

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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Table of Contents

Statement of Original Authorship.....	ii
Acknowledgements.....	iii
Abstract.....	vii
Publications and Presentations.....	ix
List of Figures.....	xi
List of Tables.....	xiii
List of Abbreviations.....	xvi
Chapter 1: Literature Review.....	1
1.1 Overview.....	2
1.2 The Anatomy of the Human Eye and its Optical System.....	6
1.3 Refractive Errors.....	10
1.4 Natural History of Eye Growth and the Development of Refractive Errors.....	24
1.5 Epidemiology of Myopia.....	36
1.6 Impact of Myopia.....	71
1.7 Strategies for Myopia Control.....	78
1.8 Aetiology of Myopia - A role for genetics in school myopia.....	98
1.9 Aetiology of Myopia - Environmental risk factors.....	103
1.10 Light Exposure and Myopia.....	128
1.11 Chapter Summary and Thesis Aims.....	149
Chapter 2: Methods.....	152
2.1 Overview.....	153
2.2 Chapter 4: Light Exposures in Young Adults.....	153
2.3 Chapter 5: Experimental Comparison of Light Data Loggers.....	156
2.4 Chapter 6: Real World Comparisons of Light Data Loggers.....	163
2.5 Chapters 7 and 8: Longitudinal Changes in Refractive Error and Ocular Biometrics in Australian Schoolchildren.....	168
Chapter 3: Methods to Measure Exposures to Environmental Risk Factors in Myopia Research ..	171
3.1 Introduction.....	172

3.2	Subjective methods of risk factor measures.....	174
3.3	Objective measures of risk factors.....	180
3.4	Conclusion.....	192
Chapter 4: Quantifying Light Exposure Patterns in Young Adults		193
4.1	Abstract.....	194
4.2	Introduction	195
4.3	Methods.....	197
4.4	Results.....	199
4.5	Discussion	206
Chapter 5: The Accuracy and Reliability of Portable Light Data Loggers for Measuring Light Intensity.....		213
5.1	Abstract.....	214
5.2	Introduction	215
5.3	Methods.....	217
5.4	Results.....	222
5.5	Discussion	235
Chapter 6: Real World Comparison of Outdoor Exposure Parameters between Wearable Light Data Loggers		240
6.1	Abstract.....	241
6.2	Introduction	242
6.3	Methods.....	244
6.4	Results.....	250
6.5	Discussion	266
Chapter 7: The Axial Length to Corneal Radius Ratio as a Determinant of Refractive Error and its Progression		277
7.1	Abstract.....	278
7.2	Introduction	279
7.3	Methods.....	282
7.4	Results.....	284

7.5	Relationship between AL/CR change and SER progression	294
7.6	Discussion	300
Chapter 8: Ocular Biometric Changes during Childhood Refractive Development and the Role of the Axial Length to Corneal Radius Ratio in Predicting Myopia Onset		305
8.1	Abstract.....	306
8.2	Introduction	307
8.3	Methods.....	310
8.4	Results.....	312
8.5	Discussion	326
Chapter 9: Summary of Findings, Conclusions and Future Directions		331
9.1	Summary of findings	332
9.2	Conclusions & future directions.....	334
9.3	Closing statement	341
References		342
Appendix 1		378
Appendix 2		396
Appendix 3		409
Appendix 4		418
Appendix 5		434
Appendix 6		436
Appendix 7		446
Appendix 8		448
Appendix 9		450
Appendix 10		452

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.
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National & International Scientific Presentations

- **Phan, L** (2018) Emerging tools in the measurement of time spent outdoors. **75th Orthoptics Australia Annual Scientific Conference**, Adelaide, Australia
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- 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)**

List of Figures

Figure 1.1: Cross-sectional view of the human eye, cut on the transverse plane.....	7
Figure 1.2: Refractive error distributions at birth.	24
Figure 1.3: Prevalence of refractive errors across age groups	33
Figure 1.4: Changes in prevalent myopia over time from repeated birth cohort studies.....	38
Figure 1.5: Differences between designs of ‘dual focus’ contact lenses.....	88
Figure 2.1: Image of a HOBO Pendant UA-002-64 LDL.....	155
Figure 2.2: Apparatus used to simultaneously collect light intensity from three pairs of different LDLs.	157
Figure 2.3: Apparatus used to simultaneously collect light intensity from five different directions.	158
Figure 2.4: Directions faced by each LDL: A) Upwards B) North C) East D) West and E) South	158
Figure 2.5: Apparatus used to simultaneously collect light intensity from four different angles.....	159
Figure 2.6: Indoor and outdoor environments used to measure angular light intensity.....	159
Figure 2.7: Image of an Actiwatch 2 LDL	160
Figure 2.8: Image of a Clouclip M2 LDL	161
Figure 2.9: Image of a Yokogawa 51012 Digital LUX meter.....	162
Figure 2.10: LDL mounting locations	166
Figure 3.1: Example of a diary designed to gather near work and outdoor exposures in university students.	179
Figure 3.2: Images of wearable light meters including the A) HOBO Pendant UA-002-64 B) Actiwatch 2 C) Clouclip M2 & D) FitSight tracker. Light sensor locations are indicated by red circles.	185
Figure 4.1: Mean light intensity over an average day	200
Figure 4.2: Mean light intensity over an average weekday.....	201
Figure 4.3: Mean light intensity over an average weekend day.....	202
Figure 5.1: LDL recordings in a “low indoor” light environment.	223
Figure 5.2: LDL recordings in a “high indoor” light environment.	224
Figure 5.3: LDL recordings in a “low outdoor” light environment.....	225
Figure 5.4: LDL recordings in a “high outdoor” light environment.	226
Figure 5.5: Scatter diagram of all portable LDLs measures against the standard light meter..	228
Figure 5.6: Bland & Altman plots showing mean differences for all portable LDLs against the standard light meter.....	230
Figure 5.7: Bland & Altman plots showing mean percentage differences for all portable LDLs against the standard light meter	231

Figure 5.8: Mean light intensity recorded by each LDL when orientated in different directions	233
Figure 6.1: Example of a subject's light exposure on one day	248
Figure 6.2: Scatter plots comparing light intensity readings	251
Figure 6.3: Bland-Altman plots comparing the agreement in light intensity readings	252
Figure 6.4: Daily time outdoors reported from the diary compared to adjusted LDL measures.	254
Figure 6.5: Comparison of mean daily light intensity using adjusted LDL measures	255
Figure 6.6: Daily time outdoors reported from the diary compared to adjusted LDL measures.	257
Figure 6.7: Bland-Altman plot comparing the agreement in estimated weekly near work time between the Clouclip LDL and the questionnaire.....	259
Figure 7.1: Scatter plots with linear regression fit lines for AL/CR vs SER during SMS and SAVES for the A) younger cohort and B) older cohort.	289
Figure 7.2: Scatter plots with LOESS smoothing curves for AL/CR vs SER during SMS and SAVES for the A) younger cohort and B) older cohort.	290
Figure 7.3: Piecewise linear regression plots for the A) younger cohort at baseline, B) younger cohort at follow-up, C) older cohort at baseline and D) older cohort at follow-up.	291
Figure 7.4: Scatter plot of AL/CR change vs SER change with linear regression (solid) and 95% confidence interval (dotted) lines drawn for the A) younger and B) older cohort.....	294
Figure 7.5: Scatter plot of AL/CR change vs SER change with linear regression (solid) and 95% confidence interval (dotted) lines drawn for baseline refractive groups in the younger cohort: A) hyperopia B) low hyperopia C) pre-myopia and D) myopia.	297
Figure 7.6: Scatter plot of AL/CR change vs SER change with linear regression (solid) and 95% confidence interval (dotted) lines drawn for baseline refractive groups in the older cohort: A) hyperopia B) low hyperopia C) pre-myopia and D) myopia	299
Figure 8.1: Baseline AL/CR vs SER progression over the 5-6 year interval for the A) younger cohort and B) older cohort.	321
Figure 8.2: Receiver operating characteristic curves for predicting incident myopia using baseline SER, AL/CR, time outdoors and near work time in the A) younger cohort (age 6 years at baseline) B) older cohort (age 12 years at baseline).	323
Figure 8.3: Receiver operating characteristic curves for predicting incident myopia using both baseline SER and AL/CR in the A) younger cohort (age 6 years at baseline) B) older cohort (age 12 years at baseline).	323
Figure 8.4: The proportion of children with incident myopia and the proportion who remained non- myopic according to baseline AL/CR in the A) younger cohort and B) older cohort.....	325

List of Tables

Table 1.1: Studies investigating the relationship between AL/CR and refractive error.	17
Table 1.2: Population-based studies reporting the prevalence of myopia in infants and children of pre-school age.....	47
Table 1.3: Population-based studies reporting the prevalence of myopia using cycloplegia in school-aged children. Prevalence values from repeated cohort studies are taken from the most recent year.	53
Table 1.4: Summary of population-based studies reporting the prevalence of myopia in young adults. Prevalence values from repeated cohort studies are taken from the most recent year.	59
Table 1.5: Summary of population-based studies reporting the prevalence of myopia in adults. Prevalence values from repeated cohort studies are taken from the most recent year.	66
Table 1.6: Summary of studies investigating pharmacological treatments for myopia control.	82
Table 1.7: Summary of peer-reviewed studies investigating under-correction (UC) or no correction (NC) compared to full correction (FC) of spectacle lenses for myopia control.	84
Table 1.8: Summary of control studies investigating bifocal (BF) and multi-focal (MF) spectacle lenses for myopia control.	85
Table 1.9: Randomised control trials investigating soft (SCL) and rigid-gas permeable (RGP) contact lenses for myopia control.	86
Table 1.10: Randomised control trials investigating orthokeratology (OK) treatment for myopia control.....	87
Table 1.11: Control trials investigating special lens designs for myopia control	91
Table 1.12: Randomised control studies investigating the addition of outdoor activity to control myopia.	94
Table 1.13: Summary of studies investigating light exposures in relation to myopia in humans.	141
Table 3.1: Comparison of device characteristics of objective near work devices.....	183
Table 3.2: Comparison of different device characteristics of portable light meter devices based on publically available specifications.	187
Table 4.1: Time spent above various light intensity thresholds, expressed as a percentage of daylight hours and in minutes during 12 and 10 daylight hour days.	203
Table 4.2: Cross-tabulation of agreement between indoor and outdoor states from the diary and from the LDL (defined as > 1,000lux).....	204
Table 4.3: Average light intensity levels recorded in various activity groups.	205

Table 4.4: Average light intensity levels recorded in various activity groups on weekdays and weekends. (*P < 0.05).....	205
Table 4.5: Activity groups sorted by indoor or outdoor environment as determined by diary entries.	205
Table 5.1: Mean ± SD illuminance measures from light meter devices over a 1-hour interval across all light environments.....	227
Table 5.2: Intra-class correlations (ICC) for each of the light meters with respect to the standard meter.....	232
Table 5.3: Concordance correlation coefficients (CCC), person’s correlation coefficients (ρ) and the bias correction factor (Cb) for each of the light meters with respect to the standard meter.....	232
Table 5.4: Angular light intensity measures from the Clouclip M2 within an indoor and outdoor environment	234
Table 6.1: Inter-rater agreements for outdoor status between LDLs and the outdoor activity diary using Cohen's kappa (κ).	253
Table 6.2: Daily time outdoors, mean outdoor light intensity and outdoor frequency captured between LDL devices and the outdoor activity diary.	256
Table 6.3: Average time outdoors determined from the LDL devices, outdoor activity questionnaire and the outdoor activity diary.	258
Table 6.4: Characteristics of myopic and non-myopic study participants.....	261
Table 6.5: Outdoor exposures and near work times between myopic and non-myopic subjects.....	261
Table 7.1: Demographic and biometric characteristics of the younger cohort at baseline and at follow-up.....	284
Table 7.2: Demographic and biometric characteristics of the older cohort at baseline and at follow-up.	285
Table 7.3: Cross-tabulation of Pearson’s correlation coefficients between ocular component measures and SER in the younger cohort at A) baseline and B) follow-up.	286
Table 7.4: Cross-tabulation of Pearson’s correlation coefficients between ocular component measures and SER in the older cohort at A) baseline and B) follow-up.	286
Table 7.5: Pearson’s correlation coefficients between AL/CR and the spherical component of refraction as well as SER.	286
Table 7.6: Cross-tabulation of Pearson’s correlation coefficients between changes in ocular component measures and changes SER in A) the younger cohort and B) the older cohort.	287
Table 7.7: Comparison of coefficients of determination (R^2) for AL/CR vs SER between linear and tri-phasic linear models.	292

Table 7.8: Optimised values from piecewise linear regression analysis for gradients and breakpoints of a tri-phasic curve.	292
Table 7.9: Pearson’s correlation coefficients between AL/CR and LP, stratified by baseline AL/CR sub-group.	293
Table 7.10: Pearson’s correlation coefficients between changes in AL/CR and changes in SER, stratified by baseline AL/CR sub-group.	293
Table 7.11: Pearson’s correlation coefficients between changes in AL/CR and changes in SER, stratified by baseline refractive error category.	293
Table 8.1: Comparison of changes in spherical equivalent refraction and optical component values across baseline to follow-up between the younger and older cohort.	313
Table 8.2: Longitudinal changes in biometric optical component measures between baseline refractive groups in the younger cohort.	315
Table 8.3: Longitudinal changes in biometric optical component measures between baseline refractive groups in the older cohort.	315
Table 8.4: Longitudinal changes in optical component measures between baseline hyperopes of the younger cohort who either remained hyperopic, became low-hyperopes or became either pre-myopic or myopic.	317
Table 8.5: Longitudinal changes in optical component measures between baseline hyperopes of the older cohort who either remained hyperopic, became low-hyperopes or became either pre-myopic or myopic.	317
Table 8.6: Longitudinal changes in optical component measures between baseline low hyperopes of the younger cohort who either remained low-hyperopes, became pre-myopic or became myopic.	318
Table 8.7: Longitudinal changes in optical component measures between baseline low hyperopes of the older cohort who either remained low-hyperopes, became pre-myopic or became myopic.	318
Table 8.8: Longitudinal changes in optical component measures in the younger cohort between children who stayed as pre-myopes, pre-myopes who became myopic, existing myopes and those who experienced hyperopic shifts in refractive category.	319
Table 8.9: Longitudinal changes in optical component measures in the older cohort between children who stayed as pre-myopes, pre-myopes who became myopic, existing myopes and those who experienced hyperopic shifts in refractive category.	319
Table 8.10: Logistic regression for predicting the development of myopia in the A) younger cohort and B) older cohort.	322

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