G. Morgan, MD,⁷ Shuyi Xiong, PhD,² Jianfeng Zhu, MD,¹ Haidong Zou, MD,^{1,2} Kathryn A. Rose, MD,⁸ Bo Zhang, MS,¹ Rebecca Weng, GD,^{3,4} Serge Resnikoff, MD,^{3,4} Xun Xu, MD,^{1,2}

Purpose: To evaluate the efficacy of time outdoors per school day over 2 years on myopia onset and shift. **Design:** A prospective, cluster-randomized, examiner-masked, 3-arm trial. **Participants:** A total of 6295 students aged 6 to 9 years from 24 primary schools in Shanghai, China, stratified and randomized by school in a 1:1:1 ratio to control (n = 2037), test I (n = 2329), or test II (n = 1929) group.

Methods: An additional 40 or 80 minutes of outdoor time was allocated to each school day for test I and II groups. Children in the control group continued their habitual outdoor time. Objective monitoring of outdoor and indoor time and light intensity each day was measured with a wrist-worn wearable during the second-year follow-up.

Main Outcome Measures: The 2-year cumulative incidence of myopia (defined as cycloplegic spherical equivalent [SE] of ≤ -0.5 diopters [D] in the right eye) among the students without myopia at baseline and changes in SE and axial length (AL) after 2 years.

Results: The unadjusted 2-year cumulative incidence of myopia was 24.9%, 20.6%, and 23.8% for control, test I, and II groups, respectively. The adjusted incidence decreased by 16% (incidence risk ratio [IRR], 0.84; 95% confidence interval [CI], 0.72–0.99; $P = 0.035$) in test I and 11% (IRR = 0.89; 95% CI, 0.79–0.99; $P = 0.041$) in test II when compared with the control group. The test groups showed less myopic shift and axial elongation compared with the control group (test I: -0.84 D and 0.55 mm, test II: -0.91 D and 0.57 mm, control: -1.04 D and 0.65 mm). There was no significant difference in the adjusted incidence of myopia and myopic shift between the 2 test groups. The test groups had similar outdoor time and light intensity (test I: 127 ± 30 minutes/day and 3557 ± 970 lux/minute; test II: 127 ± 26 minutes/day and 3662 ± 803 lux/minute) but significantly more outdoor time and higher light intensity compared with the control group (106 ± 27 minutes/day and 2984 ± 806 lux/minute). Daily outdoor time of 120 to 150 minutes at 5000 lux/minutes or cumulative outdoor light intensity of 600 000 to 750 000 lux significantly reduced the IRR by 15%–24%.

Conclusions: Increasing outdoor time reduced the risk of myopia onset and myopic shifts, especially in nonmyopic children. The protective effect of outdoor time was related to the duration of exposure and light intensity. The dose–response effect between test I and test II was not observed probably because of insufficient outdoor time achieved in the test groups, which suggests that proper monitoring on the compliance on outdoor intervention is critical if one wants to see the protective effect. *Ophthalmology* 2022;129:1245–1254 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Myopia, a condition affecting approximately one-quarter of the world's population, has been projected to double in prevalence by the year 2050.¹ The health and economic burden both to the individual and the society is substantial.^{2,3} In many East Asian countries including China, there is a trend of an early onset of myopia in childhood fueled in part by educational demands, and more than half of school-aged students are affected, with approximately 80% myopic by the end of schooling.^{4–7} Myopia shift in early years is more rapid and naturally

longer,^{8,9} thus, an early onset increases the risk of high myopia and sight-threatening complications in later life such as myopic macular degeneration (MMD).¹⁰ It has been projected that MMD could lead to 55.7 million people experiencing irreversible visual impairment and blindness globally in 2050.¹¹ Therefore, it is of importance to postpone myopia onset and slow myopia progression.

Prior evidence from controlled trials and systematic reviews has demonstrated the effectiveness of increased outdoor time in reducing the risk of myopia onset.^{12–15}



Myopia Prevention and Outdoor Light Intensity in a School-Based Cluster Randomized Trial

Pei-Chang Wu, MD, PhD,¹ Chueh-Tan Chen, MS,¹ Ken-Kuo Lin, MD,² Chi-Chin Sun, MD, PhD,³ Chien-Neng Kuo, MD,⁴ Hsiu-Mei Huang, MD,¹ Yi-Chieh Poon, MD,¹ Meng-Ling Yang, MD,² Chau-Yin Chen, MD,⁴ Jou-Chen Huang, MD,⁴ Pei-Chen Wu, MD,⁴ I-Hui Yang, MD,¹ Hui-Ju Yu, MD,¹ Po-Chiang Fang, MD,¹ Chia-Ling Tsai, DDS,⁵ Shu-Ti Chiou, PhD,^{6,7,8,*} Yi-Hsin Yang, PhD^{9,*}

Purpose: To investigate the effectiveness of a school-based program promoting outdoor activities in Taiwan for myopia prevention and to identify protective light intensities.

Design: Multi-area, cluster-randomized intervention controlled trial.

Participants: A total 693 grade 1 schoolchildren in 16 schools participated. Two hundred sixty-seven schoolchildren were in the intervention group and 426 were in the control group.

Methods: Initially, 24 schools were randomized into the intervention and control groups, but 5 and 3 schools in the intervention and control groups, respectively, withdrew before enrollment. A school-based Recess Outside Classroom Trial was implemented in the intervention group, in which schoolchildren were encouraged to go outdoors for up to 11 hours weekly. Data collection included eye examinations, cycloplegic refraction, noncontact axial length measurements, light meter recorders, diary logs, and questionnaires.

Main Outcome Measures: Change in spherical equivalent and axial length after 1 year and the intensity and duration of outdoor light exposures.

Results: The intervention group showed significantly less myopic shift and axial elongation compared with the control group (0.35 diopter [D] vs. 0.47 D; 0.28 vs. 0.33 mm; $P = 0.002$ and $P = 0.003$) and a 54% lower risk of rapid myopia progression (odds ratio, 0.46; 95% confidence interval [CI], 0.28–0.77; $P = 0.003$). The myopic protective effects were significant in both nonmyopic and myopic children compared with controls. Regarding spending outdoor time of at least 11 hours weekly with exposure to 1000 lux or more of light, the intervention group had significantly more participants compared with the control group (49.79% vs. 22.73%; $P < 0.001$). Schoolchildren with longer outdoor time in school (≥ 200 minutes) showed significantly less myopic shift (measured by light meters; ≥ 1000 lux: 0.14 D; 95% CI, 0.02–0.27; $P = 0.02$; ≥ 3000 lux: 0.16 D; 95% CI, 0.002–0.32; $P = 0.048$).

Conclusions: The school-based outdoor promotion program effectively reduced the myopia change in both nonmyopic and myopic children. Outdoor activities with strong sunlight exposure may not be necessary for myopia prevention. Relatively lower outdoor light intensity activity with longer time outdoors, such as in hallways or under trees, also can be considered. *Ophthalmology* 2018;125:1239–1250 © 2018 by the American Academy of Ophthalmology



Supplemental material available at www.aaojournal.org.

The increasing prevalence of myopia has become an important public health issue in recent decades.¹ In East Asia, myopia is found to progress rapidly, by approximately -1 diopter (D) per year in schoolchildren; up to 24% of young adults are highly myopic.² The prevalence of myopia is 20% to 30% for 6- to 7-year-old children and is as high as 84% for high school students in Taiwan.³ In contrast, a much lower prevalence of 1.6% to 1.9% for myopia was reported in cities of mainland China for children of this age.⁴ One of the reasons that a lower prevalence was reported in China may be associated with more rigorous cycloplegia and exclusion of children with

incomplete cycloplegia.⁵ However, future studies are required to determine the optimal regimen to use for cycloplegia in East Asian children of this age. In general, as soon as myopia sets in for young children, it will progress until the end of adolescence.^{6–7} Early myopia onset generally results in fast and longer duration for myopia progression and, consequently, a higher risk of becoming highly myopic later in life. High myopia (more than -5 D) can result in cataracts, glaucoma, retinal detachments, choroid neovascularization, macular degeneration, and blindness.^{8–11} Currently, myopia maculopathy is the leading cause of blindness in Taiwan, Japan,

Research

JAMA | Original Investigation

Effect of Low-Concentration Atropine Eyedrops vs Placebo on Myopia Incidence in Children The LAMP2 Randomized Clinical Trial

Jason C. Yam, MPH, Xiu Juan Zhang, PhD, Yuzhou Zhang, PhD, Benjamin H. K. Yip, PhD, Fangyao Tang, PhD, Emily S. Wong, MBChB, Christine H. T. Bui, PhD, Ka Wai Kam, MSc, Mandy P. H. Ng, MSc, Simon T. Ko, MBBS, Wilson W.K. Yip, MBChB, Alvin L. Young, MMedSc, Clement C. Tham, BM, BCh, Li Jia Chen, PhD, Chi Pui Pang, DPhil

IMPORTANCE: Early onset of myopia is associated with high myopia later in life, and myopia is irreversible once developed.

OBJECTIVE: To evaluate the efficacy of low-concentration atropine eyedrops at 0.05% and 0.01% concentration for delaying the onset of myopia.

DESIGN, SETTING, AND PARTICIPANTS: This randomized, placebo-controlled, double-masked trial conducted at the Chinese University of Hong Kong Eye Centre enrolled 474 nonmyopic children aged 4 through 9 years with cycloplegic spherical equivalent between $+1.00$ D to 0.00 D and astigmatism less than -1.00 D. The first recruited participant started treatment on July 11, 2017, and the last participant was enrolled on June 4, 2020; the date of the final follow-up session was June 4, 2022.

INTERVENTIONS: Participants were assigned at random to the 0.05% atropine (n = 160), 0.01% atropine (n = 159), and placebo (n = 155) groups and had eyedrops applied once nightly in both eyes over 2 years.

MAIN OUTCOMES AND MEASURES: The primary outcomes were the 2-year cumulative incidence rate of myopia (cycloplegic spherical equivalent of at least -0.50 D in either eye) and the percentage of participants with fast myopic shift (spherical equivalent myopic shift of at least 1.00 D).

RESULTS: Of the 474 randomized patients (mean age, 6.8 years; 50% female), 353 (74.5%) completed the trial. The 2-year cumulative incidence of myopia in the 0.05% atropine, 0.01% atropine, and placebo groups were 28.4% (33/116), 45.9% (56/122), and 53.0% (61/115), respectively, and the percentages of participants with fast myopic shift at 2 years were 25.0%, 45.1%, and 53.9%. Compared with the placebo group, the 0.05% atropine group had significantly lower 2-year cumulative myopia incidence (difference, 24.6% [95% CI, 12.0%–36.4%]) and percentage of patients with fast myopic shift (difference, 28.9% [95% CI, 16.5%–40.5%]). Compared with the 0.01% atropine group, the 0.05% atropine group had significantly lower 2-year cumulative myopia incidence (difference, 17.5% [95% CI, 5.2%–29.2%]) and percentage of patients with fast myopic shift (difference, 20.1% [95% CI, 8.0%–31.6%]). The 0.01% atropine and placebo groups were not significantly different in 2-year cumulative myopia incidence or percentage of patients with fast myopic shift. Photophobia was the most common adverse event and was reported by 12.9% of participants in the 0.05% atropine group, 18.9% in the 0.01% atropine group, and 12.2% in the placebo group in the second year.

CONCLUSIONS AND RELEVANCE: Among children aged 4 to 9 years without myopia, nightly use of 0.05% atropine eyedrops compared with placebo resulted in a significantly lower incidence of myopia and lower percentage of participants with fast myopic shift at 2 years. There was no significant difference between 0.01% atropine and placebo. Further research is needed to replicate the findings, to understand whether this represents a delay or prevention of myopia, and to assess longer-term safety.

TRIAL REGISTRATION: Chinese Clinical Trial Registry: ChiCTR18PR15006883

JAMA. 2023;329(6):472–481. doi:10.1001/jama.2022.24162
Corrected on April 4, 2023.

Visual Abstract
Editorial page 465
Supplemental content
Related article at
jamaophth.com

Author Affiliations: Author affiliations are listed at the end of this article.
Corresponding Author: Jason C. Yam, MPH, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong Eye Hospital, 147K Argyle St, Kowloon, Hong Kong (yamcheuking@cuhk.edu.hk).

We need to identify Pre-Myopic children to ensure they are getting treatment

- Combine the Polygenic Risk Score with
 - Pre-myopia (between $\leq +0.75$ dioptres and > -0.50 diopters)
 - Family History
 - At risk behaviors (indoors, near work, intense education)
 - Axial Length Trajectory

Distribution of Axial Length in Australians of Different Age Groups, Ethnicities, and Refractive Errors

Vinay Kumar Nilagiri¹, Samantha Sze-Yee Lee¹, Gareth Lingham^{1,3}, Jason Charnig^{1,2}, Seyhan Yazar⁴, Alex W. Hewitt^{5,7}, Lyn R. Griffiths⁶, Paul G. Sanfilippo⁷, Tzu-Hsun Tsai⁸, and David A. Mackey^{1,5}

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

² Department of Optometry, School of Allied Health, University of Western Australia, Perth, Western Australia, Australia

³ Centre for Eye Research Ireland, School of Physics, Clinical and Optometric Sciences, Technological University Dublin, Dublin, Ireland

⁴ Garvan-Weizmann Centre for Cell

⁵ School of Medicine, Menzies Rese

⁶ Genomics Research Centre, Centre

⁷ Technology, Queensland, Australia

⁸ Centre for Eye Research Australia, I

Melbourne, Victoria, Australia

⁸ Department of Ophthalmology, Ni

Correspondence: David A. Mackey, Lions Eye Institute, 2 Verdun St, Nedlands, WA 6009, Australia. e-mail: david.mackey@lei.org.au

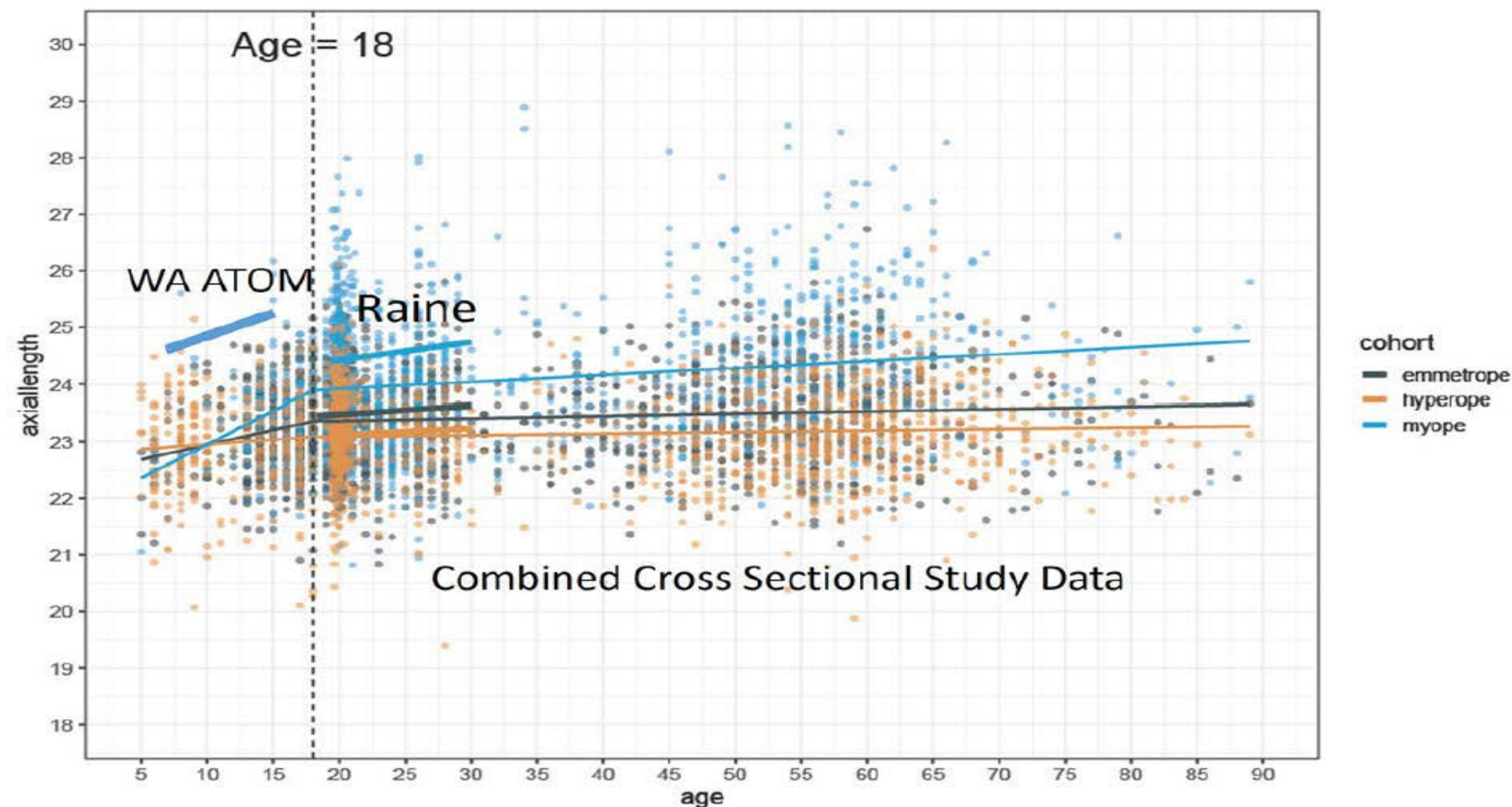
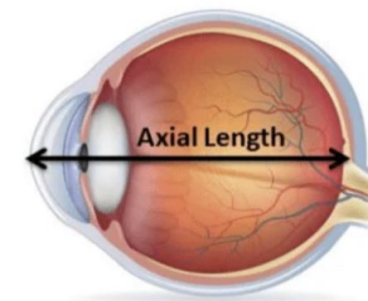
Received: March 22, 2023

Accepted: July 6, 2023

Published: August 18, 2023

Keywords: age; axial length (AL); biometry; emmetropes; hyperopes; myopes; refraction

Citation: Nilagiri VK, Lee SSY, Lingham G, Charnig J, Yazar S, Hewitt AW, Griffiths LR, Sanfilippo PG, Tsai TH, Mackey DA. Distribution of axial length in Australians of different age groups, ethnicities, and refractive errors. *Transl Vis Sci Technol.* 2023;12(8):14. <https://doi.org/10.1167/tvst.12.8.14>



Normative data for axial elongation in Asian children

Thomas Naduvilath^{1,2} | Xiangui He³ | Xun Xu³ | Padmaja Sankaridurg^{1,2}¹Brien Holden Vision Institute (BHVI), Sydney, New South Wales, Australia²School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, Australia³Shanghai Eye Disease Prevention and Treatment Centre, Shanghai Eye Hospital, Shanghai Vision Health Centre & Shanghai Children Myopia Institute, Shanghai, China

Correspondence

Thomas Naduvilath, Brien Holden Vision Institute (BHVI), Sydney, New South Wales, Australia.
Email: tjohn@bhvi.org

Funding information

Excellent Discipline Leader Cultivation Program of Shanghai Three Year Action Plan on Strengthening Public Health System Construction. Grant/Award Number: GWV-10.2-XD09; 3-year Action Program of Public Health (2020–2022). Grant/Award Number: GWV-9.1; National Key R&D Program, Grant/Award Number: 2019YFC0840607; National Science and Technology Major Project of China, Grant/Award Number: 2017ZX09304010; Brien Holden Vision Institute

Abstract

Aim: To determine the influence of refractive error (RE), age, gender and parental myopia on axial elongation in Chinese children and to develop normative data for this population.**Methods:** This is a retrospective analysis of eight longitudinal studies conducted in China between 2007 and 2017. Data of 4701 participants aged 6–16 years with spherical equivalent from +6 to −6D contributed to one, two or three annualised progression data resulting in a dataset of 11,262 eyes of 26.6%, 14.8% and 58.6% myopes, emmetropes and hyperopes, respectively. Longitudinal data included axial length and cycloplegic spherical equivalent RE. Axial elongation was log-transformed to develop an exponential model with generalised estimating equations including main effects and interactions. Model-based estimates and their confidence intervals (CIs) are reported.**Results:** Annual axial elongation decreased significantly with increasing age, with the rate of decrease specific to the RE group. Axial elongation in myopes was higher than in emmetropes and hyperopes but these differences reduced with age (0.58, 0.45 and 0.27 mm/year at 6 years and 0.13, 0.06 and 0.05 mm/year at 15 years for myopes, emmetropes and hyperopes, respectively). The rate of elongation in incident myopes was similar to that in myopes at baseline (0.33 vs. 0.34 mm/year at 10.5 years; $p=0.32$), while it was significantly lower in non-myopes (0.20 mm/year at 10.5 years, $p<0.001$). Axial elongation was greater in females than in males and in those with both parents myopic compared with one or no myopic parent, with larger differences in non-myopes than in myopes ($p<0.01$).**Conclusions:** Axial elongation varied with age, RE, gender and parental myopia. Estimated normative data with CIs could serve as a virtual control group.

KEYWORDS

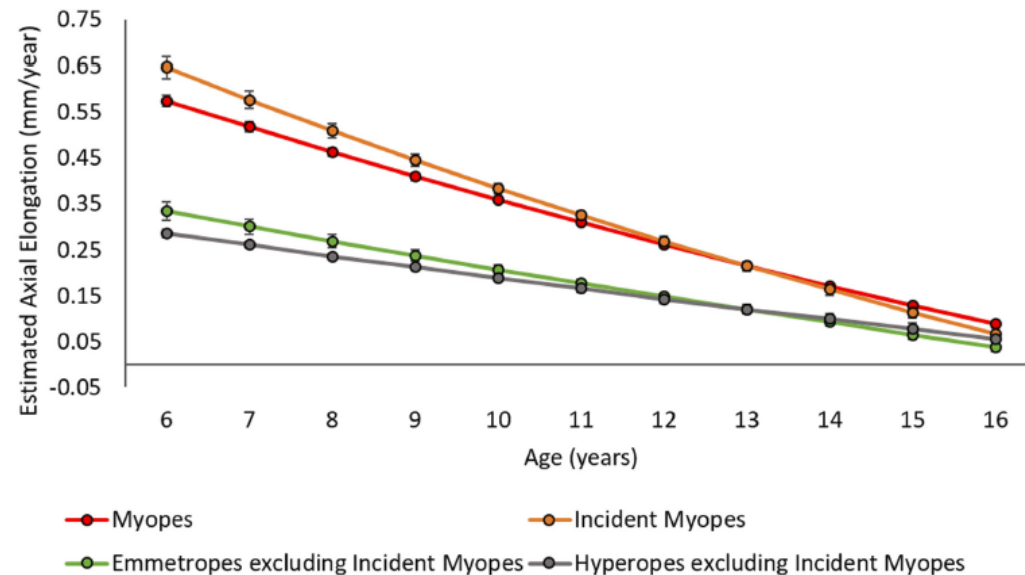
Asian, axial length, children, myopia, progression

INTRODUCTION

While myopia continues to increase globally to pandemic proportions, monitoring the progression of refractive error (RE) is key to identifying individuals at risk of myopia and high myopia.^{1–3} Although refractive measurements are the common approach to diagnosing/monitoring the progression of myopia, in recent years there is increasing use of axial length measurements. This is mostly due to recent

advances in technology affording accurate and reliable measurements of axial length in a rapid and non-invasive manner.⁴ These provide several advantages when examining young children, especially in environments where a cycloplegic assessment is not feasible and in myopia management technologies such as orthokeratology, where progression cannot be assessed with refractive measurements.⁵ Additionally, changes in axial length were found to correlate well with RE.^{6,7} Thus, it is recommended that axial

AL change in greater in children developing myopia



3 Model-based estimates of annualised axial elongation (mm/year) by age and refractive error groups. Error bars are 99% confidence

Presented as a poster at the International Myopia Conference, Rotterdam, The Netherlands, September 4–7, 2022.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](#) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2023 The Authors. *Ophthalmic and Physiological Optics* published by John Wiley & Sons Ltd on behalf of College of Optometrists.

Two recent US studies

Research

JAMA Ophthalmology | Original Investigation

Efficacy and Safety of 0.01% and 0.02% Atropine for the Treatment of Pediatric Myopia Progression Over 3 Years A Randomized Clinical Trial

Karla Zadnik, OD, PhD; Erica Schulman, OD; Ian Flitcroft, MA, MBBS, DPhil; Jennifer S. Fogt, OD, MS; Louis C. Blumenfeld, MD; Tung M. Fong, PhD; Eric Lang, MD; Houman D. Hemmati, MD, PhD; Simon P. Chandler, PhD; for the CHAMP Trial Group Investigators

IMPORTANCE The global prevalence of myopia is predicted to approach 50% by 2050, increasing the risk of visual impairment later in life. No pharmacologic therapy is approved for treating childhood myopia progression.

OBJECTIVE To assess the safety and efficacy of NVK002 (Vyluma), a novel, preservative-free, 0.01% and 0.02% low-dose atropine formulation for treating myopia progression.

DESIGN, SETTING, AND PARTICIPANTS This was a double-masked, placebo-controlled, parallel-group, randomized phase 3 clinical trial conducted from November 20, 2017, through August 22, 2022, of placebo vs low-dose atropine, 0.01% and 0.02% (2:2:3 ratio). Participants were recruited from 26 clinical sites in North America and 5 countries in Europe. Enrolled participants were 3 to 16 years of age with -0.50 diopter (D) to -6.00 D spherical equivalent refractive error (SER) and no worse than -1.50 D astigmatism.

INTERVENTIONS Once-daily placebo, low-dose atropine, 0.01%, or low-dose atropine, 0.02%, eye drops for 36 months.

MAIN OUTCOMES AND MEASURES The primary, prespecified end point was the proportion of participants' eyes responding to 0.02% atropine vs placebo therapy (<0.50 D myopia progression at 36 months [responder analysis]). Secondary efficacy end points included responder analysis for atropine, 0.01%, and mean change from baseline in SER and axial length at month 36 in a modified intention-to-treat population (mITT; participants 6-10 years of age at baseline). Safety measurements for treated participants (3-16 years of age) were reported.

RESULTS A total of 576 participants were randomly assigned to treatment groups. Of these, 573 participants (99.5%; mean [SD] age, 8.9 [2.0] years; 315 female [54.7%]) received trial treatment (3 participants who were randomized did not receive trial drug) and were included in the safety set. The 489 participants (84.9%) who were 6 to 10 years of age at randomization composed the mITT set. At month 36, compared with placebo, low-dose atropine, 0.02%, did not significantly increase the responder proportion (odds ratio [OR], 1.77; 95% CI, 0.50-6.26; $P = .37$) or slow mean SER progression (least squares mean [LSM] difference, 0.10 D; 95% CI, -0.02 D to 0.22 D; $P = .10$) but did slow mean axial elongation (LSM difference, -0.08 mm; 95% CI, -0.13 mm to -0.02 mm; $P = .005$); however, at month 36, compared with placebo, low-dose atropine, 0.01%, significantly increased the responder proportion (OR, 4.54; 95% CI, 1.15-17.97; $P = .03$), slowed mean SER progression (LSM difference, 0.24 D; 95% CI, 0.11 D-0.37 D; $P < .001$), and slowed axial elongation (LSM difference, -0.13 mm; 95% CI, -0.19 mm to -0.07 mm; $P < .001$). There were no serious ocular adverse events and few serious nonocular events; none was judged as associated with atropine.

CONCLUSIONS AND RELEVANCE This randomized clinical trial found that 0.02% atropine did not significantly increase the proportion of participants' eyes responding to therapy but suggested efficacy for 0.01% atropine across all 3 main end points compared with placebo. The efficacy and safety observed suggest that low-dose atropine may provide a treatment option for childhood myopia progression.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03350620

JAMA Ophthalmol. 2023;141(10):990-999. doi:10.1001/jamaophthalmol.2023.2097
Published online June 1, 2023. Corrected on September 14, 2023.

+ Visual Abstract
+ Supplemental content and Journal Club Slides



Author Affiliations: The Ohio State University College of Optometry, Columbus (Zadnik, Fogt); SUNY College of Optometry, New York (Schulman); Centre for Eye Research, Dublin, Ireland (Flitcroft); Eye Physicians of Central Florida, Maitland (Blumenfeld); Vyluma Inc, Bridgewater, New Jersey (Fong, Lang, Hemmati, Chandler).

Group Information: The members of the CHAMP Trial Group Investigators appear in Supplement 4.

Corresponding Author: Karla Zadnik, OD, PhD, The Ohio State University College of Optometry, 338 W 10th Ave, Columbus, OH 43210 (zadnik.4@osu.edu).

jamaophthalmology.com

Research

JAMA Ophthalmology | Original Investigation

Low-Dose 0.01% Atropine Eye Drops vs Placebo for Myopia Control A Randomized Clinical Trial

Michael X. Repka, MD, MBA; Katherine K. Weise, OD, MBA; Danielle L. Chandler, MSPH; Rui Wu, MS; B. Michele Melia, ScM; Ruth E. Manny, OD, PhD; Lori Ann F. Kehler, OD; Catherine O. Jordan, MD; Aparna Raghuram, OD, PhD; Allison L. Summers, OD, MCR; Katherine A. Lee, MD; David B. Petersen, MD; S. A. Erzurum, MD; Yi Pang, OD, PhD; Phoebe D. Lenhart, MD; Benjamin H. Ticho, MD; Roy W. Beck, MD, PhD; Raymond T. Kraker, MSPH; Jonathan M. Holmes, BM, BCh; Susan A. Cotter, OD, MS; for the Pediatric Eye Disease Investigator Group

IMPORTANCE Controlling myopia progression is of interest worldwide. Low-dose atropine eye drops have slowed progression in children in East Asia.

OBJECTIVE To compare atropine, 0.01%, eye drops with placebo for slowing myopia progression in US children.

DESIGN, SETTING, AND PARTICIPANTS This was a randomized placebo-controlled, double-masked, clinical trial conducted from June 2018 to September 2022. Children aged 5 to 12 years were recruited from 12 community- and institution-based practices in the US. Participating children had low to moderate bilateral myopia (-1.00 diopters [D] to -6.00 D spherical equivalent refractive error [SER]).

INTERVENTION Eligible children were randomly assigned 2:1 to 1 eye drop of atropine, 0.01%, nightly or 1 drop of placebo. Treatment was for 24 months followed by 6 months of observation.

MAIN OUTCOME AND MEASURES Automated cycloplegic refraction was performed by masked examiners. The primary outcome was change in SER (mean of both eyes) from baseline to 24 months (receiving treatment); other outcomes included change in SER from baseline to 30 months (not receiving treatment) and change in axial length at both time points. Differences were calculated as atropine minus placebo.

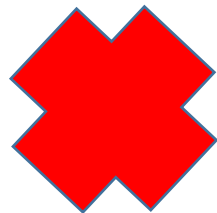
RESULTS A total of 187 children (mean [SD] age, 10.1 [1.8] years; age range, 5.1-12.9 years; 101 female [54%]; 34 Black [18%], 20 East Asian [11%], 30 Hispanic or Latino [16%], 11 multiracial [6%], 6 West/South Asian [3%], 86 White [46%]) were included in the study. A total of 125 children (67%) received atropine, 0.01%, and 62 children (33%) received placebo. Follow-up was completed at 24 months by 119 of 125 children (95%) in the atropine group and 58 of 62 children (94%) in the placebo group. At 30 months, follow-up was completed by 118 of 125 children (94%) in the atropine group and 57 of 62 children (92%) in the placebo group. At the 24-month primary outcome visit, the adjusted mean (95% CI) change in SER from baseline was -0.82 (-0.96 to -0.68) D and -0.80 (-0.98 to -0.62) D in the atropine and placebo groups, respectively (adjusted difference = -0.02 D; 95% CI, -0.19 to $+0.15$ D; $P = .83$). At 30 months (6 months not receiving treatment), the adjusted difference in mean SER change from baseline was -0.04 D (95% CI, -0.25 to $+0.17$ D). Adjusted mean (95% CI) changes in axial length from baseline to 24 months were 0.44 (0.39-0.50) mm and 0.45 (0.37-0.52) mm in the atropine and placebo groups, respectively (adjusted difference = -0.002 mm; 95% CI, -0.106 to 0.102 mm). Adjusted difference in mean axial elongation from baseline to 30 months was $+0.009$ mm (95% CI, -0.115 to 0.134 mm).

CONCLUSIONS AND RELEVANCE In this randomized clinical trial of school-aged children in the US with low to moderate myopia, atropine, 0.01%, eye drops administered nightly when compared with placebo did not slow myopia progression or axial elongation. These results do not support use of atropine, 0.01%, eye drops to slow myopia progression or axial elongation in US children.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03334253

JAMA Ophthalmol. 2023;141(8):756-765. doi:10.1001/jamaophthalmol.2023.2855
Published online July 13, 2023.

+ Visual Abstract
+ Invited Commentary page 766
+ Multimedia
+ Supplemental content



Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the Pediatric Eye Disease Investigator Group appear in Supplement 4.

Corresponding Author: Michael X. Repka, MD, MBA, c/o Jaeb Center for Health Research, 15310 Amberly Dr, Ste 350, Tampa, FL 33647 (mrepka@jhm.edu).

jamaophthalmology.com



3 harmonised low-dose Atropine studies underway



UK/Northern Ireland



Ireland



Western Australia

Clinical science

Low-dose (0.01%) atropine eye-drops to reduce progression of myopia in children: a multicentre placebo-controlled randomised trial in the UK (CHAMP-UK)—study protocol

Augusto Azuara-Blanco ¹, Nicola Logan ², Niall Strang³, Kathryn Saunders⁴, Peter M Allen⁵, Ruth Weir⁶, Paul Doherty⁷, Catherine Adams⁸, Evie Gardner⁹, Ruth Hogg ¹⁰, Margaret McFarland¹¹, Jennifer Preston¹², Rejina Verghis⁹, James J Loughman ¹³, Ian Flitcroft¹⁴, David A Mackey¹⁵, Samantha Sze-Yee Lee ¹⁶, Christopher Hammond ¹⁷, Nathan Congdon ¹⁸,^{19,20,21} Mike Clarke^{1,6}

For numbered affiliations see end of article.

Correspondence to: Professor Augusto Azuara-Blanco, Centre for Public Health, Queen's University Belfast, Belfast BT12 6BA, UK; a.azuara-blanco@qub.ac.uk

Received 26 June 2019
Revised 9 September 2019
Accepted 5 October 2019
Published Online First 25 October 2019

ABSTRACT

Background/Aims: To report the protocol of a trial designed to evaluate the efficacy, safety and mechanism of action of low-dose atropine (0.01%) eye-drops for reducing progression of myopia in UK children.

Methods: Multicentre, double-masked, superiority, placebo-controlled, randomised trial. We will enrol children aged 6–12 years with myopia of ≥ -0.50 dioptres or worse in both eyes.

We will recruit 289 participants with an allocation ratio of 2:1 (193 atropine; 96 placebo) from five centres. Participants will instil one drop in each eye every day for 2 years and attend a research centre every 6 months. The vehicle and preservative will be the same in both study arms.

The primary outcome is SER of both eyes measured by autorefractor under cycloplegia at 2 years (adjusted for baseline). Secondary outcomes include axial length, best corrected distance visual acuity, near visual acuity, reading speed, pupil diameter, accommodation, adverse event rates and allergic reactions, quality of life (EQ-5D-Y) and tolerability at 2 years. Mechanistic evaluations will include: peripheral axial length, peripheral retinal defocus, anterior chamber depth, iris colour, height and weight, activities questionnaire, ciliary body biometry and choroidal thickness. Endpoints from both eyes will be pooled in combined analysis using generalised estimating equations to allow the correlation between eyes within participant. Three years after cessation of treatment, we will also evaluate refractive error and adverse events.

Conclusions: The Childhood Atropine for Myopia Progression in the UK study will be the first randomised trial reporting outcomes of low-dose atropine eye-drops for children with myopia in a UK population.

Trial registration number: ISRCTN99883695, NCT03690089.

INTRODUCTION

In Europe, myopia prevalence has risen dramatically over the last few decades.^{1–4} Myopia appears to be occurring at a younger age, and its severity

has increased by an average of approximately 1 dioptre (D) among European-derived populations in one generation.^{5–7} In the UK, the proportion of myopic children has doubled in the last 30 years.⁸ In the USA, myopia prevalence increased from 25% to 42% in a generation.⁹

In the UK, most people with myopia have normal visual acuity when appropriately corrected, but myopia still has significant public health consequences from a variety of perspectives, educational, financial and psychological, as well as the risks of visual impairment.^{10–12} Myopia is a risk factor for myopic maculopathy, retinal detachment, cataract and glaucoma in adult life.^{13–15} and the risk increases with the degree of myopia. All these conditions are more challenging to treat than myopia itself, and reducing the risk for any of them requires interventions to slow myopia progression and thus decrease a child's severity of myopia in the long term rather than correct it optically with spectacles. Children with myopia also require frequent eye tests and change of spectacles that are funded primarily by taxpayers in the UK. Strategies to control progression of myopia are particularly meaningful in the context of WHO initiatives to eliminate preventable causes of blindness.

Atropine at low concentration has been shown to be safe and effective in slowing myopia progression in children of Chinese ethnicity,^{16,17} but its safety and effectiveness in European-derived populations has not been adequately assessed in a controlled trial. Therefore, the objective of the current study is to evaluate the efficacy, safety and mechanism of action of low-dose atropine (0.01%) in UK children with myopia. This paper describes the protocol of the randomised controlled trial called The Childhood Atropine for Myopia Progression in the UK study (CHAMP-UK).

MATERIALS AND METHODS

This is a multicentre, randomised, double-masked, placebo-controlled, superiority trial, with 2:1 allocation of intervention and control (atropine:placebo).

HRB Open Research

HRB Open Research 2019, 2:15 Last updated: 10 SEP 2019



STUDY PROTOCOL

Myopia Outcome Study of Atropine in Children (MOSAIC): an investigator-led, double-masked, placebo-controlled, randomised clinical trial protocol [version 1; peer review: 2 approved, 1 approved with reservations]

Saoirse McCrann ¹, Ian Flitcroft ², Niall C. Strang³, Kathryn J. Saunders⁴, Nicola S. Logan ⁵, Samantha Sze-Yee Lee ⁶, David A. Mackey ⁶, John S. Butler ⁷, James Loughman ¹

¹Centre for Eye Research Ireland, School of Physics, Clinical and Optometric Sciences, Technological University Dublin, Ireland, Dublin, Ireland

²Children's University Hospital, Dublin, Ireland

³Department of Vision Sciences, Glasgow Caledonian University, Glasgow, UK

⁴School of Biomedical Sciences, University of Ulster, Coleraine, UK

⁵Optometry & Vision Science Research Group, Aston Optometry School, Aston University, Birmingham, UK

⁶Centre for Ophthalmology and Visual Science (incorporating Lions Eye Institute), University of Western Australia, Perth, WA, Australia

⁷School of Mathematical Sciences, Technological University Dublin, Dublin, Ireland

V1 First published: 23 Jul 2019, 2:15 (<https://doi.org/10.12688/hrbopenres.12914.1>)

Latest published: 23 Jul 2019, 2:15 (<https://doi.org/10.12688/hrbopenres.12914.1>)

Abstract

Background: The Myopia Outcome Study of Atropine in Children (MOSAIC) aims to explore the efficacy, safety, acceptability and mechanisms of action of 0.01% unpreserved atropine for myopia control in a European population.

Methods: MOSAIC is an investigator-led, double-masked, placebo-controlled, randomised clinical trial (RCT) investigating the efficacy, safety and mechanisms of action of 0.01% atropine for managing progression of myopia. During Phase 1 of the trial, 250 children aged 6–16 years with progressive myopia instil eye drops once nightly in both eyes from randomisation to month 24. No treatment is given during Phase 2 from month 24 to 36 (washout period) for those participants initially randomised to the intervention arm (n=167), during which any potential rebound effects on cessation of treatment will be monitored. All participants initially assigned to the placebo (n=83) crossover to the intervention arm of the study for Phase 2, and from month 24 to 36, instil 0.01% atropine eye drops in both eyes once nightly. Further treatment and monitoring beyond 36 months is planned (Phase 3) and will be designed dependent on the outcomes of Phase 1.

Results: The primary outcome measure is cycloplegic spherical equivalent refractive error progression at 24 months. Secondary outcome measures include axial length change as well as the rebound, safety and acceptability profile of 0.01% atropine. Additional analyses will include the mechanisms

Open Peer Review

Reviewer Status

	Invited Reviewers		
	1	2	3
version 1 published 23 Jul 2019	 report	 report	 report

1 **Sara McCullough** , University of Ulster, Coleraine, UK

2 **Jason C. Yam** , Chinese University of Hong Kong, Hong Kong, China

3 **Jan Roelof Polling** , Erasmus University Medical Center, Rotterdam, The Netherlands
University of Applied Science, Utrecht, The Netherlands

Any reports and responses or comments on the article can be found at the end of the article.

Received: 16 January 2020 | Revised: 9 February 2020 | Accepted: 16 February 2020
DOI: 10.1111/ceo.13736

ORIGINAL ARTICLE

Clinical & Experimental Ophthalmology  WILEY

Western Australia Atropine for the Treatment of Myopia (WA-ATOM) study: Rationale, methodology and participant baseline characteristics

Samantha S.Y. Lee PhD¹  | David A. Mackey MD FRANZCO^{1,2,3}  | Gareth Lingham MOrth¹  | Julie M. Crewe BSc¹  | Michael D. Richards MD PhD FRCS^{1,4} | Fred K. Chen PhD FRANZCO^{1,5}  | Jason Charng PhD¹ | Fletcher Ng MBBS¹ | Ian Flitcroft MD⁶ | James J. Loughman PhD⁷ | Augusto Azuara-Blanco MD⁸ | Nicola S. Logan PhD⁹ | Christopher J. Hammond MD¹⁰ | Audrey Chia PhD FRANZCO^{11,12} | Tan Tai Truong MPS¹³ | Antony Clark PhD FRANZCO¹

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

²Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Victoria, Australia

³School of Medicine, Menzies Research Institute Tasmania, University of Tasmania, TAS, Australia

⁴Department of Ophthalmology, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

⁵Department of Ophthalmology, Royal Perth Hospital, Perth, Western Australia, Australia

⁶Department of Ophthalmology, Mater Misericordiae University Hospital, Dublin, Ireland

⁷Centre for Eye Research Ireland, School of Physics, Clinical and Optometric Sciences, Technological University Dublin, Dublin, Ireland

⁸School of Medicine Dentistry, and Biomedical Science, Queen's University Belfast, Belfast, Ireland

⁹School of Life & Health Sciences, Aston University, Birmingham, UK

¹⁰Department of Twin Research and Genetic Epidemiology, King's College London, St. Thomas' Hospital, London, UK

¹¹Singapore National Eye Centre, Singapore

¹²Singapore Eye Research Institute, Singapore

¹³Oxford Compounding, North Perth, Western Australia, Australia

Correspondence

Dr Antony Clark, Lions Eye Institute, Centre for Ophthalmology and Visual Science, University of Western Australia, Perth, Western Australia 6009, Australia. Email: antony.clark@lei.org.au

Funding information

Faculty of Health and Medical Sciences, University of Western Australia (Early Career Researcher Small Grant Award); Healy Medical Research Foundation (Healy Research Collaboration Award); Telethon-Perth Children's Hospital Research Fund; The Ophthalmic Research Institute of Australia; University of

Abstract

Importance: Atropine eyedrops are a promising treatment for slowing myopia progression in East Asian children. However, its effects on children in Australia, including those of non-Asian background, have not been well-studied.

Background: The Western Australia Atropine for the Treatment of Myopia (WA-ATOM) study aims to determine the efficacy and long-term effects of low-dose atropine eyedrops in myopia control. This paper describes the study rationale, methodology and participant baseline characteristics.

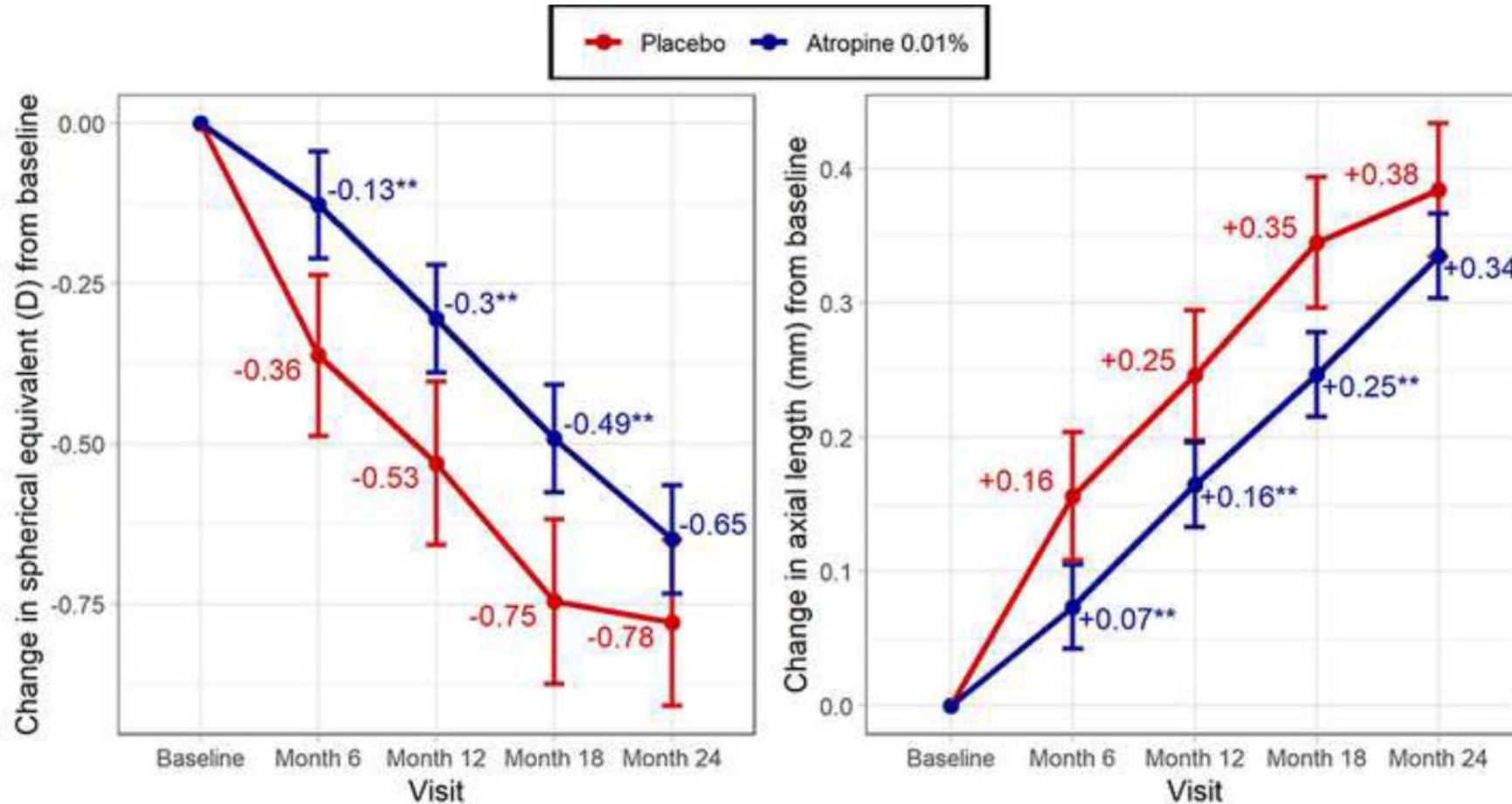
Design: Single-centre, double-masked, randomized controlled trial.

Participants: Children (6–16 years) with spherical equivalent ≤ -1.50 D in each eye, astigmatism ≤ 1.50 D and myopia progression by ≥ 0.50 D/year.



AUSTRALIAN VISION RESEARCH
australianvisionresearch.org

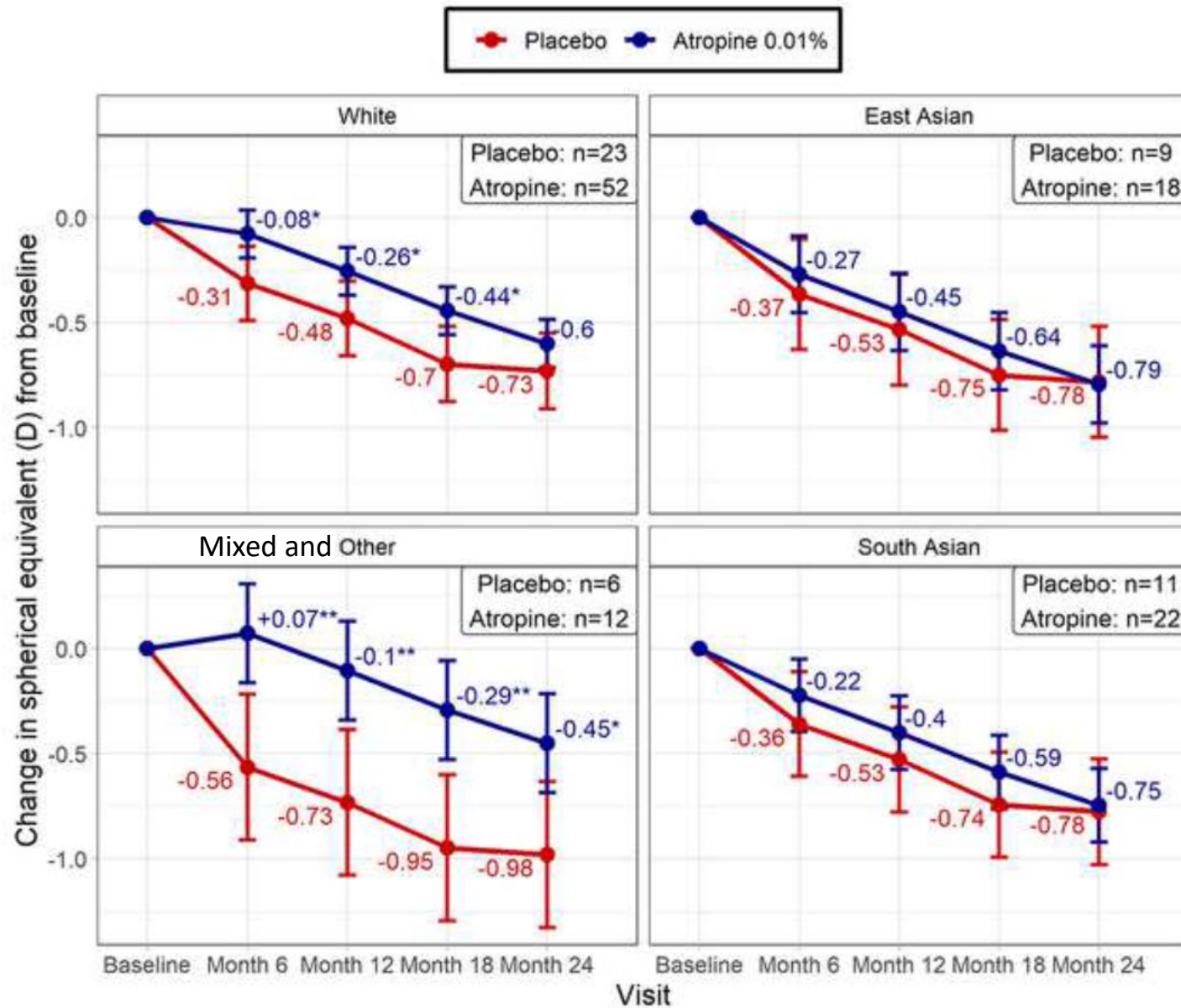
2 Year Treatment results WA ATOM Study



2-year change in Spherical Equivalent & Ethnicity

49%

12%

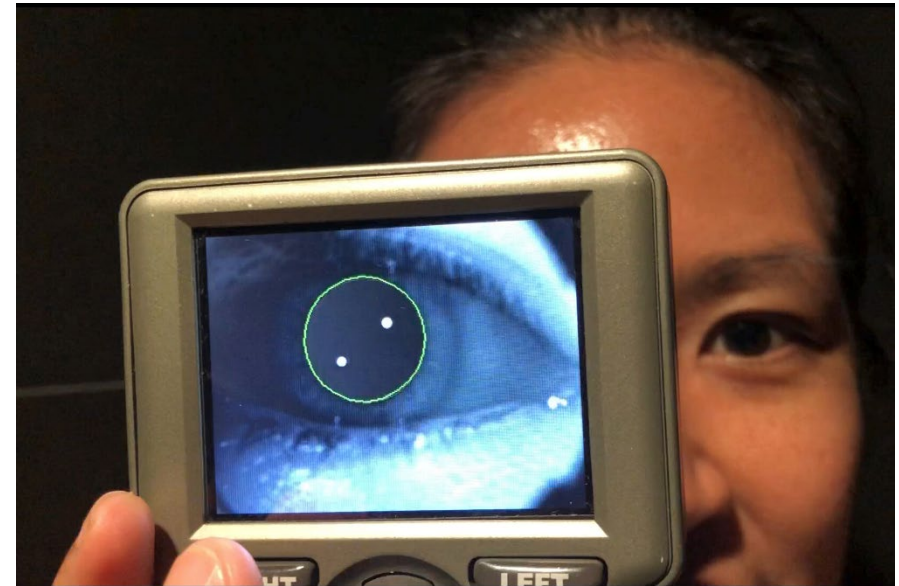


18%

22%

No difference in Glare or Difficulty with near work, Going outside or School Performance

- At all visits (6-24 months)
- Atropine group had:
- significantly increased
 - latency in pupillary constriction
 - amplitude of pupil diameter
 - pupil size at maximum constriction after light stimulus



Conclusion re Myopia Genetics

- In young onset and high myopia think Stickler syndrome and Inherited Retinal disease (ask if anyone in family has cleft palate or night blindness)
- Public Health measures such as increasing outdoor time in children can be implemented but need to be tailored to the population
- Clinical trials can use Polygenic risk score to include high risk children
- In the future combining family history with Polygenic risk scores and axial length trajectory will allow personalised intervention for high risk children

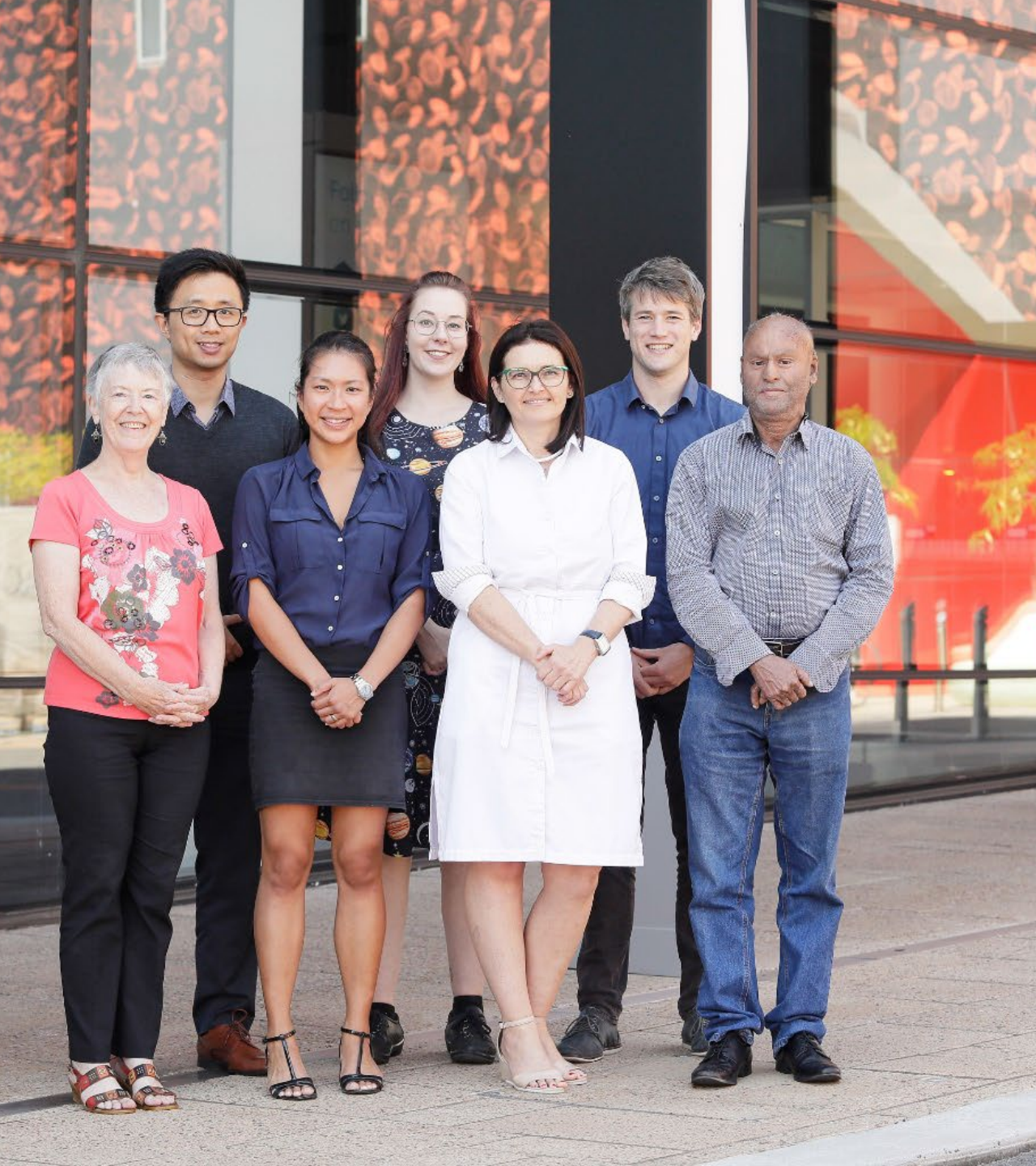
Acknowledgements:

- **CREAM CONSORTIUM MEMBERS**

- Twins Eye Study in Tasmania, Busselton Study and Raine Study participants and their families for their ongoing participation
- Busselton and Raine Study staff for study coordination & data collection
- Lions Eye Institute staff, students, and volunteers for data collection

Major Funding

- NHMRC (1021105, 1121979, 1126494)
- Alcon Research Institute
- Australian Vision Research
- Telethon
- LEI Donors



Lions Eye Institute
Raine Study
Research Team