MYOPIA RESEARCH: IMPROVING THE QUANTIFICATION OF RISK FACTORS

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Statement of Original Authorship

I, Long Phan, declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Graduate School of Health at the University of Technology Sydney.

The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made.

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Signature: Production Note: Signature removed prior to publication.

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Abstract

In recent decades, rapid increases in the prevalence and severity of myopia (short-sightedness) have been documented across the globe. In several populations, this has now reached epidemic proportions, becoming a major concern for eye care professionals. The increasing prevalence of high myopia suggest that there will be an increased risk of sight threatening pathologies that conventional treatment does not prevent. The myopia epidemic and looming rates of associated visual impairment, stimulated further studies of the aetiology of myopia, in order to develop more effective preventive intervention strategies.

This thesis aims to improve study methods in myopia research by identifying accurate and reliable tools for capturing behavioural exposures and by investigating an effective non-invasive means to relate these exposures to refractive changes. Initial direct comparisons of light intensity measures from three previously used portable light data loggers (LDLs) (Actiwatch 2, HOBO Pendant UA-002-64, and Clouclip M2) revealed strong correlations to a standard fixed industrial illuminometer (Yokogawa 51012). However, proportionally biased measurement errors were seen, indicating that light intensity measures with different portable LDL devices were reliable and reproducible, but differed between devices. These differences likely reflect the use of different sensors, and variations in control of measurement direction between different devices. Such errors inevitably lead to inaccuracies in the objective measurement of two key parameters relevant for myopia development: time spent outdoors and the intensity, duration and frequency of outdoor light exposure. Further reductions in reliability and incongruities in light exposure measures seen between LDLs during real-world validation suggested that sensor orientation was a major factor influencing device accuracy. It was concluded that spectacle-mounted LDLs appear to be the most viable option for capture of intraocular light exposures than other device wearing modalities.

In addition, by comparing longitudinal refractive and biometric data from two large population-based studies, an alternative to cycloplegic refraction using an indirect and non-contact method of determining refractive error and myopia risk was identified. In school-children aged 6 and 12 years, changes in the biometric AL/CR variable over 6–7 years were more strongly and linearly related to refractive changes than any single biometric measure. In myopic children, changes in the AL/CR variable over time could predict myopic progression with a reasonable level of accuracy. By considering this relationship, the collection of biometric data can potentially provide insight into the changes occurring in an individual's refractive status at more frequent intervals than typically able to be captured with cycloplegic refraction.

Overall, this thesis provides evidence for the presence of measurement errors occurring at several levels between commonly used portable LDL devices used to objectively capture time outdoors in myopia research. Greater knowledge of the limitations of these devices will enable more accurate capture of data and improve its interpretation. Similarly, greater understanding of the AL/CR value and its relationship to age and refractive errors can be a valuable supplement to standard cycloplegic measures in order to assess short-term refractive changes. Together this allows for more detailed measurements of causal and explanatory variables in myopia epidemiological studies. These findings also indicate a need for future methodological standardisation in myopia research, enabling more effective and reliable studies to further investigate the various relationships between behavioural environmental risk factors and myopia.

Publications and Presentations

Published Peer Reviewed Abstracts:

- **Phan, L.,** French, A. N., Rose, K. A. (2018) Emerging tools in the measurement of time spent outdoors. *Australian Orthoptic Journal*, 50.
- **Phan, L.,** French, A. N., Morgan, I. G., Rose K. A. (2019) Sunlight and myopia, how much is really enough? *Australian Orthoptic Journal*, 51.
- **Phan, L.,** French, A. N., Morgan I. G., Rose K. A. (2021) Biometric risk factors for myopia and the role of the AL/CR ratio. *Australian Orthoptic Journal*, 53.

National & International Scientific Presentations

- **Phan, L** (2018) Emerging tools in the measurement of time spent outdoors. ***75th Orthoptics Australia Annual Scientific Conference***, Adelaide, Australia
- **Phan, L** (2019) Investigating Patterns of Light Exposure in Young Adults. ***17th International Myopia Conference,*** Tokyo, Japan
- **Phan, L** (2019) Sunlight and myopia, how much is really enough? ***76th Orthoptics Australia Annual Scientific Conference***, Sydney, Australia
- **Phan, L** (2021) AL/CR for prediction of myopia and monitoring of management for progression. ***Orthoptics Australia NSW Virtual August Scientific Meeting Paediatric Symposium,*** Sydney, Australia
- **Phan, L** (2022) Ocular biometric changes during childhood refractive development and the role of the axial length to corneal radius ratio in predicting myopia onset. ***77th Orthoptics Australia Annual Scientific Conference***, Brisbane, Australia

Other Authored and Co-authored Published Peer-reviewed Papers

- **Phan, L. T**., Broadhead, G. K., Hong, T. H., & Chang, A. A. (2021). Predictors of Visual Acuity after Treatment of Neovascular Age-Related Macular Degeneration–Current Perspectives. *Clinical Ophthalmology (Auckland, NZ)*, 15, 3351. **(Appendix 1)**
- Spooner, K., **Phan, L**., Cozzi, M., Hong, T., Staurenghi, G., Chu, E., & Chang, A. A. (2021). Comparison between two multimodal imaging platforms: Nidek Mirante and Heidelberg Spectralis. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 1-12. **(Appendix 2)**
- Spooner, K., Fraser-Bell, S., Hong, T., **Phan, L.**, Wong, J. G., & Chang, A. (2021). Long-term Anti–Vascular Endothelial Growth Factor Treatment for Neovascular Age-Related Macular Degeneration: The LATAR Study: Report 1: Ten-Year, Real-World Outcomes. *Ophthalmology Retina*, 5(6), 511-518. **(Appendix 3)**

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List of Abbreviations

Abbreviation	Full term
ACD	Anterior chamber depth
AL	Axial length
AL/CR	Axial length to corneal radius ratio
ANOVA	Analysis of variance
CI	Confidence interval
CR	Corneal radius
D	Dioptre
FDM	Form deprivation myopia
GWAS	Genome-wide association study
HR	Hazard ratio
LDL	Light data logger
LIM	Lens-induced myopia
LoA	Limits of agreement
LOESS	Locally estimated scatterplot smoothing
LP	Crystalline lens power
MMD	Myopic macular degeneration
OK	Orthokeratology
OR	Odds ratio
ROC	Receiver operating curve
SAVES	Sydney Adolescent and Vascular Eye Study
SER	Spherical equivalent refraction
SD	Standard deviation
SMS	Sydney Myopia Study
SNP	Single Nucleotide Polymorphism
SPSS	Statistical Package for the Social Sciences
VA	Visual acuity
WHO	World Health Organisation