A Longitudinal Study of Lifestyle Factors and Biometric Development in Children of a Regional Population

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Thesis Abstract

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Uncorrected refractive error is one of the leading causes of blindness worldwide, occurring due to mismatch between the axial length of the eye and its refractive power. During emmetropisation, environmental influences may interrupt the coordinated growth of the eye leading to refractive error in adulthood. Elevated prevalence of myopia has led to the majority of studies focussing primarily on the risk factors leading to this condition. While no single factor has proven to be dominant, it is becoming clearer that these factors may compound, elevating risk. Studies on hyperopia and astigmatism are rarer, and understanding of the mechanisms behind these conditions is relatively poor. Interaction and modulation of the emmetropisation process represents a significant tool for the reduction of refractive error. To investigate the factors that may influence emmetropisation, cross sectional and longitudinal data were collated for 58 children aged 5 to 12 years in a regional Australian population. Mean axial length growth over 12 months for the cohort was $0.09mm$ (± 0.06), anterior chamber depth growth was $0.03mm$ (± 0.06), central corneal thickness change was $-1.18\mu m$ (± 5.36). Refractive error in the longitudinal study was stable across the study period for hyperopia (7.89%), decreased for astigmatism (18.42%) at test 1 to 13.16% at test 2), and increased for myopia (5.26% at test 1 to 7.89% at test 2). Mean change in spherical equivalent refractive error over 12 months was $-0.12D$ $(\pm 0.33D)$ with a minimum of $-0.93D$ and a maximum of $+0.69D$. Axial length and spherical equivalent refractive error exhibited change across the study period in line with published values, anterior chamber depth for the cohort tended to be greater those indicated in normative models. The results from this lifestyle survey reinforce the conclusions of published data with respect to the influence of outdoor activities as a positive influence in emmetropisation.

Keywords

Emmetropisation, axial length, refractive error, ocular biometry, regional Australian population

For Thao, Ly and Yen.

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Chapter 1: Introduction

This section serves as an introduction to the thesis outlining the background, context, purposes and questions this research project seeks to address.

1.1 BACKGROUND

Uncorrected refractive error is one of the leading causes of blindness worldwide [1] . Refractive errors are due to a mismatch between the axial length of the eye and the power of its refracting components. During the emmetropisation phase of development the eye is susceptible to environmental influences which may interrupt the coordinated growth of the eye leading to refractive error throughout childhood and into in adulthood. Due to the significant increase in the prevalence of myopia with its significant associated pathological risks, the majority of studies in this area focus primarily on the relationship between risk factors leading to this condition [2]. Risk factors ranging from genetic to environmental influences have been well studied and while no single factor has proven to be dominant, it is becoming clearer that these factors may compound, elevating risk. Studies examining risk factors for hyperopia and astigmatism are however relatively rare and understanding of the mechanisms behind the development of these refractive errors is relatively poor. The ability to interact with, and potentially modulate the emmetropisation process represents a significant tool for the reduction of refractive error as a cause of preventable blindness. This review outlines refractive errors and models of emmetropisation, risk factors and prevalence of refractive errors in their presence and potential avenues for further investigation and intervention. To date several studies have been identified which align with the goals of this current work to varying degrees which inform the structure of this research project [3-7].

1.2 CONTEXT

Research into the aetiology of myopia is a well-established field and has been the source of significant research in recent years. Despite this, current research is still

trying to understand the mechanisms behind the development of myopia and its progression[8, 9]. As emmetropisation requires the coordinated development of the optical components of the eye, an understanding of the biometry of these components during growth is important in defining the relationship between components during development. Myopia is the result of an imbalance between these optical components, where the refractive power of the cornea and lens does not offset the axial length growth[10]. With axial growth occurring during childhood, myopia generally occurs in school-age children and adolescents, typically emerging between the ages of 7-14 years with possible further progression up to late teenage to early adulthood [11]. Given variations with different populations and lifestyles in relation to myopia development, refractive and biometric development for myopes is an area of significant research with the goal of addressing ocular health issues, such as myopic maculopathy and retinal detachment, associated with the condition. Normal refractive development pathways are not fully understood. Emmetropic children have demonstrated a successful cessation of coordinated growth in the eye [12], and this process has ceased prematurely for hyperopes [13] whereas in myopes eye, growth continues beyond the normal parameters [9]. This provides an opportunity, using biometry, to identify and isolate the factors which promote cessation of emmetropisation.

1.3 STUDY RATIONALE

In this retrospective longitudinal study using biometry, relationships between ocular development and the natural progression of refractive development will be examined. This will be framed in the context of lifestyle and environmental factors for children in the most active phase of emmetropisation of 12 years of age or less. An understanding of the influence of environmental factors on emmetropisation and refractive development may provide a tool for improvement of patient management based on readily observable factors. The ability to contextualise these data with regards to lifestyle and environmental factors will facilitate more effective patient management.

This research project will implement both qualitative and quantitative data to endeavour to describe the longitudinal relationships between refractive error, measured biometric features of the cohort, and the environmental factors in which

these eyes developed. Flitcroft identified a deviation from the global tendency towards ametropia for children in Australia and Vanuatu [12], noting that the distribution of refractive error displayed stronger leptokurtosis than that of other regions. This feature of the prevalence of refractive error in the region provides the impetus for this first investigation into potential environmental and developmental conditions that may support emmetropisation.

Astigmatism may represent either overall myopia (i.e. both power meridians are myopic), overall hyperopia or a combination thereof, this condition may represent a complex presentation of the underlying refractive errors present. The overall predominance of this refractive error in adult populations warrant inclusion in this study.

Published normative curves have been used as the reference lines in this study and are presented in the context of the collected data [14].

Despite the collection of biometric data in practice becoming commonplace, devices available to practitioners are cost prohibitive, typically performing a single function. Recently, wavefront aberrometers have been implemented to refine the models used for lens generation, with potential for the application of this data in the definition of an individual's biometric data. A component of this study will compare the performance of a novel biometer (DNEye wavefront aberrometer/biometer) to that of a known device (Nidek AL-Scan).

Chapter 2: Literature Review

2.1 INTRODUCTION

At birth the human visual system is developmentally incomplete. During juvenile development the eye undergoes the process of emmetropisation which, in ideal circumstances, will result in completion of development of the eye while attaining and maintaining emmetropia [15]. The development of the human eye through its emmetropisation phase is more complex than a simple enlargement of the physiological components and is not completely understood. Neurological and ocular components of the system are therefore subject to growth and development that is strongly interdependent. Ocular growth rates are nonlinear in terms of axial length and refraction, as is the relationship between physiological components (cornea, anterior chamber depth, crystalline lens, vitreous chamber depth and the overall axial length or size of the eye) [16-18]. Each individual physiological element increases in size during the growth of the eye, and the relationship between these elements and the overall refractive power of the system is delicate and susceptible to deviation due to external influences [19]. Animal studies show that this process is dependent upon visual signals to initiate or arrest growth [20-22]. While it is possible to consider the eye as the sum of the constituent optical components it is perhaps more useful to examine the relationship between these elements and the influence of external factors on these relationships to understand the process of emmetropisation.

Failure to address deviation from normal development may have lasting consequences for the individual ranging from myopia, hyperopia and astigmatism to developmental defects in the visual system such as amblyopia [13]. Consequently, it is important to identify periods during emmetropisation where the visual system is particularly susceptible to negative developmental outcomes due to abnormalities in the initial conditions of the visual system or deviations from nominal developmental patterns.

The dominant focus of current research being conducted to date into risk factors for refractive errors and biometric component (i.e. structural) deviation is centred on the myopic population, primarily due to the recent surge in the prevalence of this condition over the last three decades [4, 23, 24]. This is perhaps due to the

tendency for risk factors to contribute more easily to the development of myopia than hyperopia, particularly in the area of excessive axial length growth. Complicating our understanding is a relative lack of studies looking at the development of biometry in healthy paediatric development [14, 25, 26], potentially due to the urgency with which the surge in myopic development demands attention. Data in this area is improving, however studies tend to focus on demographics in which myopic progression is problematic, such as East Asian populations, creating population specific data which may not reflect more general trends. Research identifying a wide range of populations, ethnicities, socio-economic conditions and refractive errors will be useful in isolating the magnitude of influence on refractive and biometric development provided by specific influences.

This review aims to examine the existing body of published studies pertaining to the development of refractive error during emmetropisation in the presence of a range of influences and risk factors. Existing review articles and studies were identified via PubMed searches. Keywords implemented in this initial phase were emmetropisation (and emmetropisation), hyperopia, myopia, astigmatism, ocular biometry and ocular aberration. These articles were then used to pursue a strategy in PubMed implementing a simplification of the systematic review methods filter from which initial articles provided references to further relevant material resulting in 621 articles via citation chasing of which 240 proved relevant. This process was performed in their individual topic areas until the citations became circularly referenced or were otherwise exhausted. While the body of research pertaining to myopic development is significant and could not be fully encompassed in this review, the relative scarcity of studies examining hyperopia and astigmatism affords greater confidence that a significant and representative portion of the extant information has been included here. The age of studies was not considered relevant unless the conclusions had been categorically disproven. However, it may be argued that even these instances present context for our current understanding, for example in the determination of biometry via calculation which was the prevalent method prior to the introduction of biometers [27]. Despite the review concentrating on risk factors during emmetropisation, studies pertaining to adult biometry and refractive error were included to provide context for the resultant refractive error development. These were subsequently divided into overall areas of compatibility describing the underlying processes for emmetropisation and the subsequent risk factors leading to deviations from emmetropic outcomes.

Relevant data from articles were identified to extract experimental and conceptual data, with points of agreement or disparity between studies identified where appropriate with experimental finding compared when possible. The overarching areas identified in this process as risk factors for deviations from ideal biometric or refractive outcomes were genetic, ethnic and socio-economic factors. The relative scarcity of biometric data on non-myopic populations presented a challenge when discussing biometric data but does identify an area of potential research.

2.2 REFRACTIVE ERROR

The progression of refractive error is often discussed in terms of the relationship between the refractive power and axial length of a given individual [3, 25, 26, 28-57]. This approach treats the eye as an optical system without considering external influences and can be problematic as this model risks being overly simplified. While the development of axial length has been demonstrated to have a strong contribution to refractive error, it is not the only contributor and may be ignoring other potential contributing factors for refractive progression. Broadly, the main source of refractive error is a deficiency or surplus of power in the refracting components of the visual system leading to a mismatch between the refractive power of these components in the total visual system (physiological) and the size of the eye due to deviation from an optimal axial length for the given power of the refracting components of the visual system (pathological).

Hashemi et al. [1] estimated the global prevalence of refractive error in children with myopia ($\leq -0.50D$), hyperopia ($\geq +2.00D$) and astigmatism ($\geq 0.75D$) to be 11.7%, 4.6% and 14.9% respectively. In the same review for adults the prevalence increased to 26.5%, 30.9% and 40.4% respectively. Prevalence rates will vary according to individual study criteria. The disproportionate increase in hyperopia as the eye ages may be indicative of the lenticular changes in the ageing visual system, however the definition of hyperopia becomes more complex in adult populations. Age related lens changes may contribute to a tendency towards hyperopia in older populations. Children are able to sustain accommodation of powers beyond the range of +2.00D, which may confound detection of hyperopia lower than this magnitude [58]. Reduced accommodation in adults progressively reduces this ability with age, making lower levels of hyperopia more reliably detected. To define hyperopia for adult

populations only the refraction for distance vision with hyperopia is considered to be present at >+0.50D [1], the same absolute magnitude as myopia and astigmatism. Due to the high density of refractive error prevalence around the -0.50D to +0.50D range, these definitions are potentially problematic. By extension, emmetropia may be considered to be any refractive error between -0.50D and +0.50D. Seemingly small changes to the reference criteria, for example ≥0.50 instead of >0.50 can significantly reduce the population of a set and skew the data accordingly. Geographical distribution of refractive error is unequal and represents a risk factor either through environmental, socioeconomic or genetic influences and will be discussed section 2.6 in more detail [3, 4, 6, 53, 59-70]. Overall, refractive error represents the most common ophthalmic impairment, so an understanding of its aetiology is key to developing management and minimisation strategies.

As light propagates through an optical system it will be subject to influence from the refracting components through which it transits. The light exiting a refracting surface or element will form a wavefront with geometry that is defined by the refracting properties of the surfaces or elements through which it has passed. The wavefront may indicate convergence or divergence of the incident light. The wavefront may be rotationally symmetrical or asymmetrical.

If a simplified model of the eye as a sphere with an internal wavefront W is considered, the following definitions apply.

1. Emmetropia - W has revolution symmetry and has an image focal point on the fovea. The power of the refracting elements of the visual system, physical distancing of these elements and the axial length of the eye are matched. This relationship is internally referenced so that regardless of the size of the eye, provided the refractive power of the cornea and crystalline lens is appropriate, emmetropia may be achieved.
2. Ametropia – Failure to meet the above condition, presents in the following three forms
    a. Myopia – W has revolution symmetry but has excess vergence and therefore has a focal point in front of the retina. This may be due to an excess of refractive power in the visual system, a failure of the relative contributions of the individual refractive elements and spacing or overly long axial length.

b. Hyperopia - W has revolution symmetry, but has insufficient vergence and therefore has a focal point behind the retina, ostensibly outside the globe of the eye. At birth hyperopia represents the most common refractive error. This may be due to a deficit of refractive power in the visual system, a failure of the relative contributions of the individual refractive elements and spacing or insufficient axial length.
c. Astigmatism – W does not have rotational symmetry. Wavefront has two orthogonal vergences which may be separately myopic, hyperopic or focus upon the retina. While axial length may contribute overall to the bias of this refractive error (either myopic or hyperopic) the source of the two power meridians is typically due to corneal or crystalline lens irregularities.

The contribution of individual elements to the overall refractive power of the eye has been well studied [31, 49, 71-73]. Each component of the system, such as the cornea, crystalline lens and axial length, exhibit a range of values that, in an ideal combination, may result in an emmetropic eye. It is possible to treat these individual elements of the visual system as a conventional optical system which are subject to known mathematical definitions and interactions [36, 49, 74-76], however the complexities of biological optics make models of these systems are far more uncertain. As the elements of the human optical system are not fully formed at birth, they are susceptible to influence from external factors during development. A mismatch in growth rates of these physiological elements will result in correlation ametropia, although the mechanisms driving this process are not fully understood [31, 32, 72]. Rather than a purely mechanical approach, an understanding of the development of each component as well as its optical contribution is required to predict final refractive outcomes in a human eye.

2.3 EMMETROPISATION

Emmetropisation attempts to describe a pathway through which the final combination of optical components in the eye results in good image formation on the

retina. All of the major determinants of refractive power, axial length, cornea curvature and lenticular power, are subject to change during this process. Simply through growth of the eye globe alone, hyperopia at birth is reduced, however a modulating effect is required to attenuate this growth in the context of the other ocular components to avoid over lengthening and subsequent myopisation. Animal models have demonstrated the negative impact of manipulating this process through spatial deprivation and artificially induced defocus [15] on axial length and refractive outcomes. These have further indicated that there is an active feedback process driven by image formation and subsequent retinal stimulation that drives the process of emmetropisation, highlighting the importance of maintaining quality visual input during childhood [15, 77, 78].

The biometry of the eye at birth is linked to gestational age and, unlike juvenile and adult biometry, is not influenced by sex. Rozema et al. [52] determined corneal radius (CR), anterior chamber depth (ACD) and lens power (P) were all correlated with the axial length of the eye indicating that prior to birth, development of the eye is scaled. Importantly none of these parameters were significantly correlated with spherical equivalent refraction (SE) other than axial length/corneal radius ratio (AL/CR). In the absence of visual input, visually mediated ocular growth does not occur so deviations from normal relationships between individual ocular components in a given eye are generally not present. The refractive errors present at birth are normally distributed, suggesting that ametropia at birth is due to factors that are present *in utero* rather than being visually mediated. In a study of neural pathway contributions to emmetropisation, Wildsoet [79] demonstrated that chick eyes, which had been isolated from the brain by optic nerve section, continued to respond to myopogenic stimuli. This further supports the ocular growth and regulatory processes occurring during emmetropisation being local to the eye and visually mediated, and the relative independence of initial biometric and refractive conditions from eventual refractive outcomes.

Refractive error present in adulthood, either myopia or hyperopia, may be considered as a failure of emmetropisation. The presence of hyperopia may be viewed as a failure of the eye to completely emmetropise, either as a result of too high an initial magnitude of hyperopia or too slow a rate of emmetropisation. Conversely myopia may be viewed as a failure of emmetropisation to be adequately maintained

once equilibrium between the physiological and refractive components has been achieved.

Hyperopia represents the most prevalent refractive error at birth with an average magnitude of +2.00D, normally distributed. Ehrlich et. al. found that the refractive error measured through cycloplegic retinoscopy decreases with age at a rate of approximately -0.75D to -0.81D per year [80] up to 20 months of age indicating an average residual hyperopic refractive error of +0.50D at that point. As the reduction in hyperopia is nonlinear this value is not necessarily indicative of the process overall. During the first two years of post-natal development the eye shifts towards emmetropia with a narrower distribution of powers than at birth, Gwiazda et al estimated that 89% of 6 year olds are effectively emmetropic, with children whose effective hyperopia had been corrected to <+1.00D also achieving a cessation of coordinated growth between ocular components [81]. Recently Hagan et al [82] observed ongoing coordinated ocular growth in 16 to 18 year emmetropes and low hyperopes. This growth was correlated to changes in other body parameters, such as height and weight, which suggests that the process may continue as long as the body is undergoing growth. The rate of change has been linked to the initial refractive error at birth. This has been observed by Atkinson et al. where the change in refractive error was proportional to the initial magnitude of hyperopia ($F=56.36$, $P<0.0001$) [32, 83]. Higher degrees of initial hyperopia will require more rapid rates of change in all of the refractive and biometric elements of the eye to achieve emmetropia by school age. Castagno et al in a meta-analysis of 40 studies observed that prevalence of hyperopia decreases with age (5% at age 7 reducing to 1% at age 15), representing a very low prevalence of hyperopia which is not in line with other studies. Prevalence ranged regionally from 0.0% in South Asian studies to 36.4% for a rural European population. Regional, demographic and environmental factors are identified as contributing to the range of prevalence across regions, however the complexity of interactions between these factors obfuscates the causal relationships. It is proposed that the causes of hyperopic decrease with age may be the same as those responsible for myopic increase with age [84]. They further indicate the scarcity of research into the association of axial length and age while highlighting the scarcity of research in distribution by specific ages.

Children with >+3.50 of hyperopia in at least one meridian have a 6x elevated risk of developing amblyopia and 13x greater risk of strabismus. Overall, hyperopia, particularly that greater than +4.00D, is associated with reduced or degraded visual

acuity [13]. These risks are reduced to 2.5 × and 4.5 × with full or partial correction of refractive error. While risk factors have been identified for inclusion in screening protocols, guidelines for prescribing are inconsistent. Under correction is posited as a means for 'restarting' the emmetropisation process, however the magnitude of under correction required is not well understood. Underscoring this is the risk that excessive under correction is linked with increased risk development of strabismus when the correction has a deficit of greater than 1.50D. Studies are inconsistent in their findings with regards to under correction and no correction on myopic development [85]. Consequently, the application of under correction as an intervention technique is not found commonly in practice.

The mechanism through which emmetropisation may be induced by under correcting in the presence of hyperopia is not well understood. It is suggested that emmetropisation is interrupted when the trigger for growth provided by visual feedback exceeds the boundary conditions of an active emmetropisation process [15]. This is in effect a reversal of the conditions through which the runaway cycle of emmetropisation for myopia is induced. By presenting partial correction of a magnitude that permits accommodation of the shortfall in refractive error, emmetropisation is restarted [13]. The authors further suggest that when fully corrected, no accommodative process is engaged, preventing the recovery of the emmetropisation process. This suggests that the transient nature of defocus in the presence of moderate hyperopia is a potential differentiating factor for the nature of defocus triggers in emmetropisation.

While hyperopia represents the most prevalent refractive error at birth, astigmatism is the most common refractive error for adult eyes , with the range of risk factors reported as age, sex, race, education, initial refractive errors, urban/rural location and axial length [86]. Given the ability of astigmatism to represent either overall myopia (i.e. both power meridians are myopic), overall hyperopia or a combination thereof, this condition may represent a complex presentation of the underlying refractive errors present.

Anterior chamber depth contributes to the refractive power of the visual system due to its placement between the two major refracting components of the eye, the cornea and the crystalline lens. Shih et al [87] indicate that ACD is deeper in myopes than emmetropes or hyperopes with stability achieved by approximately 11 years of age.

Changes to the ocular components during emmetropisation are not scaled as in prenatal conditions and are nonlinear both in development and relationships to other components. In both humans and animals, the focal plane of the eye moves away from the cornea during postnatal and juvenile development due to a reduction in lens power and flattening of the cornea. Postnatal development of the cornea has been reported with conflicting results, Wood et al [88] found a mean corneal power of 43.5D with a radius of 7.76mm (range 45.93D, 7.35mm to 39.9D, 8.46mm). Inagaki et al [89] found mean of 7.05mm suggesting a higher corneal power of 47.89D. Mutti et al [32] determined that between 3 and 9 months, on average, the lens power decreased by -3.62D and the corneal power decreased by -1.07D with the corneal power reaching approximate adult values at a younger age than the lens power. They suggest that this change in power may be due to the mechanical changes in the eye structure during growth thinning the lens and increasing corneal radii. Zadnik et al [26] found that the majority of corneal power changes had occurred by 6 years of age, with only -0.4D of change occurring between 6 and 14 years. Over the same period the lens power decreased by approximately 2.50D, further demonstrating the move away from scaled development in post-natal growth. Lenticular thickness (LT) decreases until 11 years of age then increases with age beyond this point. LT was lowest for myopes with both emmetropes and myopes displaying the greater changes during emmetropisation than hyperopes [87], it suggested that LT thinning is a compensatory response, reducing lenticular power to allow for increasing axial length.

As with refractive errors, axial length is broadly distributed at birth [90] and is also normally distributed [12, 91] suggesting it is the result of genetic factors. Mean values differ between studies centring around 18mm at birth to approximately 23mm at 3 years of age [27, 92]. As with corneal and lenticular development, axial length increases are nonlinear with average growth being approximately 1mm during emmetropisation. Change is most rapid between 3 and 9 months of age with approximately 1mm of change in the first year [25, 32] dropping to <0.5mm in the second and <0.2mm per year by 12 years of age [93]. At 12 years the relationship between axial length and SER has been described by Ip et al [34] as 1mm of increased axial length ≈ 0.96D of myopic shift. This description of emmetropisation allows us to describe the development of four main refractive outcomes with regards to the general conditions leading to them as described by Siegwart et al. [90] as:

- Born hyperopic, remains hyperopic
- Born myopic, remains myopic
- Born emmetropic, becomes hyperopic
- Born emmetropic, becomes myopic

With the implication that a failure in emmetropisation to regulate growth either compounds existing refractive error or initiates ametropia.

The relationship between ACD, LT and AL was examined by Shih et al [87] by determining the ratio of each component and relating this to refractive error. It was found that the LT/AL mean ratio in school children was 0.13 for myopes, 0.15 for emmetropes and 0.15 for hyperopes. ACD/AL mean ratios were 0.15 for myopes, 0.14 for emmetropes and 0.15 for hyperopes. Anterior segment (AS) to AL mean ratios were 0.29 for myopes, 0.30 for emmetropes and 0.31 for hyperopes. All ratios were highest for hyperopes and lowest for myopes with LT/AL increasing with age, ACD/AL decreasing with age and AS/AL remaining relatively constant with increasing age. These relationships are consistent with the concept of the axial length as a primary contributor to refractive error due to the numerical dominance of AL in the ratio.

2.4 MODELLING EMMETROPISATION

The examination of the relationship between ocular elements during growth opens the possibility of mathematical models built on the individual parameters of the eye or potentially mechanical changes over time to the eye. Rozema et al [71] implemented a statistical model incorporating 39 elements that could describe the biometric data of a population. This has utility when considered as an eye model for spectacle lens design purposes but has limited predictive value for monitoring emmetropisation. As the devices used in this study do not have the capacity for determination of lenticular power, techniques providing a calculated value that may be used to populate an eye model for an individual are required in place of direct measurement. Rozema [52] presents an application of the Bennett and Roysworth equations [94] to determine unaccommodated power of the crystalline lens in its unaccommodated state in newborn infants. While not providing a dynamic model of

the eye during growth, it does provide some insight into the complexity of modelling juvenile eyes.

$$P_L = -\frac{1000n(S_{CV}+K)}{1000n-(ACD+CCT+c_1T)(S_{CV}+K)}+\frac{1000n}{-c_2T+V}$$

$$r_{1a}=\frac{1000(n_L-n)}{QP_L}$$

$$r_{1p}=\frac{1000c_2(n_L-n)}{c_1QP_L}$$

Variable	*Description*
n	Refractive index of the aqueous and vitreous humor = 4/3
n_L	Refractive index of the crystalline lens = 1.449
S_{CV}	Subjective Cycloplegic Refraction (spherical equivalent), in diopters
K	Corneal power in diopters (measured via keratometry)
ACD	Internal anterior chamber depth (excluding corneal thickness), in mm
CCT	Central corneal thickness, in mm
T	Lens thickness in mm
V	Vitreous depth, calculated as $V = L - T - ACD_{tot}$ in mm
c_1	Position constant for the anterior lens surface (fractional distance into the lens) = 0.563
c_2	Position constant for the posterior lens surface = 0.386
Q	Ratio of anterior surface power to total lens power = 0.418
r_{1a}	Radius of curvature of the anterior lens surface, in mm
r_{1b}	Radius of curvature of the posterior lens surface, in mm

Table 2-1- List of variables and definitions used by Rozema et al. [52] for the calculation of lenticular power in the eye at birth

Utilising Mutti et al [32], values of $n_L = 1.449, c_1 = 0.563, c_2 = 0.386$ & $Q = 0.418$ were determined. Upon determination of the nominal lens power, an estimate of the

power of the entire eye may be found using the Gullstrand thick lens equation as an approximation of the eye.

$$P_{eye} = \frac{1000(n_c - 1)}{r_{ca}} + P_L - \left(\frac{1000(n_c - 1)}{r_{ca}} P_L \ \frac{ACD + CCT - c_{L1}}{1000n}\right)$$

Hung et al [18] expand upon this concept with their MATLAB model which provides simulations of axial growth incorporating defocus and genetic pathways to arrive at an estimate. They also provide scenarios in tutorials for unregulated and regulated growth environments with the ability to manipulate input data such as the introduction of lenticular blur.

Flitcroft [12] presents a single function in a discussion of emmetropisation made up of grouped biological mechanisms in turn composed of component parameters as shown below.

$$R(t) = R_0 + E_g(R_0 - R_S)\left(1 - e^{-\frac{t}{E_t}}\right) + R_c\left(0.07295^{a^{t-t_0}}\right) + G_n(t) + G_b(t)$$

Element	***Description - relevance***	***Grouping***
$R(t)$	Refraction at time (t)	--
R_0	Intrauterine/Genetic organogenesis	Early Variation
E_g	Gain of Emmetropisation	Regulation and Stability Emmetropisation
$(R_0 - R_S)$	Emmetropisation Set-point	Regulation and Stability Emmetropisation
$\left(1 - e^{-\frac{t}{E_t}}\right)$	Sensitive Period	Regulation and Stability Emmetropisation
R_c	Myopic Drift	Myopic Onset, Loss of Stability, Restabilisation
$\left(0.07295^{a^{t-t_0}}\right)$	Progression Pattern & Myopia onset (a^{t-t_0})	Myopic Onset, Loss of Stability, Restabilisation
$G_n(t)$	Growth Related Noise	Biological Noise/ Bias
$G_b(t)$	Growth Bias	Biological Noise/ Bias

Table 2-2 - Biological mechanisms associated with Flitcroft model

The development of a biexponential model by Rozema [14] permitted incorporation into a growth model of the two observed points during emmetropisation where rates of growth shift. This model provides a relatively simply means for application of normative growth curves to existing data sets that replicate observed patters across a very large (n > 650 000 individual values) data set. Table 3 presents the range of coefficients used by Rozema for the expression $a_1 \exp(a_2 \times age) + a_3 \exp(a_4 \times age) + a_5 \times age$.

	a_0	a_1	a_2	a_3	a_4	a_5	r^2
AL	23.61	-3.340	-3.006	-3.217	-0.187		0.993
ACD	3.994	-0.804	-2.695	-0.812	-0.097	-0.011	0.926
CCT	551.7	29.860	-6.731				0.643
P_{eye}	62.57	11.82	-5.845	14.96	-0.399		0.975
P_{ax}	63.04	13.29	-4.981	15.37	-0.351		0.971
SE	$P_{ax} - P_{eye}$						

Table 2-3 - Coefficients of the parameters for biometry fitted to the function $a_0 + a_1 \exp(a_2 \times age) + a_3 \exp(a_4 \times age) + a_5 \times age$ from Rozema 2023 [14]

The underlying problem for all mathematical models is the inherent noisiness of the input data and the susceptibility of the model to errors caused by the complexity of influences such as genetic and environmental factors. Ideally large-scale statistical analysis would allow the isolation and assignation of weight to the complete set of influences to allow an individual developmental model to exist for each individual. While improvements are being made in this space the realization of such a goal is perhaps too complex, so that the management of risk factors in emmetropisation must be an active process incorporating clinical observation of the individual in an ongoing context.

2.5 INTERRUPTION TO EMMETROPISATION

Form deprivation and subsequent myopia (FDM) has been consistently shown to induce axial myopia in experimental animal models, results which have been observed in humans experiencing form deprivation due to hemangioma and eyelid ptosis [95]. The degree of axial myopia correlates positively with the reduction of

retinal image contrast so even low degradation of retinal image quality can yield myopisation. This suggests that visual environmental factors as well as genetic predispositions may contribute to the risk of myopia [96]. Refractive conditions, most specifically astigmatism, can emulate the degradation in image quality caused by externally induced image degradation or physiological conditions. The resulting pattern blur mimics the initial conditions for form deprivation induced refractive errors suggesting that the presence of uncorrected astigmatism in the emmetropisation phase may lead to enhanced risk of FDM [97-99]. It has been noted in animal models that removal of the form deprival mechanisms early enough in emmetropisation permits recovery through normalization of changes to the vitreous chamber and choroidal thickness [96].

Refractive errors induced by lenses effectively modify the overall refractive power of the visual system, in turn demanding that emmetropisation occur in such a way that neutralizes this change in power [95]. In humans this may be encountered through inappropriate prescribing of spectacles in children, although even correctly prescribed powers that utilize an inappropriate lens design may contribute to this effect through the association between binocular vision disfunction and refractive error [100]. Changes due to lens induced effects choroidal thickness; myopic defocus (induced with positive lenses) thickens the choroid, slowing axial growth and shifting the refraction hyperopic. The opposite effect occurs when hyperopic defocus is induced with negative lenses. Once the imposed defocus has been resolved through changes in growth of the vitreous chamber the process ceases [96]. In animal models defocus imposed beyond the limits of the linear response range of the emmetropisation mechanism elicited no response. There may be a risk in these cases of FDM induced by the degradation of image quality however animal models have shown reversal of choroidal changes on removal of the induced refractive error. Atkinson et al [83], in their study of infants with spectacle correction, showed hyperopes who had not worn spectacle correction or wore their spectacles infrequently did not experience any discernible effect on emmetropisation. Children who wore their spectacles consistently were more hyperopic by 3 years of age, suggesting that the lower level of retinal defocus removed a driver for active emmetropisation.

Periodic cycles of hyperopic and myopic defocus have been observed to reduce axial elongation in chicks [22], which has in turn led to the development of multifocal lenses for human use that attempt to replicate this effect. Compared to the cyclical

presentation of defocus used in the research, multifocal lenses are used to present simultaneously competing images with both hyperopic and myopic signals across the visual field. Animal models have shown the effect of refractive change to be equal to the average of the two powers presented to the visual system [101] suggesting that careful manipulation of this effect may help with management of myopisation. Recently spectacle lens designs have leveraged the results of these studies to provide simultaneous defocus across the visual field to interrupt axial length growth. Currently two distinct spectacle lens designs have been released which implement this concept via differing mechanisms. Defocus Integrated Multiple Segment (DIMS) lenses comprise a nine millimetre central zone of distance refraction with a twenty four millimetre ring comprised of approximately 400 1.3mm aspheric lenslets with an apical power of +3.50D providing competing hyperopic and myopic signals. The results of this two-year trial of 160 individuals indicated an attenuation of myopic progression compared to single vision lens wear. Mean refraction difference was -0.44 +/-0.09D (52%), and reduction of axial length growth mean difference of 0.34 +/- 0.04mm (62%)[102]. Three-year results presented an addition line of treatment through the addition of a group of subjects transitioned into DIMS lens wear to evaluate the effect of change of treatment modality. Relative to the historical control group DIMS lens wear attenuated mean myopic progression in line with previous years by 0.18 +/-0.42D and axial length growth by 0.08 +/-0.15mm [103]. Switching to DIMS lenses in the third year of the trial slowed myopic progression by 0.30 +/-0.42D and axial length by 0.12 +/-0.16mm. The DIMS study concluded that the optimal age for interventive strategies had yet to be determined and the long-term efficacy of the treatment was not known due to the relatively short timescale of the studies.

An alternative approach uses concentric aspheric rings of power in the lens to induce defocus across a volume as opposed to the individually defined lenslets of the DIMS design. Bao et al [57] in their 2021 study compared slightly aspheric zones (SAL) and highly aspheric zones (HAL) with single vision lenses across a twelve-month period to gauge the efficacy of this approach. At twelve months the change in SER for HAL was -0.27 +/- 0.04D, SAL -0.48 +/- 0.05D and SV -0.81 +/- 0.06D indicating an efficacy of 67% myopia attenuation for HAL lenses compared to SV (SAL 41% compared to SV). Axial length results at twelve months were HAL 0.13 +/- 0.02mm, SAL 0.25 +/-0.02mm and SV 0.36 +/-0.02mm, indicating a reduction of axial length growth of 0.23mm (63.8%) for the HAL lens over SV. This study observed an

association between lower age with faster myopic progression and axial lengthening for SV wear, an association that was not found in the HAL group where change was consistent across all age groups. This suggests HAL type lenses may be an effective intervention technique for younger individuals. The authors indicated a significant hyperopic shift was observed in 20% of individuals with AL reduction in 26% of individuals although the magnitude of hyperopic shift was not indicated, and the statement of AL reduction was also not substantiated beyond a percentage. It is unclear whether the claim is that AL was physically reduced, or the AL was reduced in relation to the SE and other metrics for emmetropisation. These two applications of peripheral defocus (HAL and DIMS) yielded similar overall results in terms of axial length progression with the HAL lens exhibiting slightly more refractive error progression over the same period. As axial length provides a more objective result than refractive error it will prove to be the more reliable indicator of progression when comparing these studies.

Participants in the preceding studies had similar inclusion criteria (up to -5.00D and -4.00 SER respectively) and exhibited similar results in attenuation of myopic progression and axial length growth. Of interest is the mean refractive error, which in both studies was in the order of -3.00D SER. This indicates the effect of either DIMS lenslets or HALT regions resulted in the areas of peripheral blur being positive powered (>0.00D) compared to the overall negative power of the individuals' correction and therefore majority of the lens power. The results given thus far for these two lenses designs would therefore appear to indicate good efficacy in cases where the absolute magnitude of distance refraction is less than the absolute magnitude of the defocus provided in the peripheral regions of the lens. The limited time scale of the studies only allows application of the results to the period represented by the studies and does not permit extrapolation. While specific results are not provided for cases where the distance refraction exceeds the magnitude of the peripheral defocus it would provide further insight into the role of defocus in the attenuation of myopisation.

Accommodation was speculated to be a contributing factor in myopisation with compensation for the defocus that drives accommodation influencing emmetropisation either through lenticular compensation or atropine. Animal studies have since decoupled the effects of atropine and lens induced defocus correction [96]. Diether and Wildsoet found in their investigation of accommodation in chicks [20] that when accommodation was impaired, the decoding and compensation for defocus was

similarly inhibited. This suggests that accommodation may play a role in emmetropisation by decoding the defocus presented at the retina although the proposed mechanisms for this interaction are complex and poorly understood [99].

An alternative approach to optical defocus as a control mechanism for myopic development is the use of contrast to attenuate axial growth initiation signals in the developing eye. Rappon et. al. in the Control of Myopia Using Peripheral Diffusion Lenses Efficacy and Safety Study, suggested that a cellular defect in cone receptors causes abnormal contrast signalling between neighbouring cells, and this false high contrast signal is an initiator of axial growth [104-106]. It was posited that due to the accommodated eye experiencing less vergence related blur during indoor activities, that optically imposed diffusion or contrast reduction may provide a control mechanism for myopisation. Unlike optically imposed blur through the application of defocus, contrast reduction was achieved through translucent diffusers approximately 0.14mm in diameter and 0.2mm in height. Radial curvature was irregular with steeper sies and a flattened top with the intention of scattering light (i.e. diffusion) to reduce contrast. A central aperture of approximated 5mm was left clear of diffusers. For the study two spacings were tested (test 1 = 0.365mm spacing, and test 2 = 0.240mm), with the lower density, or greater spacing, showing greater efficacy in reducing axial elongation (0.15mm, $p<0.0001$ reduction) compared with higher density (0.10mm $p=0.0018$). Spherical equivalent refraction progression was reduced by 74% (-0.40D $p<0.0001$) for test 1 and 59% (-0.32D $p<0.0001$) for test 2 compared to the control group.

Measurement of biometric components of the eye to understand the progression and potential deviation of emmetropisation is becoming an increasingly prevalent feature of developmental optometry. For determination of these parameters the most common devices used are biometers which utilise optical partial coherence interferometry [107] which in effect are re tasked devices for the calculation of replacement intraocular lenses [108]. Compared to previous measurement techniques utilising A-Scan ultrasound, optical biometry techniques are up to 10 times more accurate [109] with repeatability of approximately +/-0.04mm [110-112]. In practice, optical biometry is preferred as there is no need for anaesthetic or direct contact with the eye. While the preceding references all tend to be oriented to the determination of optical biometry for myopia, the techniques are directly transferrable to all refractive conditions and biometric development, including emmetropia [43].

The usage of optical biometers for the determination of biometry is subject to the limitations of the devices initial purpose, namely the determination of the required power for an intraocular lens. Consequently, the parameters of the existing crystalline lens are not commonly determined, as these represent values that are not relevant to the requirements of the optical system post-surgery. For the device used in this study (Nidek AL-Scan) the unit allows implementation of one of several formulae to determine the required power of the IOL in the context of the other measured biometric elements in the eye [113]:

- SRK (Sanders-Retzlaff-Kraff), SRK II and SRK/T
- Carmellin-Calossi
- Shammas-PL
- Binkhorst
- Hoffer Q
- Holladay 1
- Haigis

Using the SRK expression as an example

$$IOL = A - 2.5AL - 0.9K - DR(0.0875A - 8.55)$$

Where A='A constant' for a given IOL, AL=axial length (mm), DR=desired postoperative refractive error, K=corneal refractive power (D) ($K = (n_k - 1000)\frac{1000}{R^{-1}}$. Or for zero refractive error:

$$IOL = A - 2.5AL - 0.9K$$

This indicates that despite the increased range of measured values incorporated into the biometric environment, there are still several normative or *a priori* values being applied (*A, DR,* n_k). Knowledge of these values is important in practice, particularly when results of differing units are being compared. The Nidek AL-Scan has been the subject of 9 studies indicating good alignment with the results of other known devices used in biometric monitoring during emmetropisation, such as the IOL-Master [114-122]. Studies such as Hoffer et al [118] have indicated that overall axial length results are in close agreement between the IOL Master and AL-Scan, with

differences appearing in the composition and ratio of the individual refracting elements of the eye. Comparison between the DNEye Scanner and established devices such as the AL-Scan do not currently exist, the section of this research project pertaining to the comparison of the DNEye Scanner to a known known measurement device represents new data for the field. As the DNEye Scanner is a currently unique application of an existing hardware platform in the market, the patent documents have been used to outline the techniques and methodology by which the results are determined [123, 124].

The Rodenstock DNEye unit represents a novel application of an established wavefront biometer (Visionix VX110) incorporating an autorefractor, corneal topographer, pachymeter, and aberrometer [124]. The biometry of the eye may be defined as a sequence of 12 degrees of freedom, of which it is not necessary for all to be known or defined by direct measurement in any given case, although the robustness of a specific case may be defined by the ratio of measured to calculated values. The elements are defined as the refractive surface power matrix of the cornea C (3), surface refractive matrices of the lens L (L_1=3, L_2=3), the length parameter of the anterior chamber d_{CL}, lens thickness d_L, and the vitreous body depth d_{LR}, totalling 12 elements [124]. This patent document provides sources for this data (i) direct measurement, (ii) values described in literature (a priori), and (iii) calculations from consistency conditions such as known relationships to refractive errors. The authors describe these collectively as $df_{2,}$ which is comprised of the combination of the three defined sources, in turn which must total 12 in order to provide definition of the overall biometry of the refracting system. While any combination of the elements is possible, the most advantageous combination is one that is biased towards measurements in category d(i) e.g. df2=6+4+2, however in these cases the system risks being mathematically overdetermined (i.e. df2>12). As a spot source of light may be used to propagate a wavefront from the retinal surface it is possible to determine values for the vergence of light at the posterior (L2) and anterior (L1) surfaces of the crystalline lens via calculation. The inventors of the device note that while it is possible to arrive at values for the complete biometry of the eye, this does not constitute measurement except in the case of those elements whose parameters have been directly measured.

Beyond the patent documents there are currently no published research data investigating the repeatability of the results of this process, or comparisons to known optical biometers currently in common usage. This represents a novel area for

exploration in the context of this study. The application of this process in the generation of individual best form designs for spectacle lenses has, however, resulted in a significant database of over 500,000 eyes, from which normative models have been developed for eyes grouped according to refractive error. As these are proprietary techniques, there is again no published data on the results. However, their implantation into commercially delivered products suggests a confidence in the success of the modelling which warrants further study outside of the industrial development groups.

2.6 GENETIC FACTORS

As refractive error is comprised of a deviation from an optimal relationship between the biometry and refracting elements of the eye, genetic variation plays a significant role in the initial conditions and eventual susceptibility to refractive error.

Developments in genome mapping have allowed for the relationship between specific single nucleotide polymorphisms (SNP) and the refractive outcomes of an individual, in effect looking for a genetic predisposition towards specific conditions. Genome wide association studies (GWAS) rely in significant data sets to extrapolate relationships with both 23andME and the Consortium of Refractive Error and Myopia (CREAM) providing large sets. It should be noted that both of these data sets are European, so linkages to refractive and biometric outcomes are still subject to confounding effects from environmental factors.

As with many of the current studies in refractive outcomes during emmetropisation, the primary focus is identification of factors and triggers for myopisation. Identification of a gene linked to a single ocular function may however generate results relevant to other refractive outcomes. The number of biometric ocular components and processes involved in emmetropisation and the number and relationship between loci is quite large, and has been steadily identified despite the current bias towards identifying loci involved in myopisation. Given this complexity of interaction leading to ametropia, the observed overlap between genes identified for differing refractive outcomes is unsurprising, it may therefore be difficult to separate the pathways leading to specific outcomes from those more generally associated with ametropia.

Currently GWAS studies have identified approximately 30 points of susceptibility with associations to refractive outcomes with an overall contribution of

under 12% [125-128]. An association with between one specific SNP (rs12193446) and risk of myopic progression was found to be age dependent with a peak risk at 11 years of age, dropping thereafter [127]. Using the Online Mendelian Inheritance in Man (OMIM) database, Flitcroft et al. [129] identified 219 individual cases of ametropia with 167 of these having had at least one causative SNP isolated. From this set 154 unique genes associated with refractive error were identified, 119 associated with myopia, 42 with hyperopia and 23 with astigmatism. The majority of these were autosomal, for myopia 107 vs 12, indicating significant gender independence for the genetic influence on refractive errors [129]. Of note is this study's ability to associate ametropic conditions with genetic pathways. Myopia was linked with processes such as lens development, gliogenesis and Schwann cell differential while hyperopia appeared to be linked more strongly with processes associated with organogenesis. Lin et al. [130] confirmed a reported association between the AREG gene and myopia [125] which had been observed as increasing axial length in guinea pig studies. The AREG gene is specifically expressed in human retinal pigment epithelium and is therefore related to the structural changes of the eye that occur during emmetropisation, notably those associated with axial length. In their discussion of genetic influence on emmetropisation, Siegwart et al [90] indicate that axial length development during the infantile and juvenile periods is driven by genetic factors rather than environmental.

Classical twin studies represent the earliest attempts to isolate genetic causes for ametropia, with the earliest reoccurring in 1922 [131]. The results of this study found monozygotic twins displayed greater similarity than dizygotic twins and heritability of refractive conditions of 85%. Flitcroft proposed that anisometropia is evidence of stochastic influences on the aetiology of refractive error as two different refractive outcomes are observed between the eyes of a single individual [12]. He further noted that the significance of the association between twins decreased with an increase in refractive error beyond 0.50D difference between SE for twins and with higher magnitude spherical equivalent powers. Using data from Sorsby et al. [132], Flitcroft observed that for SE powers up to 0.50D 4% of twins displayed a difference in SE of >0.50D. Beyond the 0.50D threshold up to 2.00D 30% of twins displayed a difference of SE of 0.50D or more while beyond 4.25D SE 80% of twins had greater than 0.50D difference in SE. More generally, recent research has displayed a range of heritability results from 8-14% in the case of Angi et al [133] to 90% for Hammond et

al. [134]. The IMI Myopia-Genetics report, as part of its review of genetic contribution, indicates that studies assessment of contribution of heritable factors to refractive error range between 15% and 98% [135]. This broad range of estimated contributions from heredities is indicative of the complexity of interaction between environmental and genetic factors. Axial length, lens thickness and corneal power display varying degrees of heritability from 40% to 90% with emmetropic children of myopic parents exhibiting longer axial lengths in line with their parents [90, 136]. As classical twin studies heritability results are representative of both environmental and genetic influences on refractive outcomes for a population, they may not reflect individual risk assignation [136]. Furthermore, there is an assumption of complete matching of environmental influences which may overstate the influence of heritability as it is unclear whether environmental factors work independently or in concert with genetic factors [136, 137].

There are a limited number of situations in which emmetropisation fails to occur, such as Down's syndrome [28, 138]. In the matched cohort study by Doyle et al. of 50 individuals with Down's syndrome, emmetropisation failed to happen in a majority of children, with most (80%) displaying hyperopia at 15-22 years in line with initial birth conditions for the general population of +2.50D [28]. Myopia was present in 18% of individuals, emmetropia in 2% and visual acuity was 6/12 or better in 63% of individuals. In similar aged cohorts without Down's syndrome emmetropia represents 83% of individuals with myopia and hyperopia in 13% and 4% respectively. The continuity between numbers of myopic individuals and inversion of hyperopic and emmetropic individuals provides further confirmation of the existence of the failure of emmetropisation in these cases. The same linear relationship between axial length and refractive error was observed between both groups. The distribution of refractive error at birth is also similar between both groups indicating the failure of emmetropisation in the children with Down's syndrome. While change in refractive error has been observed in children with Down's syndrome it tends to be an exacerbation of existing refractive error rather than a trend towards emmetropia [138]. Also, in contrast to normal emmetropisation the rate of change in power was not related to initial refractive error but to the error observed later in life with the rate of change to thirty months of age providing an indicator of future development. This has led to the suggestion that in this particular cohort, an opportunity exists to examine the influence of genetic factors on refractive and biometric conditions within the eye without the confounding

effects of environmental influences [90]. This particular set of conditions, while presenting a unique opportunity to look more deeply at genetic factors in ametropic development requires further investigation.

Parental ametropia also points to future ametropia risks for children, particularly for myopia to the extent that it has become one of the most common points addressed in clinical practice when assessing risk. Mutti [139] indicates that one myopic parent gives an odds ratio of 2.05 while two parents increases the ratio to 4.92 for myopic progression with heritability in the order of 80% to 100%. This is supported by family aggregation studies which have shown risks of 1.3 and 9.5 respectively for one and two myopic parents respectively [140].

Ehrlich et al. [80] observed that refractive error at birth has been observed to be correlated to the rate of emmetropisation and eventual refractive outcomes. The overall tendency to hyperopia at birth and subsequent emmetropisation displaying a negative power trend indicates that low hyperopic powers (+2.00D) at birth will tend towards emmetropia while powers below this threshold will be at greater risk of myopisation. Zadnik et al. [141] indicate that powers at or below +0.75D, measured under cycloplegic condition, at 6 years of age are considered to be at risk of myopisation, providing a set of initial conditions that may point to future refractive results during and after emmetropisation.

2.7 ETHNICITY

Along with parental history of refractive error, ethnicity represents one of the simplest ways to identify risk factors for refractive error in a normal clinical setting as it may be determined simply through direct questioning of the individual or family members.

The influence of ethnicity on deviation from normal biometric and refractive development has received increasing attention over recent years. The most prominent relationships appear to be those between myopisation and people of East Asian backgrounds. Logan et al [4] who looked at 327 children aged between 6 to 7 years old and 269 children aged 12 to 13 years old and investigated the prevalence of refractive error and ocular biometry across multiple ethnicities. It was found that myopia was more prevalent in the older group being 29.4% versus 9.4% and also higher in South Asian children in the older group compared to White European children being 36.8% and 18.6% respectively [4]. This is in line with an older study

by Rudnicka,. et al [67] in the Child Heart and Health Study England (CHASE) study where South Asians had the highest prevalence, followed by African Caribbean when compared to White Europeans. Similarly, the Sydney Myopia Study by Ip, et al[65] examined 2353 Australian students of various ethnic groups aged between 11 and 15 years. It was found that myopia prevalence was lower among White European children (4.6%) and Middle Eastern children (6.1%) than among East Asian (39.5%) and South Asian (31.5%) children [65].

The CLEERE study provided a direct comparison of ethnicities within one study [142] coming from one country. In this examination of 2523 children, it was found that the prevalence of myopia was greatest for Asian children (18.5%) and Hispanic children (13.2%), while African American children (6.6%) and white European children (4.4%) were lowest. By examining differences due to ethnicity within a single country this study provides a meaningful look at ethnicity in isolation from other factors such as geographical, education and socio-economic difference between nations. This study nonetheless demonstrates the observed tendency towards myopia for children of Asian and East Asian ethnicities compared to other groups.

Kleinstein et al. indicate that the prevalence of hyperopia is greatest among white populations, 19.3% >+1.25D but as high as 32.4% >+1.00D [63]. Hispanic children (12.7%) were the next highest representative group, while African American populations exhibited a 6.4% and East Asian populations exhibited a 6.3% rate of hyperopia presentation among children. Similar relationships between groups were shown by the Logan et al. Aston Eye Study [4] with white European (22.9%,), South Asian (10.3%) and African Caribbean (9.1%), These results also agree with those of Borchert et al which indicate rates of hyperopia for white European descent children (25%) and Hispanic children (23%). There is variation in the representation of African American children with hyperopia (17%) compared with the CLEERE results (6.4%). This may be due to the age of the participants in each study, approximately 10 years of age for CLEERE and <72 months in the case of Borchert et al. as the rates for older children in the other ethnicities decrease as well.

While the prevalence of hyperopia among ethnicities is greatest for white populations, the classification is broad and makes it difficult to draw conclusions regarding the significance of this data for more specific groups within the White European population. Nonetheless, Foster et al [143] determined axial length to be strongly inversely correlated with refractive error with a similar association between

anterior chamber depth in women, but not men. In this adult population myopia accounted for 27% (<-0.50D) of the 2210 individuals, emmetropia 21% (-0.49D to +0.49D) and hyperopia 52.2% (>+0.50D).

The presence of significant (>1.00D) astigmatism may be linked to ethnicity and have longer reaching effects, such as blurred pattern vision due to astigmatism which itself may be a contributing factor to myopic progression [144, 145].

In the longitudinal study of 522 eyes in East Asian children by Fan et al [144], astigmatic error > 0.50D was observed in 55.8% of children, with 21.1% of children exhibiting astigmatism of >1.00D. At the initial presentation it was noted that higher astigmatic results tended to correspond with higher hyperopic spherical readings which then changed to an association with higher myopic readings five years later indicating a relationship between astigmatism and myopic shift. Compared to the results of the CLEERE study where Asian populations were studied in a geographically distant location (the USA), Asian children appear to be more likely to have astigmatism >1.00D in the USA (33.6%) compared to China (21.1%).

The CLEERE study also indicated a high prevalence of astigmatism among North American Hispanic populations, 36.9% for >1.00D and 20.5% >1.25D, with East Asians and Hispanics exhibiting the same risk regardless of age or sex. Brazilian indigenous populations are notable in that they displayed very low rates of myopia (2.7%) and hyperopia (5.05%) [63]. Astigmatism occurred in 13.2% of the individuals, however was observed to be present in 78.6% of myopes and 29.6% of hyperopes, which is in keeping with the reported higher incidence of astigmatism among myopes and hyperopes but still higher than other populations in the same geographical area.

Ip et al [34] in a study of 6- and 12-year-old children of East Asian and White European determined at 6 years of age there was no significant difference between ethnic groups and the correlation between SER and axial length (13% and 19% respectively). By 12 years of age continuing axial elongation in the East Asian cohort was identified as a contributing factor in the differing rates of myopia relative to the White European cohort. This process of continuing elongation was also more prevalent in the East Asian cohort and was associated with greater variability in corneal curvature. There was no other relationship determined with anterior chamber depth and lens power. The relationship between ocular biometric parameters and ethnicity appears to gain significance after emmetropisation has taken place and once refractive errors have established.

Native American populations have displayed rates of astigmatism greater than 1.00D of over 45%, significantly greater than 5% incidence for the same geographical population of approximately six years of age [146-148]. Goss [147] observed a correlation between parental lineage and prevalence of astigmatism. Children with both parents of full American Indian ethnicity made up 39% of the astigmats and 23% of overall participants in the study, declining to 19% (11% of total) who identified as ¼ Native American. In this particular study 59.33% of the total participants exhibited astigmatism suggesting a ratio of 1.46 astigmats to non-astigmats. Social and genetic influences cannot be ruled out in this instance, with high numbers of observed cases of albinism suggesting inter-familial relationships could play a part in these figures. Similarly, many subjects in these studies displayed signs of current or past chronic lid infections, which may contribute to the rates of astigmatism due to pressure from the lids on the cornea during emmetropisation [148, 149].

2.8 ACCESS TO HEALTH CARE

The twentieth century has seen one of the greatest upheavals in global socio-economic conditions in human history with significant changes to the way in which populations access health care, education, and development opportunities.

Limited access to health care was identified as an independent risk factor for development of refractive error in the study by Borchert et al. of 9970 children aged 6 to 72 months of age [6]. Similarly, multivariate logistic regression indicated astigmatism, age <36 months, ethnicity (African American or Hispanic) and testing location to be independent risk factors. Access to health care and health insurance is most often linked to the socio-economic status of a region which may be indicative of a link between ethnicity, affluence and elevated risk of refractive error due to reduced access to early intervention strategies for ophthalmic complaints. This is at least partially supported by the studies in Native American populations in which refractive error was observed at higher rates with evidence of current or pre-existing chronic lid infection [147-149].

A marked difference in distribution of refractive errors has been noted between urban and rural populations during and after the process of emmetropisation. Studies conducted on Chinese populations have noted relatively consistent findings between urban and rural populations < 5 years of age, with myopia being relatively rare (<5%

incidence) [150]. These results are consistent globally with South Africa, Chile, Malaysia, Nepal, and India reporting similar findings for consistent testing protocols (1% cyclopentolate and refraction using autorefractor confirmed by retinoscopy) [59-61, 151, 152]. By 15 years of age the prevalence of myopia in urban Chinese populations increased to 78.4% while rural populations from Northern China reported rates of 36.7% for males and 55% for females. Other confounding factors such as ethnicity and genetics may not be accounted for in this instance, so it is of note that while the initial conditions for refractive error are relatively consistent globally, differentiation arises during emmetropisation that correlates with the population density of the local area. This study noted that the risk of myopisation nearly doubled for children in an urban setting with no influence from gender, grade level or parental education. These results have been replicated in other regions such as India, Nepal, and Malaysia, all suggesting that individuals of the same ethnicity will experience differing refractive outcomes depending on urban density and time spent in education [153-156].

Considering the relationship between education levels and ametropia, Fan et al. [125] determined high education levels are associated with 0.59D greater magnitude of myopia (or weaker hyperopia) compared with the lower education group. The meta-study grouped 50 351 individuals from 34 studies into two educational categories, individuals with higher or university education and those with lower secondary education or less. A total of 50.4% of European participants and 30% of Asian participants satisfied the higher education criteria. The study also confirmed links between ethnicity and ametropia with students of Asian descent exhibiting greater magnitude of myopia (-1.09D) compared to European descent (-0.49D) with Singapore Chinese (-1.75D) exhibited greater than other Asian Cohorts (-0.60D) [125].

A study into the prevalence of refractive errors in adopted children from eastern Europe indicated a higher than normal frequency of ophthalmological findings [157]. These individuals were often from lower socio-economic groups yet were of White European or Caucasian ethnicity, allowing an analysis of individuals of an ethnic group with relatively scarce access to health service. In this study 30% of the children were born preterm and 47% were considered to be of low birth weight. 10% of the children were myopic, 22% hyperopic and 55% astigmatic, compared to the control group these individuals had at least twice the prevalence of each of these refractive

errors. Overall, 78% of the children had some form of ophthalmological finding when including visual acuity, strabismus, amblyopia, stereo vision defects, refractive error, glaucoma and cognitive visual issues [157]. Evidence of prenatal alcohol abuse was extant in 33% of the children in this study which is a higher rate than the generally stated 19%. Other studies of adoptees performed internationally have been longitudinal which precludes meaningful comparison between studies, however the socio-economic conditions that lead to higher likelihood of adoption have been observed as a common thread. Looking at immunization as an indicator of access to primary health care, Hostetter et al. determined that up to 77% of adopted children had not completed immunization schedules [158]. Taken as a general indicator of the deleterious health conditions experienced by the children, a correlation is seen between the initial health care, socio-economic conditions, and the likelihood of poor refractive outcomes later in life.

Perhaps the strongest conclusion that may be drawn from the consideration of environmental factors on ophthalmic outcomes is that understanding is confounded by the sheer complexity of interactions between influential factors. It appears that, sadly, while multifactorial influences such as ethnicity and geographic location may exacerbate negative outcomes, the only factors that may have protective effects are those pertaining to daylight exposure [159].

2.9 BIRTH WEIGHT

Preterm births have been associated with elevated incidence of refractive abnormalities with up to eight times the rate of incidence compared to full term births as well a linkage with impaired emmetropisation [39]. Potential causes of this include complications stemming from preterm birth, disease, or premature stimulation of the visual system too early in its development. Refractive impairment presents as a failure of the refracting components and physiological elements of the anterior eye with increased corneal curvature, higher power of the crystalline lens and relatively shallow anterior chamber [160, 161]. This is in contrast to myopisation during emmetropisation where axial length is the dominant cause of refractive error [162].

Early studies indicated a linkage between low birth weight in premature babies and elevated incidence of myopia [163]. In normal birth weights of 2500 grams or higher the distribution of refractive error observed was normal with mean refraction

of +0.62D at 10 days or less after birth, a value which differs from current data and may suggest a degree of unreliability in the findings at that point in time. Nonetheless, low birth weights of less than 2000 grams were observed to be predominantly myopic, particularly in the presence of retrolental fibroplasia or retinopathy of prematurity (ROP) [164, 165]. Choi et. al [160] indicated that myopia was found in 67.2% of subjects studied with ROP suggesting strong linkages between preterm birth, ROP and refractive error, although the relationship between treatment for birth complications and preterm birth itself on refractive error is yet to be established. In these cases, the magnitude of refractive error present at young ages appears to remain once established, at one year [166-168], potentially continuing to develop up to three years of age [160], suggesting emmetropisation does not occur in these cases, or is attenuated in the presence of ROP.

More recently, studies have supported the early evidence that low birth weight may be linked to refractive error in later years [169-172], again with a bias towards myopia. Fiess, et al [172] in their research found that low birth weight was linked to visual acuity and long term refractive outcome and that low birth weight babies were more likely to have lower visual acuities and higher myopic refractive error in adulthood. In another paper by Fiess, et al [169] linear regression showed axial length as the reason behind 58% of variance in spherical equivalent on low birth weight subjects and 54% in normal subjects while corneal power only accounted for 1% of the variance in both groups, highlighting axial elongation as the more likely mechanism behind myopia development. Similarly, Plotnikov, et al [170] in their research found that lower birth weights within the normal range was causally associated with more myopia, however the impact of the effect was modest being 1.00D across 95% of the population.

Smoking by either parent during pregnancy has been associated with decreased risk of myopia and maternal smoking in particular with increased prevalence of hyperopia (27%) [5, 6] after adjustment for ethnicity, income and education. These results are similar to those of Ip et al. [173] which indicated maternal smoking was more frequent among hyperopes at six years (16.4%) and 12 years (21.6%). Jiang et al. [174] found risk increased with severity of hyperopia, with low to moderate hyperopia (28%) risk increasing to high hyperopia (64%), however even a low amount of smoking was associated with some elevated risk of high hyperopia developing. Studies have suggested that nicotinic acetylcholine receptors may regulate ocular

growth, inhibiting axial elongation through the suppression of the muscarinic acetylcholine receptors and subsequent form deprivation myopia [175]. Low corneal curvature radii to axial length ratios rather than solely low axial length have been observed to be a primary contributor in hyperopia in children, while maternal smoking has been linked to abnormally low axial length [174]. These mechanisms are not well understood in relation to the persistence of hyperopia but may be linked to the suppression of emmetropisation.

2.10 STUDY HABITS

Plotnikov et al [176] examined the relationship between education and refractive outcomes as a function of time spent in education. This study recruited 502,649 participants aged between 37 and 73 years of age encompassing the period when the Raising of the School Leaving Age (ROSLA) from 15 to 16 years of age was implemented in England and Wales in 1972 [176]. The ROSLA 1972 reform was associated with a −0.29 D more negative refractive error and regression discontinuity analysis estimated the causal effect on refractive error as −0.77 D [176]. He et al. [150] noted that the development of ametropia roughly coincided with the commencement of formal schooling while the study by Sun et al. of 5060 university students found that myopia was more prevalent in post graduate students (96.9%) compared to undergraduates (94.9%) suggesting some linkage between time in study and refractive outcome [156] . The 2002 study by Loman et al. also found similar results with a myopic increase in 86% of participants, which was associated with a reduction in daylight exposure [177]. Studies on Native Alaskan, Yupik and Inuit populations in the mid twentieth century also suggest an increase the prevalence of myopia with the introduction of formal schooling [98, 178, 179], these studies represent an interesting set of data through their ability to track changes in refractive outcomes through a period of significant socio-economic development. Young et al. [98] in a cohort of 41 family units with 197 individuals noted the correlation for ametropia between siblings was highest, suggesting environmental factors were contributing to the refractive outcomes. Additionally, despite a relative absence of myopia among parents (1.5%), myopic prevalence among the children was 44.7%. It was postulated that in addition to changes in education, additional interrelated influences such as changes to housing and diet contributed to such a significant change across a single generation.

Developing the idea of a link between education, intelligence and refractive outcomes, very early studies used intelligence quotient to determine risk for myopia [180]. The results have not been consistently replicated in modern studies which more effectively differentiate between the contribution of multifactorial influences. The Twin Early Development Study was only able to find a weak relationship between intelligence quotient (IQ) and refractive outcome, with a 1.5% myopic variance attributable to IQ alone [181]. Contrasting this are the results of Williams et al. who in a study of 2871 children found a risk for myopic increase for 7 to 10 year old children which was linked to their performance in reading and maths tests [182]. They found IQ scores to be predictive with Weschler Objective Reading Tests (Odds Ratio (OR) 4.64 $p=0.001$), SATS tests (reading OR 4.19 $p<0.001$, maths OR 3.05 $p=0.008$) with verbal IQ tests performing more weakly (OR3.52 $p=0.055$) as a predictor for myopia. Parental assessment of the child's engagement with education related tasks showed more significant results, a parental indication of the child enjoying reading showing an odds ratio of 12.89 ($p=0.031$). As there is a strong association between results for IQ tests, education, and other environmental factors the ability to effectively isolate the confounding environmental influences is key to assigning reliability to results in this space, currently it may not be possible to confidently achieve this. In the case of Williams et al. one further outcome was the confirmation of the linkage between ethnicity ($p=0.129$) and number of myopic parents ($p=0.014$) and risk of ametropia in a UK population [182].

Near induced transient myopia (NITM) has been defined as the short-term myopic far point shift immediately following a sustained near visual task [183]. The relationship between NITM and progression of refractive error amongst 223 students of the Beijing Myopia Progression Study was examined by Lin et al.[184]. After adjusting for risk factors it was found that NITM was associated with hyperopic children for every 1D increase in the initial NITM at baseline there was a relative -1.48D myopic refractive shift [184]. A possible cause of this is increased variability of the NITM response and ciliary muscle spasm, however no association was found between NITM conditions and refractive change for either emmetropic of myopic students when adjusted for the same risk factors as hyperopes [184]. These findings differ from those of the same author in 2013 in respect to anisometropes. where for two thirds of the subjects the initial NITM and subsequent decay was notably higher in the more myopic eye [185]. Similarly, Sivaraman et al [186] in a study of NITM in

two groups of Indian subjects viewing targets at 0.2m for 5 minutes and another group viewing for 60 minutes, found the magnitude of the NITM was higher in myopes compared to emmetropes for both groups.

2.11 NEAR WORK

The relationship between time spent on near tasks and myopia may be subject to a complex interplay between elevated time performing near work tasks related to education, the impact of this on outdoor time and binocular vision effects and gaze behaviours. In the International Myopia Institute white papers in clinical management guidelines, Gifford et al [100] report binocular vision assessment is an important tool in risk management of myopia. AC/A ratios, esophoria, and accommodative facility deviate from normal values although if this is a causal relationship is still unclear.

While studies have been performed examining the role of time spent on near tasks in ametropic development, the linkage is not as clear as early studies into education and myopia risk suggested. The work of Lanca and Saw was unable to establish an association between screen time and myopisation in a cohort of children aged 3 to 19 years [187]. Confounding factors such as ethnicity, genetics and socio economic conditions are difficult to isolate, furthermore the identification of the specific nature of near work being performed (reading, computer, hand held device etc) is also a confounding element [99]. This is exacerbated by the variability of distances at which an individual will hold material for near vision tasks. The Harman distance from the elbow to the middle knuckle has been examined by Richards et al, with no association found between this physiologically defined unit of measurement and the habitual working distance for near tasks [188]. Metrics used for definition of near work are also inconsistent, primarily concentrating on time spent on near work as a common thread. Hybrid units such as dioptre-hours look at working distance and time relationships but are not consistently implemented across the assorted studies.

The Handan Offspring Myopia Study, after adjusting for confounding factors, also failed to establish a causative relationship between near work and myopia [189]. The only meaningful association for this study occurred in the high near work, relatively low outdoor time subgroup, further suggesting a more complex interplay of factors than near work alone. Longitudinal studies, such as that performed by Zadnik

et al. [190] examined populations from the United States, Australia, Taiwan and Singapore and also did not find near work as a risk factor in isolation.

Hyperopic retinal defocus experienced during accommodative lag has been observed in animal studies to trigger axial lengthening [191, 192] however the results from human studies are inconsistent. It has been suggested by Mutti et al. [192, 193] that hyperopic defocus in humans may be an effect rather than a cause of axial lengthening. Accommodative lag has been observed as occurring both prior to myopic onset [194, 195] and post onset [192] making the role of accommodative lag as an isolated risk factor inconclusive. Conversely, Yu et al. [196] found a significant correlation between accommodative lag value at 20cm and the magnitude of myopia in a study of accommodative accuracy at a range of near work distances. Harb et al [99] suggest that the vergence system be considered in conjunction with accommodative function and offer indirect evidence of this linkage. They suggest that the relatively increased efficacy of progressive powered spectacle lenses (compared to single vision) in the control of myopia with large accommodative lag and near esophoria is evidence of this effect, as observed by Mutti et al. [93]. Secondly, near addition prismatic bifocal lenses were observed by Cheng et al [197] to slow myopic progression in children with low accommodative lag and annual progression rates of 0.50D or greater.

Studies on gaze behaviour are relatively rare, however, Harb et al [198] determined that myopic adults take fewer breaks from sustained near work, potentially due to the relative ease of maintaining near focus due to the nature of their refractive error. Taking fewer breaks from near tasks may reduce the protective effect of gaze breaks as the retinal defocus pattern experienced during distance vision aids in emmetropisation [191].

2.12 OUTDOOR ACTIVITY

Recently, multiple studies have indicated outdoor activity provides a protective effect with regards to myopisation. As with many other aspects of risk identification there is a lack of standardization of methods which complicates comparison of results, however the emerging consensus is that reduced outdoor activity combined with high levels of near work represents a significant risk of myopisation, as indicated by Rose et al. in the Sydney Myopia Study [199]. Jiang et al observed a 31% risk reduction

linked to longer time spent outdoors [200], however there was no observed effect on the progression of preexisting myopia. Lower levels of outdoor time displayed longer axial lengths and faster axial elongation [200]. This effect was also observed by Guo et al in their 4-year study which associated shorter axial length with outdoor exposure [201]. The IMI White Papers concluded that 8-15 hours of outdoor exposure per week provides a reduced risk of onset, but not protection against existing development [100]. Further establishing the multifactorial nature of ametropic risk is the findings by Jiang et al and Guo et al that outdoor time reduced myopisation risk by up to 58% in the children with one myopic parent [200, 201]. In a meta-analysis Sherwin et al [202]and Xiong et al [203] found similar patterns in the relationship between time spent outdoors, including a 9% reduction in risk per hour of outdoor time of non-myopes developing the condition.

The specific elements of outdoor time that lead to this protective effect are as yet undetermined, but a number of candidates have been identified, the experience of the visual environment, the nature of the light itself and activity. The activity is difficult to separate from the very fact that the individual has gone outdoors to engage in a sport and while it may not be discounted is very susceptible to confounding factors.

From an optical perspective, the structure of the visual environment is of interest as a risk factor in the development of ametropia. Studies of military personnel in confined environments, such as submarines, show an association between a visual environment with limited distance vision potential as compared with those in more varied visual environments [204]. In a review of the interaction between factors in myopia development, Flitcroft [9] provides a description of the dioptric structure of the environment with relation to working distances. Using this technique demonstrates the relative dioptric complexity of near work environments as compared to outdoor environments. A desk with object distances varying from 30cm to 2 metres will require more significant accommodative effort to shift over a 2.8D range of distances whereas an outdoor scene is unlikely to exert more than 0.50D of change in demand between objects. Indoor environments will therefore have objects in the field of vision exerting a range of demands in the visual system and exist in a range of states of focus when not in attentive gaze. A further consequence of this is the presence of higher variation in dioptric variation and defocus as the eye moves around the structure of the indoor scene with up to ten times the dioptric change in peripheral retinal image when compared to changes at the fovea [9]. The implication of this being that the more

dioptrically complex environments are more myopogenic due to higher and more complex levels of hyperopic retinal defocus. If this is indeed borne out, then it may provide support for the relationship between urbanization and myopisation due to living conditions.

The relative light intensity between indoor and outdoor locations has been reported as a factor in emmetropisation and has been associated with the reported protective effects of increased time outdoors [205, 206]. Yotsukura et al. [55] in a study of myopia in Brazilian school children found shorter axial lengths (22.98+/-0.87mm) associated with high luminance (100 lux). This supports animal studies indicating an association between high light intensity and protection from form deprivation myopia [95, 207] however the same magnitude of protective effect has not been observed in lens induced myopia [208]. In a study of light dosing regimens Lan et al. [209]determined continuous exposure to bright light provided a protective effect for form deprivation myopia after 5 hours with no additional benefit if extended to 10 hours or beyond. Limited benefit was observed for 1 to 2 hour period of exposure. Cyclic dosing of 1:1 or 7:7 minutes gave the greatest protection and, in some cases, fully suppressed myopic development. This supports the epidemiological study by Feldkaemper et al. [210] and Zhang [211] which suggest dopamine release induced by changes in luminance and outdoor light intensity helps regulate axial length development.

Wavelength is associated with suppression of myopia in animal and human studies with greatest effect in the 360 to 400nm range [212, 213]. Animal studies have shown wavelength may be used to induce ametropia, longer wavelengths inducing myopia and shorter inducing hyperopia in chicks and guinea pigs [214, 215]. Conversely primates developed hyperopia associate with shorter vitreous chambers when exposed to long wavelength light [21]. Perhaps the only conclusion we may draw here is that emmetropisation may involve chromatic aberration and that this process may be manipulated using narrow band lighting.

Like dopamine, vitamin D release is stimulated through higher intensity and specific wavelength light exposure. Smooth muscle of the ciliary body has been found to be larger in myopic children [216] and since vitamin D may regulate the length and refractive degree of the eye [217] deficiency may present elevated risk of ametropia [211]. Birth season has been associated with in utero vitamin D exposure, higher birth weight and adult height. As axial length is associated with overall body height there

may be a link between biometric values and birth season, although this appears to be independent of refractive outcomes.

The COVID-19 pandemic forced significant lifestyle changes upon entire populations, with the most pronounced impact being on cities and dense urban settings. Home confinement has exacerbated the effects of reduced outdoor time and limited variety in the optical structure of the visual environment. Compounding these effects was the increased reliance on remote learning and technology to provide education and workplace continuity. The study of Wang et al [218] was well positioned to examine the impact of this event as it encompassed a significant period prior to the pandemic lockdown with study completion occurring in July 2020. Myopic shift during the period covered by the lockdowns relative to previous periods was substantial for children aged 6 (-0.32D), 7 (-0.28D) and 8 (-0.29D). Myopic prevalence increased for the same ages compared to previous periods, 6 (21.5% vs 5.7%), 7 (26.2% vs 16.2%) and 8 (37.2% vs 27.7%). Smaller shifts were observed in older children (-0.1D) which were considered statistically, but not clinically significant. The screening date was noted as a potential confounding factor as it was moved from September to June, immediately after lockdown. While this may prove problematic when considering the data across the entirety of the study and limit the ability to provide meaningful forecasts, it does allow the significance to the lockdown itself to be isolated. Chang et al [219] conducted a study of 29,719 students commencing in 2019 and completing after the local lockdown in China had been lifted with follow up approximately 6 months later. During lockdown the rate of myopic progression was elevated relative to the preceding and following periods. Period 1 (pre lockdown) rate of myopic progress was -0.030D/month, period 2 (during lockdown) -0.074D/month and period 3 (post lockdown) 0.016D/month. Overall trends for SER were negative prior to the lockdown event and positive after the event indicating a partial reversal of the myopogenic effect of enforced periods of confinement. Some of the myopic progression may be due to accommodative spasm due to lockdown which in turn may account for the hyperopic effect during period 3. Overall, these results link well with those of the DIMS and HAL lens studies which also found younger children were more susceptible to myopisation [57, 103] but also more responsive to treatment suggesting that earlier intervention is more effective than later in life. Improvements in spectacle lens intervention techniques provide greater opportunity to treat younger children, with

greater compliance compared to other modes of intervention due to increased comfort and reduced implementation complexity.

In this retrospective longitudinal study biometry will be used to examine the relationships between ocular development and the natural progression of refractive development. Both qualitative and quantitative data will be used to describe the longitudinal relationships between refractive error, measured ocular biometry, and environmental factors for development. These data are collected from a regional Australian cohort that displays homogeneity for a large range of variables that typically operate as confounding elements, such as ethnicity and geography. This will be framed in the context of lifestyle and environmental factors for children in the most active phase of emmetropisation of 12 years of age or less. Management of emmetropisation is increasingly of interest in practice, particularly in regional Australia where clinical resources are relatively sparse. The implementation and re-tasking of existing devices for determination of biometric development is attractive as it permits the elevation of clinical management of emmetropisation without significant additional investment. An examination of two commercially available biometers is also undertaken to compare the validity of results obtained via calculations from a wavefront aberrometer (DNEye/Visionix) against those from a known biometer (Nidek AL-Scan) to determine the suitability of the wavefront aberrometer device for patient emmetropisation management.

Chapter 3: Research Design

Research into the aetiology of myopia is well-established and has been the source of significant attention in recent years. As emmetropisation requires the coordinated development of the optical components of the eye, an understanding of the biometry of these components during growth is important in understanding the relationship between components during development. Refractive errors, including myopia, are the result of an imbalance between these optical components, where the refractive power of the cornea and lens does not offset the axial length growth[10]. With axial growth almost exclusively occurring during childhood ametropia typically emerges between the ages of 7-14 years, with possible further progression up to late teenage to early adulthood [11]. Given variations with different populations and lifestyles in relation to myopia development, refractive and biometric development for myopes is an area of significant research. Normal refractive development pathways are not fully understood. Emmetropic children have demonstrated a successful cessation of coordinated growth in the eye [12], and this process has ceased prematurely for hyperopes [13] whereas in myopes eye growth continues beyond the normal parameters [9]. This provides an opportunity, using biometry as a metric, to identify and isolate the factors which promote cessation of emmetropisation.

Section 3.1 discusses the methodology implemented in the study; section 3.2 lists all the instruments used in the study and rationale for their use; sections 3.3 to 3.5 describes the participant selection criteria, the procedure used and the timeline for completion of each stage of the study; section 3.6 discusses how the data were analysed; finally, section 3.7 discusses the ethical considerations of the research and limitations.

3.1 METHODOLOGY AND RESEARCH DESIGN

Purposes

The minimum age for candidates is 5 years of age to allow for the inclusion of school and educational environmental factors for all candidates. While biometric and refractive data provide objective measurements of refractive conditions, context will

be given through a survey of family history and the social and environmental conditions present during emmetropisation and comparison of biometric and refractive development between individuals. In particular, aspects of lifestyle involving time spent outside in daylight hours along with time spent on near work and digital devices will be examined given the emerging evidence with links to myopia in this field [2, 220]. Data will be drawn from practice records at Hannaford Eyewear, Bowral, located in the regional area of the Southern Highlands, NSW, Australia. As such it will be representative of a regional Australian population, which in terms of representation of age distribution is broadly in line with the rest of the country. However, notable differences exist in terms of parental education, ethnicity, and employment. Ethnicity is relatively homogenous compared to the urban centres in Australia. The population is predominantly of White European ethnicity, with the top five census responses for ancestry (English, Australian, Irish, Scottish and German) 47.6% greater than the state average and 32.0% greater than the national average [221]. Employment data indicates there is a higher percentage of retirees in the region, resulting in lower employment figures for the inhabitants. Corrected for this factor, employment is in line with national averages and in line with the median income figures. Housing type is an indicator of household income as well as environment. The Southern Highlands is out of line with national averages for this measure, which is indicative of the nature of regional towns where separate dwellings (houses) are the dominant structure type. Following is a sample of the relevant data that have been drawn from the 2021 national census [221]

	Bowral	*National*
% of population meeting age eligibility for inclusion in study	6.2	6.2
% of school aged students in primary school	27.5	27
Median weekly income (Household) $	2,204	2,120
% Separate Houses	83.9	72.3

Table 3-1 - Eligibility & inclusion data from the Commonwealth Census 2021

Retrospective study data has been drawn from existing patient records and data collected during the course of regular clinical attendances at the practice. Biometric and refractive data will include:

1. Refraction – non-cycloplegic indicating habitual refractive power. Autorefraction is conducted as part of the biometric assessment to provide an objective measure of refractive error.
2. Axial Length (AL) – the correlation between refractive error and AL is well established. This is useful as a metric for ocular development and will provide context for refractive error (if any).
3. Corneal Radius (CR) – is routinely measured as part of the biometry data collection, however this parameter was not selected for inclusion in this study as there was no capacity to assess the impact of CR without further consideration of the confounding effects of lenticular parameters on refractive error.
4. Central Corneal Thickness (CCT) – despite CCT being relatively stable after early infancy, it is useful as it provides a control, or reference, metric for other parameters.

5. Anterior Chamber Depth (ACD) – ACD has not been strongly associated with SE refractive error [52], correlations have been reported between ACD, AL and lens power.

Environmental factors surveyed via questionnaire:

1. Parental ethnicity
2. Birth country
3. Health care access
4. Birth conditions – weight and maturity
5. Visual environment– near work duration and type, dioptric composition of home environment, outdoor exposure duration/regularity
6. Developmental milestones

Gaining a better understanding of these factors will potentially allow practitioners to identify risk factors in the full range of refractive errors using surveys for patients which, while not necessarily providing predictive data, may allow a clearer assessment of risk for a given patients and therefore inform treatment pathways.

Secondary questions

The monitoring and management of emmetropisation in a practice setting typically requires dedicated instrumentation, which is often cost prohibitive to implement in smaller practice settings. Recently a number of wavefront aberrometers based on the Visionix aberrometry platform such as the DNEye have been introduced to the market to facilitate in the development of customised lens designs. The design of lenses implementing these data aims to provide a customized eye model for a given patient's biometric data. This approach differs form that currently implemented by the ophthalmic industry where the eye used in a lens design is defined via published models which may not represent the biometry of a specific eye [31, 222]. It is possible that these data may also provide a pathway for the determination of a more detailed

set of aberrometry measurements than otherwise available in the absence of direct measurements. Importantly, some elements of these data such as axial length are determined via calculation rather than direct measurement. Consequently, understanding of the relative utility of these types of measurements compared to direct measurement devices is of interest.

Secondary questions that will be addressed are:

An examination of the correlations between DNEye & Nidek AL-Scan data. The DNEye aberrometer from Rodenstock uses a proprietary algorithm to determine overall axial length from measured anterior biometric data. Comparison of measurements from this device and the measurements taken with a Nidek AL-scan will assess the usefulness of determined (as opposed to directly measured) biometry for patient management.

This represents an examination of the suitability of wavefront aberrometry to determine axial length. In this method employed by this portion of the study, axial length is determined through the direct comparison of biometric data from a known device (Nidek AL-Scan)[115, 118, 119, 121, 223] to the derived biometric output from a relatively new device (Rodenstock DNEye Scanner) [124, 224]. This device is currently used in the refinement of commercially available lens designs for patients and is of interest as a diagnostic tool. The DNEye unit uses anterior biometric data to derive axial length via a proprietary algorithm. This method does not provide axial length data via direct measurement. It is of interest to determine the reliability of the biometric data provided by this device as the range of functions (tonometry, pachymetry, topography and aberrometry) provided by the unit make it an attractive proposition for practitioners in entrance testing for patients. The ability to use such a device as a management tool for patients during emmetropisation may allow practitioners to engage more effectively in patient management during emmetropisation without the additional investment in devices devoted to a single purpose.

3.1.1 Methodology

The study was reviewed and received approval from the Aston University Research Ethics Committee (AU REC) as described in Appendix A. The protocol of this study adheres to the Declaration of Helsinki and the WMA declaration of Taipei on Ethical Consideration regarding Health Databases and Biobanks.

You et al. [225] indicated that the change in refractive error during emmetropisation, while non-linear, is consistent. This, in conjunction with the work of Lv and Zhang [226] suggests that detection of change in refractive and biometric parameters requires 12 months between data collection points, with greater change detected for 24 months. For this study a period of 12 months was selected to maximise potential for candidate eligibility. The Kruskal - Wallis test was used for examining the distribution of variables as the data are non-parametric. Categorical variables may be defined as a percentage, with quantitative variables described as a mean +/- standard deviation. Multiple linear regression analyses will be performed to evaluate independent influence of the individual risk factors.

The participants were drawn from the patient base at a practice in regional NSW, Australia. As such they were potentially engaged in interventions consistent with normal treatment regimens for the correction of ametropia. None of the candidates were subject to any intervention specifically designed for the attenuation of myopic progression.

The study was conducted at the practice location in regional NSW, Australia (Hannaford Eyewear).

3.1.2 Research Design

The study consists of collection of biometric parameters from a cohort of 5 to 12 year old children across a one year time period during their normal clinical interaction with a regional practice in NSW, Australia. A survey was presented to the parents/carers of the children to determine key developmental milestones and environmental factors.

As normality is not displayed across the entirety of the data set, and there are predominantly three or more categories for each response, the Kruskal-Wallis test is indicated to examine the data with respect to the survey responses. Groups were

defined as the environmental or lifestyle factor assigned to a categorical numerical definition and the dependent variable is the biometric component (axial length, corneal thickness, anterior chamber depth or spherical equivalent refractive error) as a continuous scale that does not display normal distribution. As the candidates represent a mix of ages, and hence different points in the emmetropisation process, there was concern that an obfuscating effect caused by age in the statistical model due to the established link between axial length and age may be present. The ordinal logistic regression of the generalised Kruskal-Wallis model will also generalise to mixed effects, accounting for age.

The cohort size was based on G*Power (version 3.1.9.6, Franz Faul, Universitat Kiel, Germany) calculations using ANOVA: repeated measures, within-between interaction, effect size $f^2 = 0.35$ (large), α err prob = 0.05, Power (1-β err prob)= 0.8 number of groups = 4 (maximum number of categories assigned to each environmental factor) and number of measurements = 2. Number of groups varied according the to the variable being examined and ranged from 2 for simple binary (yes/no, public school/private school etc) responses, to 4 (home type, time spent at tasks). As the larger group size resulted in the largest requirement for sample size, this was taken as the minimum cohort size for this study. These definitions yielded a total sample size of 28. The cohort was drawn from individuals responding to displayed material in the practice advising of the study. To allow for dropout across the duration of the study, and provide a nonresponse adjustment for invalid or unusable data, additional participants were permitted to respond to the invitation. This resulted in 58 individuals fulfilling the initial criteria for a single attendance, 38 (66.52%) individuals fulfilling the criteria of two or more attendances, and 36 (62.07%) satisfactorily fulfilling all criteria (including completion of the survey materials fully).

The results of this particular test were repeated for the second set of data which was intended to correspond with the participants regular consultation schedule of twelve months after the initial data collection date. In practice the participants returned an average of 13.6 ($\pm$5.32) months after the initial consultation The same set of tests via Kruskal-Wallis are repeated in this later set of data, providing two cross sectional sets of data across the timeline. An analysis of these two cross section tests will be compared to provide a measure of internal referencing to validate the accuracy of the data.

To fulfil the requirements of the longitudinal study, the magnitude of change for each of the biometric parameters for each candidate has been determined for each candidate. The nature of candidate attendance has resulted in inequality of periods between measurements so that the annual rate of change has been determined for the candidates as well. It is acknowledged that this a coarse measure, subject to uncertainty due to the effects of nonlinear growth rates across the timeframe, there is still utility in providing both scales for comparison to the range of environmental factors. Consequently, both the overall magnitude of change in biometric data and the rate of change across the testing period are subject to the Kruskal-Wallis test with respect to the range of environmental factors and survey responses. One eye was selected from the data set provided by each candidate using the signal to noise ratio provided by the NIDEK AL-Scan as the determining factor. Biometry measurements were taken as close to a 12-month gap as reasonable possible, given the limitations of patient compliance with regular clinical attendance. This timescale permitted inclusion of the full range of seasons for the region and the accompanying variation in daylight hours Where multiple measurements exist the two data points closest to 12 months, and with the most favourable SNR relationships were selected (as described in chapter 3.6.1).

The survey used was an elaboration on that used by the Joint Writing committee for the Multi-Ethnic Paediatric Eye Diseases Study [5] and the Aston Eye Study [4] with additional questions pertaining to visual environment and developmental milestones. Prevalence of refractive error and biometric development in the presence of environmental factors was determined. A comparison of rates of biometric and refractive change was performed between individuals as well as published normative data in the presence of environmental influences. Appendix G contains the questionnaire in full which describe the questions, explanations, and range of potential responses for reference to the data discussion in this section. Chapter 3.4 describes the questions included in the questionnaire in detail with descriptions. The data returned from these responses is a combination of measured data from biometric and test results conducted in practice and responses to the survey questions presented to the parents/carers. Consequently, the data describes the relationship between categorical results from surveys (which are from ordinal and nominal sets), and quantitative continuous results (refractive error and biometric results).

To determine the agreement of the measurements taken with the DNEye unit with those determined by the Nidek AL-Scan, sample size was again determined. The

data for both devices was evaluated for normal distribution using the Shapiro-Wilk test. With the exception of CCT data for both devices, normal distribution was present. As the data for axial length and anterior chamber depth are normally distributed, a paired t-test was performed on this data. As this component of the analysis was directed at the comparison of measurement data between devices, a Bland-Altman Analysis was also conducted comparing the difference between measurements to the mean. A preliminary analysis of the calibration data set used in practice using MedCalc (Version 22.021, Ostend, Belgium) and a study by Hoffer et al [118] indicated a minimum sample size of 48 pairs of measurements was sufficient to produce the required plot, (Type I error (α, Sig) = 0.05, Type II error (β, 1-power) = 0.1 (90% confidence), expected mean of difference = 0.01mm, expected SD of differences = 0.02)

Note: As G*Power does not provide an effect size equation for this test, the effect sizes suggested by Cohen [227] were applied for the Kruskal Wallis test (small = 0.01, medium = 0.06, and large = 0.14). For the Mann-Whitney U test Cohen's suggested effect sizes (small = 0.1, medium = 0.3, and large = 0.5) were used.

3.2 INSTRUMENTS

Subjective refraction was undertaken using the Rodenstock Phorovist 800 Phoropter (Appendix D) (Rodenstock GMBH, Munich, Germany).

Biometric measurements were captured using the Nidek AL-Scan (Nidek Co. Ltd, Aichi, Japan), and the Rodenstock DNEye scanner (Rodenstock GMBH, Munich, Germany), and using the techniques described in section 3.2.4 Ocular Biometry (above).

The Nidek Al-Scan (software version 1.12.02) is an optical biometry device using partial-coherence interferometry. Axial length is determined from partial coherence superposition of light waves emitted from an 830 nm super luminescent diode laser. A 970nm LED is used for corneal curvature assessment and a 525nm LED is used for determination of corneal diameter. It was developed initially for applications in ophthalmology, principally the determination of ocular biometry for the calculation of intra ocular lens parameters. Sectional images of the eye are provided (Scheimpflug image) as well as the pupil image and the reflected image of the mire

rings used for alignment during measurements. Measurements take approximately 8-10 seconds for a complete set of biometric data for one eye. Anterior chamber depth is measured from the posterior of the cornea to the anterior of the lens.

The Rodenstock DNEye wavefront aberrometer is derived from the Visionix VX120 aberrometer (Visionix-Lunaeu Technology Chartres, France), with the addition of proprietary software for the determination of optical biometry to be applied to lens designs (CNXT Version 23.11.8 release 2024-01-31T15:42:18+1:00). The device uses Shack-Hartman wavefront analysis. Lower and higher order aberrations, brightness dependent pupillometry, placido disk videokeratography, and Scheimpflug pachymetry [228]. Axial length is determined by calculation based on biometric measurements, not by interferometry as in the Nidek AL-Scan. Anterior chamber depth is measured from the anterior corneal surface to the anterior lens surface. Wavefront aberrometry output is defined using Zernike coefficients Z_n^m and expressed in μm. Zernike coefficients are defined by an order (n) and meridional frequency (m) in the form Z_n^m with the complexity of the component surfaces increasing with radial order commencing with $n = 0$. Each order n contains $m = n + 1$ elements. Within each radial order modes of the same absolute value represent aberrations of the same shape rotated with respect to each other. This permits aberrations with direction dependence (eg prism) or angular components (eg astigmatism) to be expressed clearly. Consequently, meridional modes $m = 0$ in each order are rotationally symmetrical which occurs in all even numbered radial orders. Corresponding to each Zernike mode is a coefficient C_m^n which defines the magnitude of a given mode to the total wavefront. Their coefficients are consistent and therefore additive, as opposed to the traditional spherocylindrical power representations. Low order aberrations are defined as $n \leq 2$, with high order aberrations being $n \geq 3$. The contribution of each mode is independent of other modes, so the inclusion or omission of higher order aberrations does not influence the quantification of the lower order modes. However, the inclusion of higher order modes can only increase the magnitude of the total wavefront error. The variance of each aberration mode is the square of the corresponding coefficient and the total variance of the wavefront from the ideal is the sum of the variances of each aberration mode.

3.3 PARTICIPANTS

3.3.1 Recruitment and Eligibility

Participants were recruited via non probabilistic direct contact and through direct referral from their attending optometrist when undertaking regular optometric care at the practice (Hannaford Eyewear, Bowral). To recruit participants, relevant material was placed in the practice waiting areas, consultation rooms, and in newsletters sent as part of regular contact with patients. No advertisements, preselection, or data mining of the practice database was undertaken with the goal of identifying and engaging in unsolicited contact of individual patients.

Participants who did not have at least one set of refraction results and biometric data were excluded from the study. Age was limited to participants aged from 5 to 12 years of age. There was no minimum requirement for visual performance for inclusion in the study, beyond the ability to obtain biometric and autorefraction data. A total of 76 participants initially engaged with the study, all of whom had at least one data point for refraction and biometric data. Of these, 58 parents or carers of participants completed consent forms, with 55 of these continuing to complete the survey. Within this group 38 participants had 2 sets of complete data (refraction and biometry).

As the project was undertaken over a period of over 24 months, participants would attend for consultation at a range of intervals, thus it was not possible to provide a fixed baseline and interval period for measurements to be taken. Similarly, follow up consultations were dictated by clinical necessity, it is therefore not possible for the interval between measurements to comply with the ideal 12 month goal in all cases.
After consent was received from the carer or parent, the participants name and reference number from the practice management software was recorded. A unique reference number for the study was allocated to the participant for usage in the electronic submission pathway (the reference used by the individual completing the questionnaire), a second unrelated reference number was allocated to the participant which was then used in subsequent data analysis.

3.3.2 Consultation Procedures

The standard consultation procedures for each attendance are outlined in table 3.

	Initial Consultation (Baseline)	*Subsequent Consultation*
Subjective Refraction	✓	✓
Ocular Biometry (Nidek)	✓	✓
Wavefront Aberrometry (DNEye)	✓	✓
Autorefraction (DNEye)	✓	✓
Questionnaire	(✓)	(✓)

Table 3-2 - Consultation Procedures

If the participant had completed the questionnaire on their initial attendance, confirmation was sought at their subsequent visit that any pertinent environmental factors (outdoor time, domicile arrangement etc) had not been modified in the intervening period. In all instances all variables were consistent for the duration of the study.

3.3.3 Subjective Refraction

Subjective refraction was performed for all participants with the Rodenstock Phorovist 800 phoropter with confirmation performed via trial frame as part of their normal attendance regimen. Cycloplegic refraction is not normally performed in children at this practice unless clinically indicated. In cases where cycloplegic refraction was required, this is performed at a specially arranged subsequent consultation. This arrangement fit well with the requirements of the study as it permitted determination of habitual refractive error in normal conditions.

Subjective refractions were performed by one of three attending optometrists in the practice. In cases where previous refractive error was unknown, or when pre-existing optical appliances were not available for examination, an initial assessment of refractive error was performed via static distance fixation retinoscopy. Refraction was initially performed at 6 metres using the phoropter on the right eye, with the left eye occluded. Spherical power was refined first until no improvement was detected. Cylinder and axis was determined using the Jackson cross cylinder in the phoropter after which final refinement of the spherical power was performed to achieve the least

minus refraction. Upon completion of the refraction of the right eye the process was repeated for the left, with the right eye occluded. In the cases where the child was found to have a refractive error, verification and refinement of the prescription was finally performed in a trial frame in free space.

A source of potential variation was identified due to the necessity to have the child's regular practitioner perform their consultation. The results of the study into reproducibility of refraction results by Mackenzie in 2008 [229], indicate 95% limits of agreement refraction by multiple optometrists to be 0.78D. This figure is significant in the context of this study as it exceeds the totality of expected changes in refractive error across 12 months for a normally emmetropising eye. To address this, the results of the subjective refraction were treated as ancillary to the result obtained from the autorefraction performed by the DNEye unit. The attending optometrist performed this part of the consultation.

The DNEye unit is based on the Visionix XV120+, a multidiagnostic unit providing a range of clinical data including refraction estimation using a Hartmann-Shack sensor system. Sanchez et al. indicate that intrasession repeatability is good with limited difference (<0.04D) detected for subjects between sessions [230]. In a comparison of subjective refraction to the results of the Visionix VX120 mean difference for sphere, cylinder and spherical equivalent was found to be $0.01 \pm 0.43D$, $0.14 \pm 0.47D$, and $-0.26 \pm 0.30D$ respectively. Correlation was high ($r > 0.75$) across these measurements [231].

3.3.4 Ocular Biometry

Ocular biometry was performed for all subjects as part of their routine attendance using the Nidek AL-Scan (Nidek, Aichi, Japan) and the Rodenstock DNEye (Rodenstock, Munich, Germany). The Nidek AL-Scan is calibrated daily as prompted by the use interface, the Rodenstock DNEye units is calibrated as prompted via the user interface.

When performing the ocular biometry measurements with the Nidek AL-Scan, the child was instructed to rest their chin upon the chinrest and rotate their forehead forward until it came firmly in contact with the forehead rest. In the case of a child being too short to correctly align with the device a parent or carer held the child on their lap during the measurement. The device was positioned in front of the child's

right eye prior to commencement of measurement and the subject instructed to fix their gaze upon the red fixation light inside the unit and blink freely until instructed otherwise. The device was aligned vertically to align with the patient's eye line, then the joy stick is moved to achieve a sharp image of the mires on the child's cornea, this is supplemented by the self-focussing systems within the device. The child was then instructed to hold their gaze steady and refrain from blinking until instructed. Upon achieving good alignment, the device automatically commences measurement. Keratometry is performed initially, followed by axial length measurement and finally corneal thickness and anterior chamber depth. A minimum of five measurements are taken by the device over approximately 8 seconds. In the event of poor signal to noise ratio the user will be prompted to repeat measurements. The child was then instructed to blink normally as the device was moved to the left and the process was repeated. The data was collected by the Nidek Navis Software package which is integrated into the practices record management software. Biometric data collected by this device (per eye) were:

- Axial length (AL) in mm - minimum 5 measurements
- Signal to noise ratio (SNR)
- Average axial length in mm
- Average signal to noise ratio
- Graphical representation of the signal to noise ratio
- Keratometry @ 2.4mm and 3.3mm
- Central corneal thickness in μm(CCT)
- Anterior chamber depth in mm (ACD)
- White to white distance in mm
- Pupil diameter in mm (mesopic)

A sample of the output is provided in Appendix E. The signal to noise ratio is dimensionless.

Biometric measurements were also performed using the DNEye wavefront aberrometer. When performing the ocular biometry measurements with the unit, the child was instructed to rest their chin upon the chinrest and rotate their forehead

forward until it came firmly in contact with the forehead rest. The device was positioned in front of the child's right eye prior to commencement of measurement and the child instructed to fix their gaze upon the image of a hot air balloon. The child was instructed that the image will regularly move in and out of focus and was reassured that this was normal. Furthermore, they were not required to attempt to keep the image in focus through effort, rather that the preference was for them to simply fixate their gaze upon the balloon. The measurement process for the DNEye device consists of three stages. In the initial stage wavefront aberrometry is performed for both distance and near vision. The child may blink freely but was instructed to hold their gaze steady. In the second phase the display changes to an array of red rings, at which time corneal topography is measured. During this phase the subject is required to refrain from blinking and hold their gaze steady. In the final stage Scheimpflug imagery is performed, with the child required to hold their head and gaze steady and refrain from blinking. The process in total takes approximately 60 seconds per eye, with the initial phase taking approximately 40 seconds and the subsequent phases approximately 10 seconds each. Due to the longer time taken for this test it was necessary to ensure proper engagement of the child with the test to reduce fixation losses. The data collected by this device was, per eye:

- Far mesopic refraction (Sphere (D), cylinder (D) and axis (°))
- Far photopic refraction (Sphere (D), cylinder (D) and axis (°))
- Near photopic refraction (Sphere (D), cylinder (D) and axis (°))
- Graphical representations of the refractive error (power heat map)
- Subjective refraction (as entered by the operator)
- Corneal topography
- Anterior chamber depth (ACD)
- Axial eye length (AL)
- DNEye order values
- Wavefront aberrations (Zernike meridional modes 2 to 4)

A sample of the output is provided in Appendix F.

The data for refractive error selected for use in this study were drawn from the photopic distance vision results of the DNEye scan as this most closely represented the real-world condition in which the participant will be interacting with their environmental stimuli.

3.4 QUESTIONNAIRE

Upon acceptance of participation and completion of the consent, the parents/carers of the child were presented with a questionnaire. This was an elaboration on that used by the Joint Writing committee for the Multi-Ethnic Pediatric Eye Diseases Study [5] and the Aston Eye Study [4] with additional questions pertaining to visual environment and developmental milestones (Appendix G). The questionnaire was presented in paper form at the clinical attendance. Results were held within the principal researcher's account and only accessible to them via two factor authentication.

3.4.1 Birth Conditions

To determine the influence of biometric and physiological parameters at birth on subsequent development, the carers were asked to provide information on these factors. The Australian government provides a resource known as the 'Blue Book' in which data drawn from clinical interactions as well as developmental milestones and vaccination records are recorded. As weight and height have been associated with refractive development [232], these were selected for inclusion. Similarly, maturity at birth as well as complications have been associated with development of refractive error and have been included in this section. Values were recorded as continuous data for birth maturity in weeks (negative values for preterm), birth weight in kilograms and height in centimetres. Pre-term births, on time births and post term births were assigned category values (1,2 and three respectively). Complications at birth were assigned a value of 1 (= no complications) or 2 (= complications at birth). The limited number of participants coupled with the large array of reported complications at birth made statistical of the relationship between specific birth complication untenable.

3.4.2 Developmental Milestones

Data in the 'Blue Book' are recorded at birth, 1-4 weeks, 6-8 weeks, 6 months, 12 months, 18 months, 24 months, 36 months, and 48 months. An assessment is provided to the parent or carer indicating their child's development relative to normative age values for the population at each of these milestones. The milestones selected for this study commenced at 18 months as this aligns with the closest period after the most commonly reported ages for talking and walking (12 months). Data from these milestones were unlikely to be reliably recorded and so responses were divided into categories of lower than average/average/higher than average to facilitate responses from the carer. Each of these categories was assigned a numerical categorical value to facilitate analysis ('Lower' = 1, 'Average' = 2, 'Higher' = 3).

Respondents were asked to indicate the age at which the child first crawled or shuffled and the age at which the child first spoke. While these are subjective and therefore prone to significant variance in assessment of fulfilment, they are also indicative of the commencement of interaction with the surrounding environment.

Handedness (right or left dominance) was recorded and assigned a numerical value (right = 1, left = 2).

Respondents were asked if the subject had been diagnosed with behavioural difficulties (No = 1, Yes = 2).

Respondents were asked if the child wore spectacles or corrective lenses (No = 1, Yes = 2). They were also asked to report the age at which wear was commenced, which was recorded as a continuous value.

3.4.3 Education

Performance at school was included in the questionnaire as a series of queries related to the overall performance of the child in a range of areas at the time of completion of the survey.

Year at school was recorded as a continuous value with kindergarten represented by 0 and all other responses represented by their actual value.

Type of school was recorded, with responses public (assigned category 2) or private (assigned category 3), as these represent to two dominant forms of school mode in Australia. Public schools are run by the state governments with federal government

support and are subject to standardised syllabi. Private schools range from religious based facilities to selective schools with performance-based admission criteria. These schools are also subject to the national syllabus requirements but often include additional content or supplementary course materials and support structures. Private school predominately implement a fee structure for attendance, while public schools are subsidised by the government and attract no school fees. In Australian nationally standardised testing (NAPLAN), of the top 100 performing schools 53% were private and 47% public. 90% of the top 100 performing schools were from areas considered to be socially and/or economically advantaged, of which the southern highlands is included [233]. No respondents indicated home schooling (assigned category 1).

3.4.4 Visual Environment

Assessment of visual environment was divided into subcategories of outdoor light exposure, time spent on near work tasks, sports, type of domicile and time spent in lockdown during covid.

Time spent outdoors for play or recreation per day during daylight hours was recorded to assess the amount of daylight exposure experienced by the child. It was categorised and allocated a numerical value, <30 minutes (1), 30 minutes to 1 hour (2), > 1 hour (3), and nil (4).

Time spent outdoors for play or recreation per day during evening hours was recorded to assess the amount of outdoor exposure experienced by the subject under artificial lighting. It was categorised and allocated a numerical value, <30 minutes (1), 30 minutes to 1 hour (2), > 1 hour (3), and nil (4).

Overall study time was queried to determine the total amount of time per day spent at concentrated near tasks required to meet educational demands. It was categorised and allocated a numerical value, <30 minutes (1), 30 minutes to 1 hour (2), > 1 hour (3), and nil (4).

Screen based study time was queried to determine the total amount of time per day spent at concentrated near tasks required to meet educational demands on screens or devices. It was categorised and allocated a numerical value, <30 minutes (1), 30 minutes to 1 hour (2), > 1 hour (3), and nil (4).

Screen based recreational time was queried to determine the total amount of time per day spent at recreational near tasks that utilise screens or devices. It was categorised and allocated a numerical value, <30 minutes (1), 30 minutes to 1 hour (2), > 1 hour (3), and nil (4).

The type of study site was queried with two options, a dedicated study area set up for that purpose only (categorised as 1), and a communal area such as the kitchen or living room of the home (categorised 2).

Sports participation was queried and defined according to type of sport, categorised according to none (1), indoor (2), or outdoor (3). The amount of time spent at this sport was recorded as a continuous numerical value in hours.

The type of home structure was recorded as an indicator of the expected dioptric complexity of visual demand of their home environment. Categories were assigned according to the following responses Apartment/Flat (1), Townhouse/Semidetached (2), Small Residential (3), Large Residential (4), and Semi-Rural/Rural (5). While not observed as an item of interest in other studies, the type of home structure was included as it represents a means for the definition of the home visual environment. Factors potentially influenced by this include light exposure and the variability of the dioptric demand on the visual system, proximity and access to outdoor play, near work behaviour, and also as a proxy for socioeconomic status.

As the Southern Highlands were categorised as regional during the lockdown phase of the COVID-19 response, longer lockdown times indicated that the child had sent that period in a major urban centre. Periods of time spent off school less than 3 months indicated that the child was in the Southern Highlands or other regional area for the duration of the lockdowns. Categories were assigned as regional lockdown =1 and urban lockdown = 2. Both the length of time spent in lockdown as a continuous variable and the location implied by the lockdown period as a category were examined. There were a number of instances where children moved to the highlands in between lockdown periods, as indicated by the range of values for time spent in lockdown instead of distinct sets of periods.

3.4.5 Parental Survey

As ethnicity, parental visual conditions, and parental education have been associated with visual development, the parents or carers of the child were asked to complete a series of questions based on the ethnicity, education and visual performance of the child's birth parents.

Maternal age at time of completing the questionnaire was recorded as a continuous value. From this value it was possible to determine maternal age at the birth of the child.

As ethnicity is associated with risk for development of visual conditionals, maternal birth country was recorded and assigned a numerical categorical value. Responses were not pre-defined and based upon the respondent's assessment of the most appropriate name for their birth country, this may reflect a political view rather than the actual recognised name for their birth country at the time of writing. Responses were assigned values according to order of appearance in the surveys, Australia (1), Czechoslovakia (2) [note: not the Czech Republic], Vietnam (3), Hong Kong (4), United Kingdom (5), USA (6), Canada (7) and South Africa (8).

Further to the determination of birth country, a specific question was asked to determine maternal ethnicity. Numerical categorical values were assigned to responses in the order of their appearance in the responses, White European (1), and East Asian (2).

Maternal highest education level was queried with numerical categories assigned to the responses as follows, High School (1), TAFE (Technical and Further Education College) (2) and University (3).

Maternal employment at the time of completion of the survey was queried and categorised numerically as N/A (1), Part Time (2), and Full Time (3).

Predominant mode of maternal spectacle or corrective lens wear was queried and assigned a numerical category as None (1), Spectacles (2), and Contact Lenses (3).

Maternal visual condition was queried and assigned a numerical category as Emmetropia/no visual condition (1), Myopia (2), Hyperopia (3), Astigmatism (4), and Presbyopia (5).

Refractive error has been defined using the method described in the Aston Eye Study [4, 67, 234]. Myopia is defined as spherical equivalent refraction (SER) of $\leq -0.50D$ and hyperopia as $\geq +2.00D$.

Paternal birth country was also queried. Responses were assigned values according to order of appearance in the surveys, Australia (1), Czechoslovakia (2) [note: not the Czech Republic], Vietnam (3), Hong Kong (4), United Kingdom (5), USA (6), Canada (7) and South Africa (8).

Further to the determination of birth country, a specific question was asked to determine paternal ethnicity. Numerical categorical values were assigned to responses in the order of their appearance in the responses, White European (1), and East Asian (2).

Paternal highest education level was queried with numerical categories assigned to the responses as follows, High School (1), TAFE (2) and University (3).

Paternal employment at the time of completion of the survey was queried and categorised numerically as N/A (1), Part Time (2), and Full Time (3).

Predominant mode of paternal spectacle or corrective lens wear was queried and assigned a numerical category as None (1), Spectacles (2), and Contact Lenses (3).

Paternal visual condition was queried and assigned a numerical category as Emmetropia/no visual condition (1), Myopia (2), Hyperopia (3), Astigmatism (4), and Presbyopia (5).

3.5 FOLLOW UP VISIT

Participants who attended for their scheduled clinical follow up consultations during the timescale of the study, and who had already completed the questionnaire, were not required to complete another questionnaire. They were, however queried to ensure that no parameters or answers from the initial responses had changed. There were no changes to response in this manner.

Participants who were eligible for inclusion in the study, had not opted to participate at their initial visit, but did opt to participate at their subsequent visit were presented with the questionnaire to fill out at that time. A potential weakness of this approach was identified where it was possible for the child's home environment

conditions to have modified between their initial and subsequent visits. There was no scope in the ethics approval to make secondary contact with the participant, so this factor was identified and accepted.

Of the complete cohort of 58, n=46 (79.1%) completed the survey at the initial consultation. Two of these candidates (3.45%) had incomplete surveys or did not complete the survey. This ratio was maintained in the longitudinal cohort where n=29 (80.56%) completed their surveys at the initial consultation.

The twelve-month duration of the study was selected to minimise the impact of seasonality on the longitudinal results by ensuring the individuals had experienced the full range of seasonal environmental factors between visits. In the longitudinal cohort of 38 individuals, 12 (31.58%) returned for their subsequent consultation in the same season as the initial. 18 (47.37%) individuals returned one season later than their initial test, in keeping with the average time of 13.60 months. This suggests that there was no significant difference in climate or daylight hours that may have resulted in variances in responses due to season. Most consultations were undertaken in summer (36.84%) followed by autumn (26.32%), winter (21.05%), and spring (15.79%). This was not included as a factor in this study, however would warrant inclusion in future examinations of the data set.

As the time between initial and subsequent visits was dependent on participant compliance with their clinical recall schedule, the interval values are variable. This was accepted as feature of a study utilising data from regular clinical attendances as opposed to a study based on active recruitment.

Participants undertook their subsequent consultation as part of their normal routine attendance which included subjective refraction and biometric data collection as outlined in the processes for the initial consultation. Data recorded at the subsequent visit mirrored that at the initial visit with the addition of the recording of the time interval between consultations.

3.6 STATISTICAL ANALYSIS

The collected data were entered into Microsoft Excel (Microsoft Corporation, Redmond, Washington United States of America) for collation and initial analysis.

The master record created in Microsoft Excel for the collation of data prior to export to SPSS was comprised of a set of four sheets with fields as indicated:

Sheet 1

- Reference number
- Age at test
- Sex
- Biometry from initial collection date
  - Nidek AL-Scan biometry
    - RE Axial Length (mm)
    - RE Anterior Chamber Depth (mm)
    - RE Central Corneal Thickness (μm)
    - RE Signal to Noise Ratio
    - LE Axial Length (mm)
    - LE Anterior Chamber Depth (mm)
    - LE Central Corneal Thickness (μm)
    - LE Signal to Noise Ratio
  - Rodenstock DNEye Biometry
    - RE Axial Length (mm)
    - RE Anterior Chamber Depth (mm)
    - RE Central Corneal Thickness (μm)
    - LE Axial Length (mm)
    - LE Anterior Chamber Depth (mm)
    - LE Central Corneal Thickness (μm)
  - Autorefraction Results
    - RE Sphere Power (D)
    - RE Cylinder Power (D)
    - RE Axis $(°)$
    - LE Sphere Power (D)
    - LE Cylinder Power (D)
    - LE Axis $(°)$

Sheet 2 Biometry from subsequent collection date

- Age at subsequent consultation
- Time since initial consultation
- Biometry from second (subsequent) collection date
  - Nidek AL-Scan Biometry
    - RE Axial Length (mm)
    - RE Anterior Chamber Depth (mm)
    - RE Central Corneal Thickness (μm)
    - RE Signal to Noise Ratio
    - LE Axial Length (mm)
    - LE Anterior Chamber Depth (mm)
    - LE Central Corneal Thickness (μm)
    - LE Signal to Noise Ratio
  - Rodenstock DNEye Biometry
    - RE Axial Length (mm)
    - RE Anterior Chamber Depth (mm)
    - RE Central Corneal Thickness (μm)
    - LE Axial Length (mm)
    - LE Anterior Chamber Depth (mm)
    - LE Central Corneal Thickness (μm)
  - Autorefraction Results
    - RE Sphere Power (D)
    - RE Cylinder Power (D)
    - RE Axis (°)
    - LE Sphere Power (D)
    - LE Cylinder Power (D)
    - LE Axis (°)

Sheet 3 Survey responses

Sheet 5 All results combined for export to SPSS

Test dates were selected from the individual's record which is representative of the initial capture of biometric data and a capture twelve months after this. Additional data points for individual participants that also fit the inclusion criteria of the 12-month interval were assessed in comparison to the other data points in the individual's clinical record. Signal to noise ratio was used as a deciding factor where multiple data points fulfilled the selection criteria.

Further to the recorded data the following derived relationships were included on the sheet to facilitate analysis:

Derived Data and Relationships

- Age @ Test Date #2
- Interval between test dates

The following data was derived in line with the techniques used by Atchison et al [235]. Refractions were converted from the accepted sphero-cylindrical notation (S\C $\times \theta$) to spherical equivalent (M).

$$M = S + \frac{C}{2}$$

Giving the following output fields:

- RE spherical equivalent refraction
- LE spherical equivalent refraction.

Additionally, the following relationships have been added to the record to facilitate comparison between measuring devices:

- RE axial length difference (AL-Scan vs DNEye)
- RE axial length mean (AL-Scan vs DNEye)
- LE axial length difference (AL-Scan vs DNEye)
- LE axial length mean (AL-Scan vs DNEye)
- RE ACD difference (AL-Scan vs DNEye)
- RE ACD mean (AL-Scan vs DNEye)
- LE ACD difference (AL-Scan vs DNEye)
- LE ACD mean (AL-Scan vs DNEye)
- RE CCD difference (AL-Scan vs DNEye)

- RE CCD mean (AL-Scan vs DNEye)
- LE CCD difference (AL-Scan vs DNEye)
- LE CCD mean (AL-Scan vs DNEye)

3.6.1 Eye Selection Criteria

In several cases it was noted that initial data was either only available for one eye, or that data was unreliable for one eye due to non-compliance with protocols by the child. One eye was selected for inclusion in the study by examining the signal to noise ratio for each measurement as a clinical tool for differentiation between results in line with the results of Armstrong [236]. After this the comparison data for the second data point was drawn from the same eye when possible. Cases were present in which despite the SNR being higher for a given eye on the initial consultation, failure to capture any data for that eye on a subsequent visit demanded the selection of the alternate eye. The following hierarchy for selection of eye data was developed to address this.

1. All data points completed (AL, ACD, CCT) Test 1
2. All data points completed Test 2
3. SNR Test 1 select highest eye
4. SNR Test 2 select highest eye
5. If match – proceed with that eye (right or left for comparison)
    a. Otherwise select eye with least SNR variation between tests

The data was then transferred to SPSS Statistics 29 (IBM, Armonk, North Castle, New York, United States of America) for analysis.

3.6.2 Examination of Lifestyle and Environment Factors on Ocular biometry of Regional Population

The demographics of the participants were analysed and statistics not specific to consultation date were reported for range and distribution:

- Sex
- Maturity at birth
- Birth complication

- Hight and weight statistics
- Milestones
- Educational environment
- Visual environment
- Parental statistics

Biometric and refractive results were collated according to consultation (test 1 or test 2), analysed and reported:

- Test 1
    - Age
    - Biometry
    - Refractive error
- Test 2
    - Age
    - Interval since previous test
    - Biometry
    - Refractive error

Ocular biometry parameters and refractive error were compared with the range of categorical survey results using Kruskal-Wallis analysis to identify correlations between development, visual environment, educational and parental influences. These analyses were performed independently as a cross-sectional study of data from both test 1 and test 2.

The change in biometric parameters between tests was determined, with annual and monthly rates of change calculated. Ocular biometry parameters and refractive error changes and rates of change were compared with the range of categorical survey results using a Kruskal-Wallis analysis to identify correlations between development, visual environment, educational and parental influences. As the sample size is small and the assumption for normality was not met across all variables, a Kruskal-Wallis test was determined to be the most appropriate test as we are comparing the mean rank

of three or more different groups. The dependent variables (Test Fields) are continuous variables and not normally distributed:

- Axial Length
- Anterior Chamber Depth
- Central Corneal Thickness
- Refractive error

The independent variables (Groups) are the categorical (nominal) responses outlined in the questionnaire. The test was conducted for the range of dependent variables listed above on a case-by-case basis for each of the independent nominal responses from the questionnaire using SPSS – Non-Parametric Tests – Legacy Dialogs – K Independent Samples – Kruskal Wallis.

3.6.3 Comparative Analysis of Biometry Devices and Applicability of Existing Model Eyes

Not all candidates have data from the Rodenstock DNEye Scanner unit linked to each Nidek data capture. This is due to the Rodenstock unit primarily being used in the context of lens design, therefore participants who have not had spectacles prescribed may not have had measurements taken on both units at the same attendance. Capture of this data is dependent upon the decision of the attending optometrist; however it is noted that this data is increasingly being captured as there are clinically relevant outputs such as objective refraction that can assist with clinical assessment of an individual.

Using the existing calibration data sets from the practice, test analysis was performed to ensure the mobility of the data between this master excel sheet and SPSS. These results were examined for reliability using SPSS to perform a Wilcoxon Signed Rank Test for one sample in the difference between measurements to determine bias between the two devices (Nidek AL-Scan and DNEye Scanner) and a Wilcoxon signed rank test for two samples to determine effect sizes on the differences between measurements. Additionally, Bland-Altman plots for the major biometric data sets were conducted for agreement between measurements on the two devices.

The relative performance of the of the measuring devices against each other and the Gullstrand model eye was also performed by examining the relationship between the models eye and measured data.

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3.7 ETHICS AND LIMITATIONS

A primary source of uncertainty in the data is the quality of measurements taken from the children during the testing process. The time taken for the Nidek AL-Scan is approximately 8 seconds per eye, with half of that time requiring stable fixation. The DNEye Scanner unit requires more engagement from the individual. The test is comprised of three main components, wavefront aberrometry, topography and pachymetry via Scheimpflug imagery. The topography and pachymetry require stability for <5 seconds per test, the aberrometry is in two phases (distance and near) which under ideal conditions take approximately 15 seconds per test. A compliant and stable subject will perform the test in under 90 seconds. Compliant children will perform in roughly the same time frame yielding reliable results. Non-compliant children with poor attention or fixation can require repetition of the aberrometry in particular, which often results in frustration from the child, in turn causing poor fixation. It was found that if a child is immediately struggling to maintain fixation it is best to disengage from the DNEye test and perform the AL-Scan to increase confidence and compliance. Nonetheless, the possibility of a shorter version of the test for children with the design team at Rodenstock has been discussed, examination of potential trade-offs between accuracy and time for the aberrometry portion of the test process is underway.

While refraction during cycloplegia is a more common source of data in the literature, this study makes use of autorefractor results under no other influence. This decision was made to determine the patient's habitual performance in terms of refraction, with the results being more reflective of their daily optical performance. As this is a study of lifestyle influences in the context of daily life, and dilation is not a feature of that, it was felt that this was a reasonable course of action. Additionally, cycloplegia was not a part of the regular clinical consultation for the patients' regular reviews. The terms of the ethics approval indicated that the data was to be drawn from normal practice attendance, which supported the decision to not introduce additional elements to the testing regime. The participants saw their habitual optometrist, and while this introduced a level of uncertainty, this was again addressed through the use of objective autorefraction data rather than subjective refraction results.

Chapter 4: Comparison of Biometers

There is interest in developing novel methods for recording biometry in a practice setting. A relatively cost-effective device that fulfils multiple roles with the practice is a desirable tool for implementation from a patient care and financial perspective. However, biometers have typically not been designed for use with children. Additionally, the concept of utilising measured anterior biometric elements combined with normative data to calculate other biometric values has not yielded data in line with that of known biometers [228]. This component of the study aims to compare biometric data from the Nidek AL-Scan and the Rodenstock DNEye to determine their level of agreement and assess whether the DNEye can reliably substitute for traditional biometry devices in optometric practice.

4.1 METHODS

A comparison of the relative performance of the Nidek AL -Scan and the DNEye biometers was performed for the data collected from the cohort described in Chapter 3. As this component of the study examines the relative performance of the device, both eyes were included in each instance where paired measurements were available (n = 121 for AL and n=125 for ACD). The data for both devices was evaluated for normal distribution using the Shapiro-Wilk test, with the null hypothesis that the data is normally distributed. With the exception of CCT data for the Nidek AL-Scan ($p=0.449$), p was <0.05 for the remaining data, the null hypothesis was rejected indicating that normal distribution was not present. As the number of data points for axial length and anterior chamber depth are considered large, a paired t-test was determined to be satisfactory due to the applicability of the Central Limit Theorem in this set size. Additionally, a Bland-Altman analysis was performed using the same data set.

4.2 RESULTS

The data collected from the cohort described in Chapter three included measurements taken with both the Nidek AL-Scan and the DNEye wavefront aberrometer.

The cohort consisted of 63 (49.22%) female participants and 65 (50.78%) male participants. The mean age was 10.10 (±1.55) years, ranging from 6.67 to 12.97. Refractive error was recorded as indicated in tables 4-1 to 4-4.

Refractive Error (D) (all participants n = 128)	*Value*	*Min*	*Max*
Mean spherical equivalent power	+0.67 (±1.62)	-2.87	+6.47
Mean cylindrical power	-0.38 (±0.45)	-2.34	0.00

Table 4-1- Refractive error for the Comparison of Biometers cohort n=128

Refractive Error (D) (female participants n = 63)	*Value*	*Min*	*Max*
Mean spherical equivalent power	+1.07 (±1.97)	-0.57	+6.47
Mean cylindrical power	-0.35 (±0.41)	-1.89	0.00

Table 4-2 - Refractive error of female participants (n=63)

Refractive Error (D) (male participants n = 65)	*Value*	*Min*	*Max*
Mean spherical equivalent power	+0.28 (±1.07)	-2.87	+4.34
Mean cylindrical power	-0.41 (±0.48)	-2.34	0.00

Table 4-3 - Refractive error of male participants (n=65)

Refractive Error Definition	*Total cohort*	*Female*	*Male*
Hyperopia $(\geq +2.00D)$	10 (7.81%)	8 (6.25%)	2 (1.56%)
Myopia $(\leq -0.50D)$	7(5.47%)	1 (0.78%)	5 (4.69%)
Astigmatism $\geq 0.75D)$	17 (13.28%)	9 (7.03%)	8 (6.25%)

Table 4-4 - Refractive error defined by type for cohort (n=128)

The biometry measurements for axial length, anterior chamber depth and corneal thickness were compared. The mean values indicate that AL measurements were higher for the DNEye whereas ACD values were higher for the Nidek. There was a significant difference between AL measurements for Nidek (mean = 22.96mm, standard deviation = 0.73mm) and DNEye (mean = 23.80mm, standard deviation = 0.72mm; t=-18.06, p =<0.001, two tailed). The magnitude of the difference in the means (mean difference = -0.84mm, 95% confidence limits: -0.94 to -0.75mm) was large (Cohen's d = 1.64). Similarly, there was a significant difference between ACD measurements for Nidek (mean = 3.66mm, standard deviation = 0.21mm) and DNEye (mean = 3.15, standard deviation = 0.37mm; t = 20.14, p =<0.001, two tailed). The magnitude of the difference in the means (mean difference = 0.51mm, 95% confidence limits: 0.46 to 0.56mm) was large (Cohen's d = 1.81). These results indicate that the DNEye unit provides data that varies significantly from the Nidek AL-Scan. As the AL-Scan has been found to agree well with other known biometers in the industry [118] it is concluded that the calculated biometry data from the DNEye would, by extension, vary from other devices such as the IOL Master.

	Statistic	*df*	*Sig.*
Axial length (Nidek)	0.967	121	0.005
Axial length (DNEye)	0.936	121	<0.001
Anterior chamber Depth (Nidek)	0.972	125	0.011
Anterior chamber depth (DNEye)	0.872	125	<0.001
Corneal thickness (Nidek)	0.989	117	0.449
Corneal thickness (DNEye)	0.944	117	<0.001

Table 4-5 - Tests of Normality for Nidek AL-Scan and DNEye data

		Mean (mm)	*N*	*Std. Deviation*	*Std. Mean Error*
Pair 1	Axial Length (Nidek)	22.96	121	0.73	0.067
	Axial Length (DNEye)	23.80	121	0.72	0.065
Pair 2	ACD (Nidek)	3.66	125	0.21	0.019
	ACD (DNEye)	3.156	125	0.37	0.033

Table 4-6 - Paired samples statistics (T-test)

		N	*Correlation*	*Sig. One sided p*	*Sig. Two sided p*
Pair 1	AL Nidek – AL DNEye	121	0.750	<0.001	<0.001
Pair 2	ACD Nidek – ACD DNEye	125	0.645	<0.001	<0.001

Table 4-7 - Paired samples correlation (T-test)

					95% Confidence interval of the difference				*Significance*	
		Mean	Std. Dev	Std. Error Mean	Lower	Upper	t	df	One sided p	Two sided p
Pair 1	AL Nidek – AL DNEye	-0.845	0.515	0.047	-0.937	-0.752	-18.062	120	<0.001	<0.001
Pair 2	ACD Nidek – ACD DNEye	0.508	0.282	0.253	0.459	0.559	20.137	124	<0.001	<0.001

Table 4-8 - Paired samples test (T-test)

A Bland-Altman plot was generated using the data in table 4-9 for AL, ACD, and CCT measurements for the two devices. The difference is calculated as Nidek results – DNEye results.

	N	*Mean*	*Std. Deviation*	*Std Err. Mean*	*Upper Confidence*	*Lower confidence*
AL Difference (mm)	123	-0.845	0.515	0.047	0.164	-1.854
AL Mean (mm)	123	23.2798	1.341	0.141	25.909	20.650
ACD Difference (mm)	125	0.509	0.282	0.025	1.062	-0.045
ACD Mean (mm)	125	3.412	0.264	0.024	3.930	2.895
CCT Difference (µm)	118	-9.45	29.840	2.759	49.033	-67.939
CCT Mean (µm)	118	558.5	32.125	2.957	621.466	495.534

Table 4-9 - One sample statistics for Bland - Altman plot

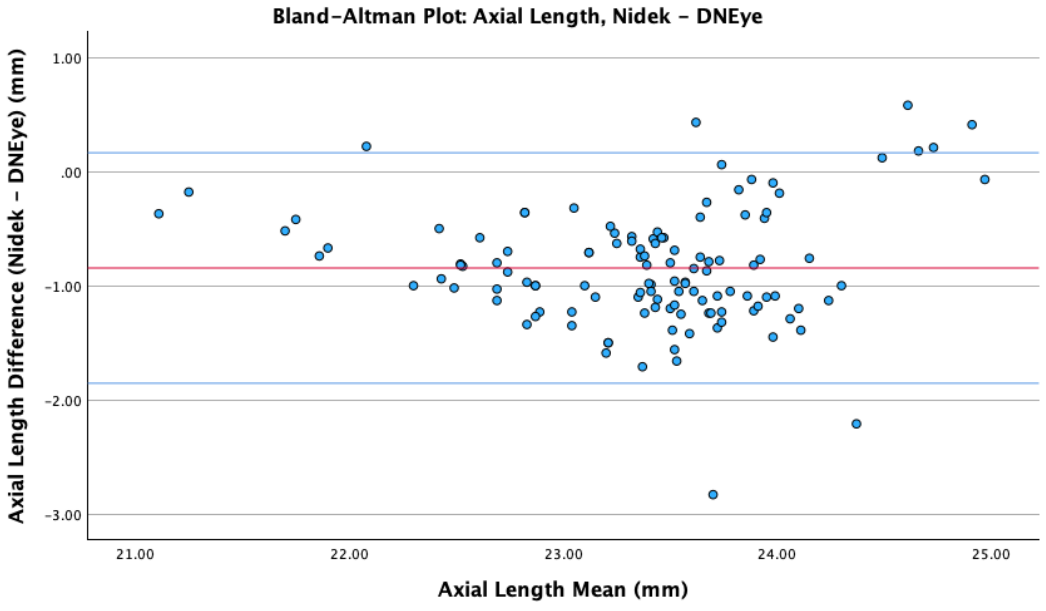

Figure 4-1 - Bland-Altman plot for Nidek - DNEye measurements for axial length (mm)

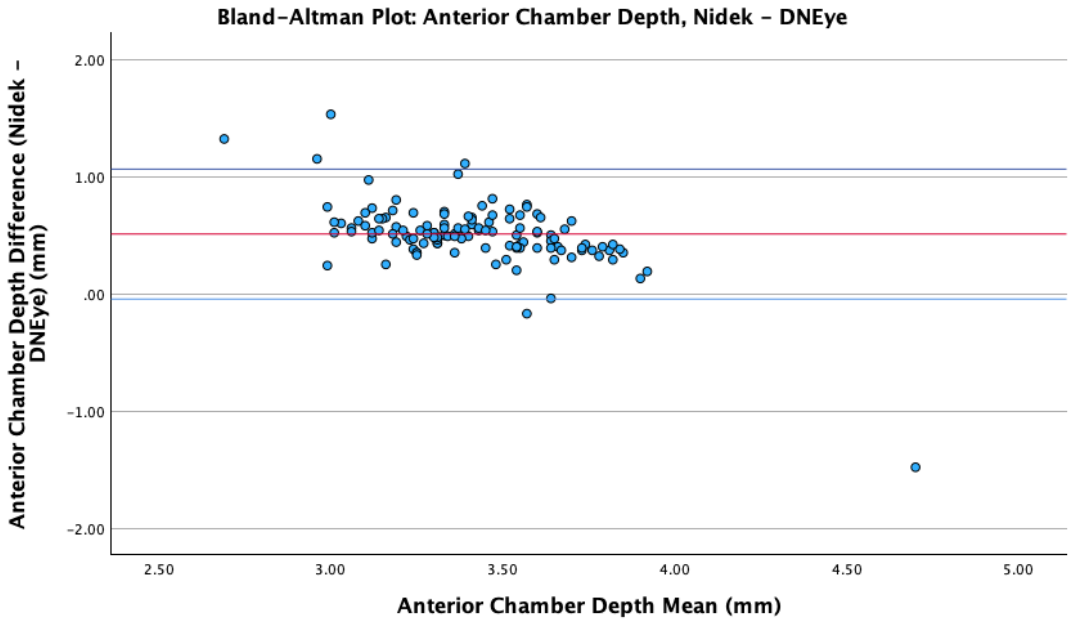

Figure 4-2 Bland-Altman plot for Nidek - DNEye measurements for anterior chamber depth (mm)

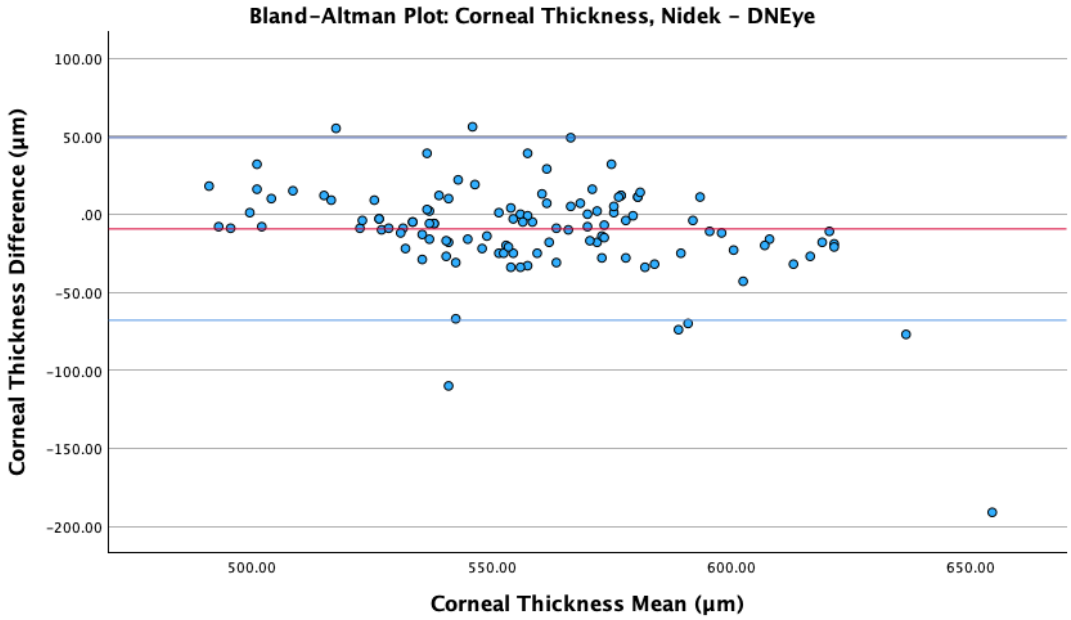

Figure 4-3 Bland-Altman plot for Nidek - DNEye measurements for corneal thickness (µm)

4.2.1 Comparison Of Observed Biometry To Applied Gullstrand Eye

To assess the applicability of the Gullstrand schematic eye to the study population axial length was compared to that of the Gullstrand model. Using the full data set of eyes (n=128) as well as the two measurements for the longitudinal cohort, a one sample T test was performed to compare the measured results.

The cohort of n=128 included both eyes for all participants regardless of the number of attendees (i.e. inclusion in the longitudinal study). The mean was $22.95 \pm 0.8mm$ with a t value of $-20.42,$ p=<0.001 two sided. The effect size was 1.8 (large).

Further analysis was performed for the cohort of n=38 (test 1) which included one eye for all participants who had attended two consultations (i.e. fulfilled criteria for inclusion in the longitudinal study). The mean was $23.03 \pm 0.94mm$ with a t value of $-9.411,$ p=<0.001 two sided. The effect size was 1.53 (large).

Similarly, analysis was performed for the cohort of n=38 (test 2) which included one eye for all participants who had attended two consultations (i.e. fulfilled criteria for inclusion in the longitudinal study. The mean was $22.93 \pm 0.96mm$ with a t value of $-8.954,$ p=<0.001 two sided. The effect size was 1.454 (large).

4.3 DISCUSSION

The axial length results for the DNEye device of this cohort of $23.80(\pm 0.72)\ mm, p = 0.001$ are consistent with those found by Hessler et al. [228] of $24.74(\pm 1.22)\ mm,\ p = 0.001$. The difference in mean can be accounted for by the differing age between the Hessler cohort and that of this study. The source of this variation is unclear, however as the biometry for the DNEye unit is determined via calculation it is conjectured that the use or a higher number of normative values may be the source of deviation.

While the DNEye unit makes use of direct measurement of anterior, other values such as crystalline lens geometry and posterior chamber depth are drawn from published data. Additionally, the Nidek anterior measurement point for the Nidek device is the posterior cornea, while the DNEye measures to the anterior pole of the cornea. It is postulated that these may represent the source of deviation from the Nidek data.

In all three instances the axial length of the cohort differed by a statistically significant amount from the Gullstrand model eye, with the measured values being consistently shorter. In the larger cohort only 6 eyes exceeded 24mm, for the longitudinal cohort this number was 3, despite the growth in AL shown across the 12 months. In none of the test sets did the Gullstrand model eye fall within one SD of the mean of the measured values. This suggests that the Gullstrand eye, and potentially the range of adult fixed model eyes, are potentially inappropriate for implementation on children's lens designs. This result warrants further examination as study to ascertain the effect of variations in axial length on far point sphere and lens design for children. Furthermore, the consistent deviation highlights the importance of using population-specific biometric data in clinical applications and research, particularly for predictive modelling, lens design, and optical simulation.

While the DNEye biometric data is not in line with data from known biometers, it is seen that there is potential utility in applying this data to lens designs from two perspectives. The first is that despite the variance from other biometers, the results indicate a movement towards the actual biometry of a given eye compared to a static Gullstrand model. Further investigation of how the optical model for the DNEye data is generated is warranted. Despite the difference in means due to age, the data found in this study are consistent with other published data [228] and exhibit large effect sizes (≈ 1.5), suggesting refinement of the model through inclusion of more detailed modelling of the biometric components may yield improvements. One source of this may be via the development of age specific eye models, as the current process is performed with an ignorance of age. Given the difference between Hessler [228] and the results shown in this study, further analysis would be warranted to determine the viability of age-related normative models for eyes. The second is the concept of an optical model of the eye, as opposed to physical for the purposes of lens design. As lens designs for the attenuation of myopisation are blur dependent, the implementation of age-related models may provide an avenue for refinement of these designs.

Consequently, the data from the DNEye may not be deemed appropriate for the acquisition of data in the course of myopia management, but does provide novel data for the generation of lens designs. The consistent deviation of the measured data from this cohort and the Gullstrand model also highlights the importance of using population

specific biometric data in clinical applications and research, particularly for predictive modelling and lens design.

Despite the opportunities that this approach to generating biometric data present in a practice setting, the outcome of this comparative analysis preclude inclusion of DNEye results in the cross sectional and longitudinal analysis performed in this study in subsequent chapters.

Chapter 5: Baseline Data – A Cross-Sectional Study of Lifestyle Factors on the Biometry of Children in a Regional Australian Population

The Southern Highlands of NSW, Australia represents an ethnically homogenous population with access to healthcare and education that is in line with the rest of the population. A cross-sectional study of the cohort, while not as robust as a longitudinal analysis, permits the examination of the cohort in the context of published data while framing the limital conditions for the longitudinal element of the study in chapter 6 [237, 238].

This chapter provides a description of the cohort in terms of demographics, refractive, and biometric data. Further to this is an analysis of the lifestyle factors potentially influencing the refractive and ophthalmic biometric state of the individuals at the time of their initial consultation (test 1) in this study. While providing a baseline reference for subsequent longitudinal analysis in Chapter 6, the larger sample size available due to the single interaction nature of the cross-sectional study also provides an opportunity to identify relationships between data that may inform future analysis.

5.1 METHODS

A total of 78 participants indicated verbal consent to take part in the research project. 16 (20.51%) participants did not return consent forms and did not have data extracted form patient records. 4 (5.13%) participants sought inclusion in the study, but did not meet the age criteria of 5-12 years of age, leaving a total of 58 of the initial 78 participants (74.36%) who had consented to participate and had at least one data collection event for inclusion in the study. Three individuals did return consent forms for inclusion in the study but failed to return surveys. Of the range of data collected, some elements, such as wavefront aberrometry, did not return significant results and were not reported upon in the following chapter.

5.2 RESULTS - CROSS SECTIONAL COHORT

5.2.1 Demographics of Participants

The total number of participants for whom an initial data point was extracted was 58. All were patients at Hannaford Eyewear, Bowral, NSW, Australia. There were 30 (51.72%) female participants and 28 (48.28%) male participants. The mean age of the participants at this first consultation was 9.13 ±1.83 years, ranging from 5.0 to 12.97 years (Figure 5-1). Despite superficially fulfilling normality tests for skew and kurtosis, the Shapiro-Wilk test indicates that the data is not normally distributed. Age distribution was negatively skewed and platykurtic.

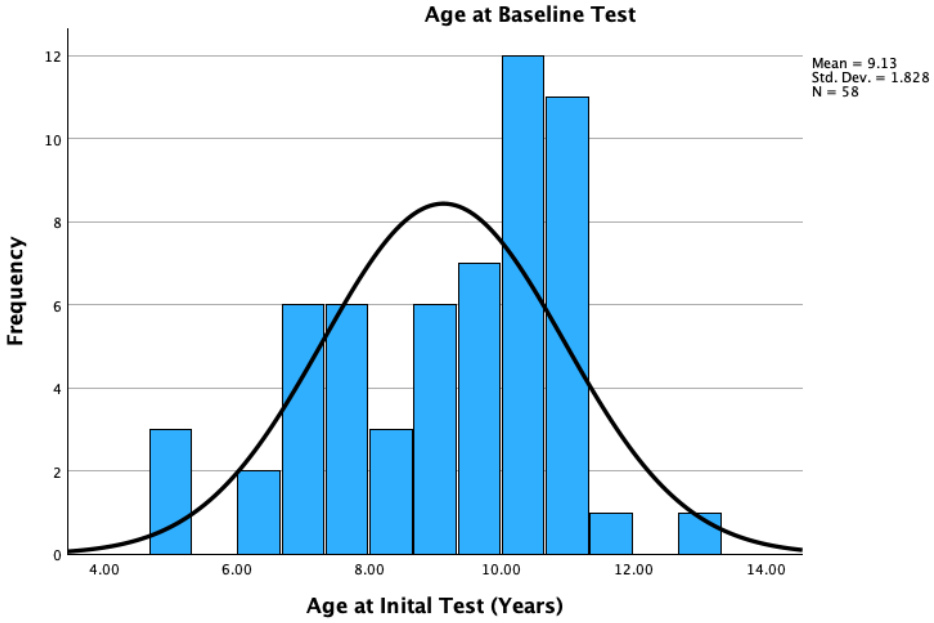

Figure 5-1 Age at which first consultation for inclusion in the study occurred
Note: 3 respondents (5.17%) did not complete or return the questionnaire.

The majority of parental respondents included in the study were of white European ethnicity (95.45%), with the rest being of East Asian ethnicity (4.55%). The children were also predominantly of White European ethnicity (92.73% both parents), maternal East Asian ethnicity and paternal White European ethnicity (5.45%), and one of both parents with East Asian ethnicity (1.82%).

5.2.2 Refractive Error

The mean spherical equivalent (SE) correction for all eyes (n=58), determined by autorefraction, was $+0.60D \pm 1.53$, with a range of $-2.87D$ to $+6.47D$. Right eye mean spherical equivalent correction was $+0.58D \pm 1.57$, with a range of $-2.69D$ to

$+6.23D$ and left eye mean spherical equivalent correction $+0.62D \pm 1.62$, with a range of $-2.87D$ to $+6.47D$. Data for the refractive error detected at the first consultation for the cohort is presented in tables 5-1 and 5-2.

Refractive Error	*Mean*	*Min*	*Max*
Mean spherical power (all)	$+0.78D \pm 1.59$	$-2.68D$	$+7.41D$
Mean spherical power RE	$+0.75D \pm 1.52$	$-2.66D$	$+6.60D$
Mean spherical power LE	$+0.81D \pm 1.66$	$-2.68D$	$+7.41D$
Mean cylindrical power (all)	$-0.34D \pm 0.45$	$-2.34D$	$0.00D$
Mean cylindrical power RE	$-0.33D \pm 0.47$	$-2.34D$	$0.00D$
Mean cylindrical power LE	$-0.36D \pm 0.44$	$-2.26D$	$0.00D$

Table 5-1 – Refractive error of all eyes in cohort for cross sectional study n=58

Refractive Error Definition	*RE*	*LE*
Hyperopia $(\geq +2.00D)$	5 (8.62%)	5 (8.62%)
Myopia $(\leq -0.50D)$	3 (5.17%)	6 (10.34%)
Astigmatism $\geq 0.75D)$	9 (15.52%)	13 (22.41%)
Hyperope (incl astigmatism)	3 (5.17%)	2 (3.45%)
Myope (incl astigmatism)	1 (1.72%)	1 (1.72%)

Table 5-2 Refractive error defined by type for both eyes n=58

The refractive error was examined using Wilcoxon Signed Ranks Test. No statistically significant differences were found between right and left eyes with regards to spherical equivalent ($p = 0.948$), spherical ($p = 0.615$), or cylindrical powers ($p = 0.103$). To select one eye for inclusion from each candidate SNR results from the Nidek AL-Scan were used as the determining factor, where the eye with the highest

and most consistent SNR was selected (as described in chapter 3.6.1). For the eye selected for inclusion in the study 39 (67.24%) were right eyes and 19 (32.76%) were left eyes. Data for the selected eyes is presented in tables 5-3 and 5-4.

Refractive Error (selected eye)	*Mean*	*Min*	*Max*
Mean spherical equivalent power	$+0.63D \pm 1.67$	$-2.87D$	$+6.23D$
Mean spherical power	$+0.80D \pm 1.68$	$-2.68D$	$+6.60D$
Mean cylindrical power	$-0.34D \pm 0.45$	$-2.26D$	$0.00D$

Table 5-3 Refractive error of selected eyes in cohort for cross sectional study n=58

Refractive Error Definition n=58	
Hyperopia $(\geq +2.00D)$	5 (8.62%)
Myopia $(\leq -0.50D)$	3 (5.18%)
Astigmatism $\geq 0.75D$)	9 (15.52%)

Table 5-4 Refractive error defined by type for selected eyes n=58

5.2.3 Biometry

Normality tests were performed on the data using the Shapiro – Wilk test as shown in table 5-5. The null hypothesis is that the data are normally distributed indicating that only the spherical equivalent refraction is not normally distributed in this case.

	Statistic	*df*	*Sig.*
Axial length	0.974	58	0.244
Anterior Chamber Depth	0.984	58	0.638
Corneal Thickness	0.989	58	0.885
Spherical Equivalent Refraction	0.697	58	<0.001

Table 5-5 Tests of Normality for data from first data collection for initial cohort (at least one test)

The biometry of the selected eye as measured using the Nidek AL-Scan is presented in table 5-6 and following figures.

Biometry (selected eye)	*Mean*	*Min*	*Max*
Axial length	$22.81mm \pm 0.93$	$20.36mm$	$24.93mm$
Anterior chamber depth	$3.64mm \pm 0.21$	$3.03mm$	$4.05mm$
Central Corneal Thickness	$557\mu m \pm 31.94$	$484\mu m$	$639\mu m$

Table 5-6 Biometry data of cohort for selected eye n=58

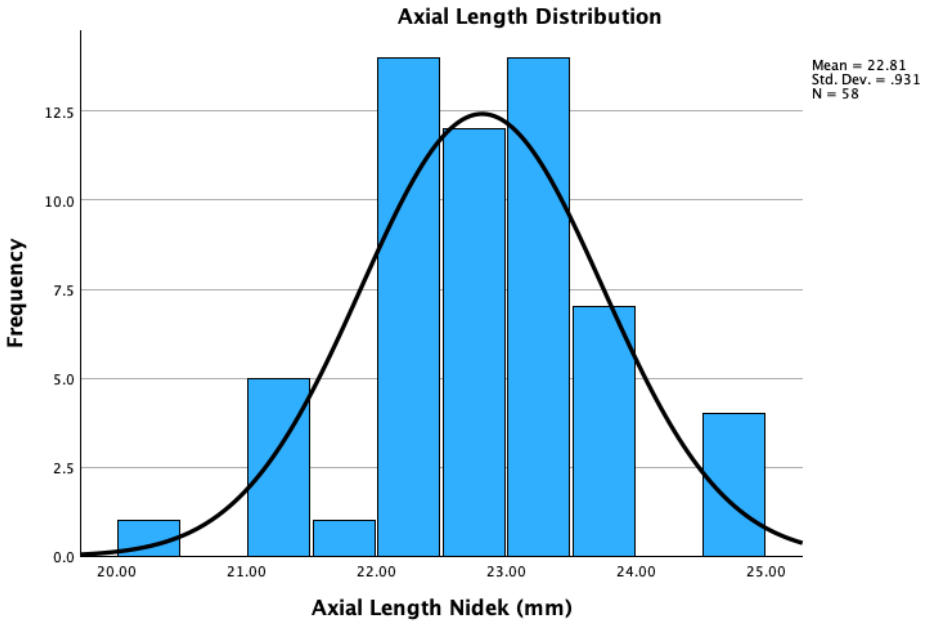

Figure 5-2 Axial length (mm) distribution for cross sectional study cohort.

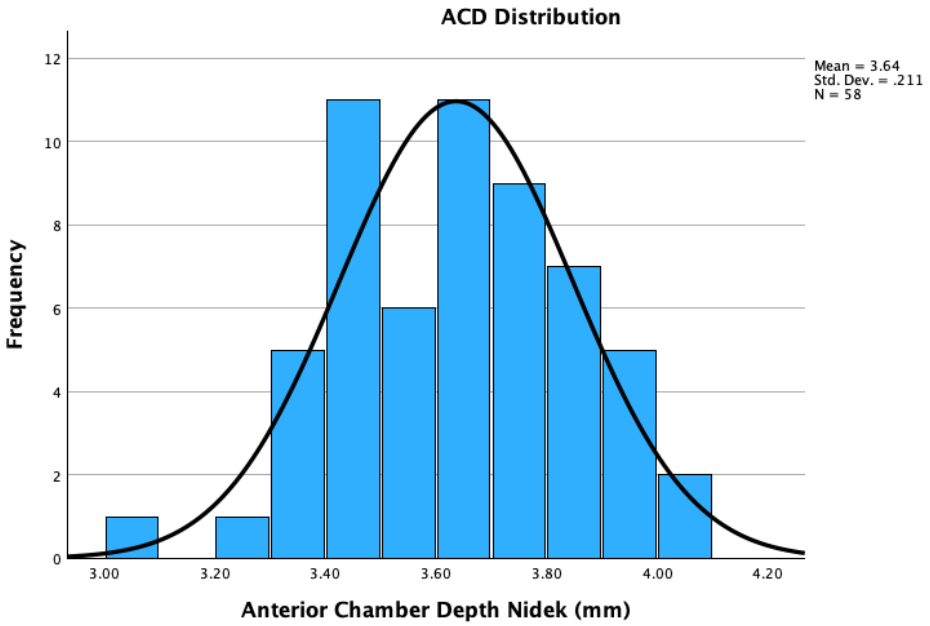

Figure 5-3 Anterior chamber depth (mm) distribution cross sectional study cohort.

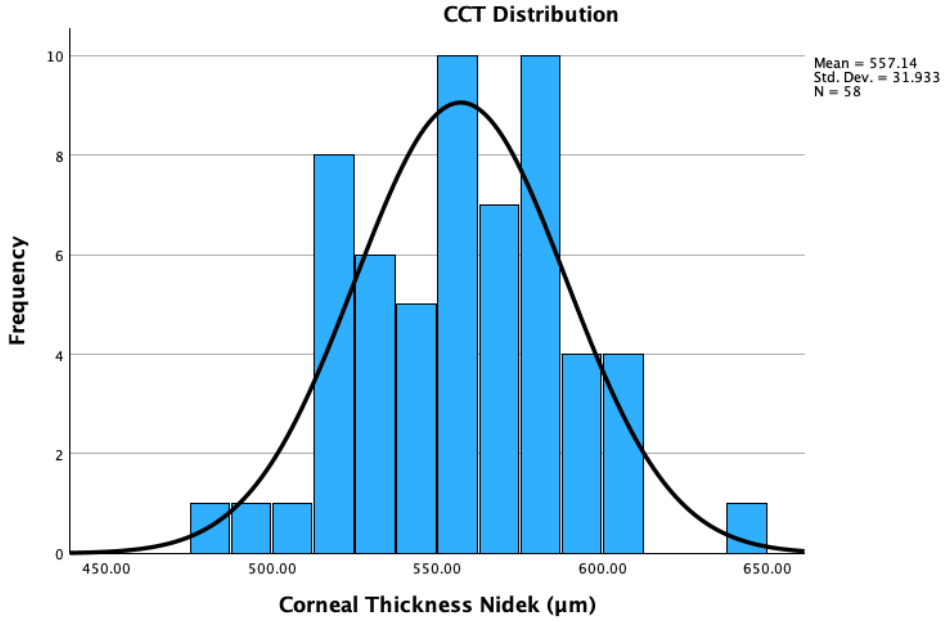

Figure 5-4 Corneal thickness (µm) distribution for cross sectional study cohort.

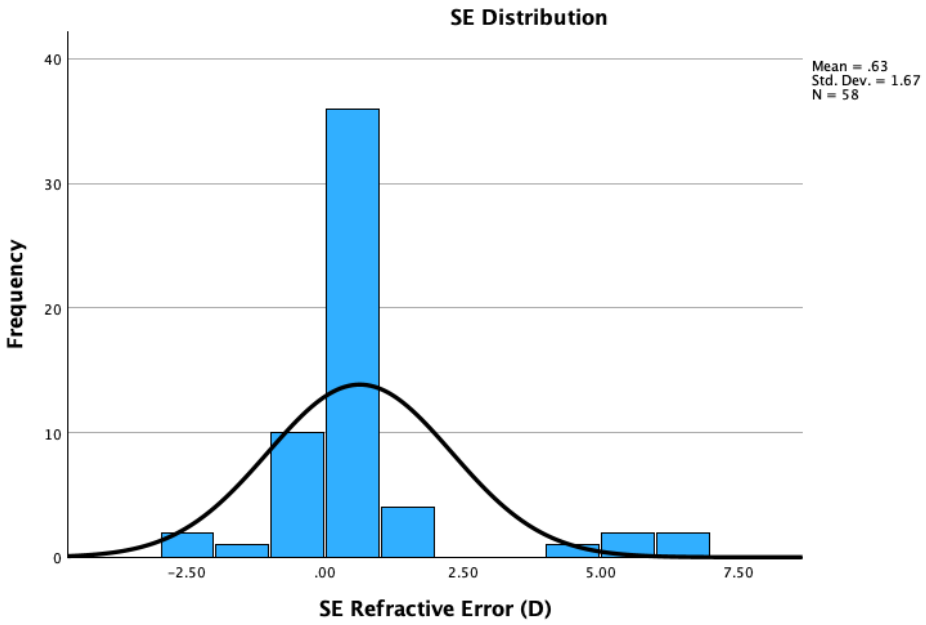

Figure 5-5 Spherical equivalent refractive error (D) distribution for cross sectional study cohort.

As the SE data (figure 5-5) is not normally distributed (Shapiro-Wilk $p = < 0.001$) a Spearman Rank Correlation was performed to examine the relationship between refractive error and biometry. SE and axial length showed a negative correlation (Pearson correlation = -0.451, sig 2 tailed = < 0.001, Spearman's rho = -0.263, sig 2 tailed = 0.046) with a medium effect size (> 0.30). This is in line with the established negative correlation between refractive error and axial length. These results reflect the strong tendency towards emmetropia in the cohort. Figure 5-6 shows the scatter plots for the above tests and linear regression lines. G*Power was used to confirm the sample size for future studies using the Pearsons coefficient for effect size, which indicated a total sample size of 56 candidates required to confirm the results found here.

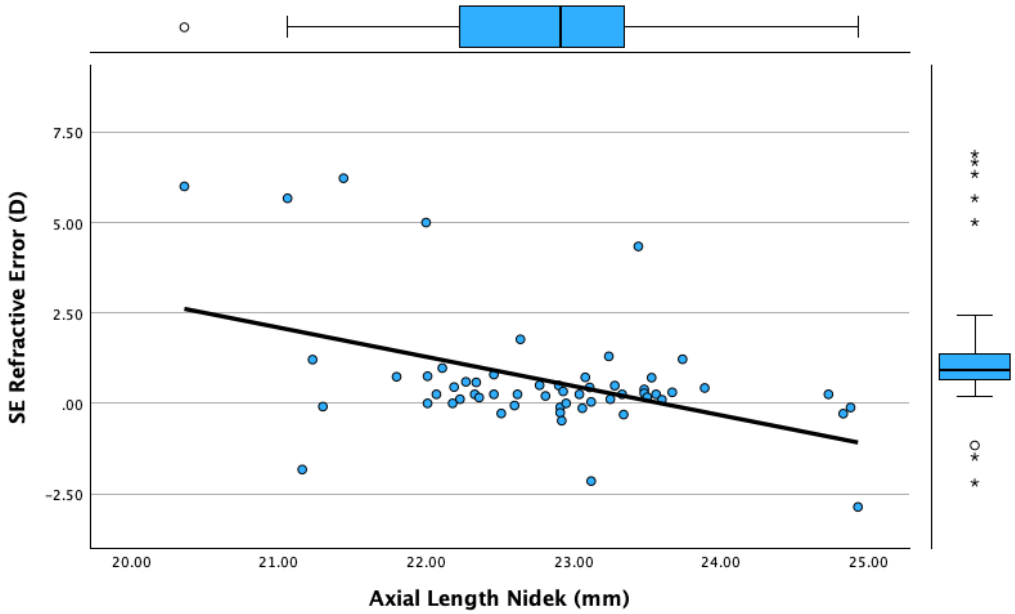

Figure 5-6 Linear regression plot of Spherical Equivalent Refraction (SE) in dioptres and Axial Length (AL) in mm.

This test was repeated for ACD and CCT with no significant results. SE and ACD results yielded a Pearson Correlation of -0.148 (sig. 2 tailed = 0.268) and Spearman's rho = 0.020 (sig 2 tailed = 0.884). CCT results were Pearson Correlation of 0.114 (sig. 2 tailed = 0.396) and Spearman's rho = 0.069 (sig 2 tailed = 0.607).

Scatter plots of axial length of the selected eye as a function of age were produced to examine the relationship between age and overall eye length. Normative lines for growth were overlaid to examine the age and axial length relationships in the context of publish normative models. This process was repeated for ACD, CCT, and SE refractive error (figures 5-7 to 5-10). These models were reproduced from Rozema's bi exponential functions describing emmetropisation and applied to figures where appropriate [14].

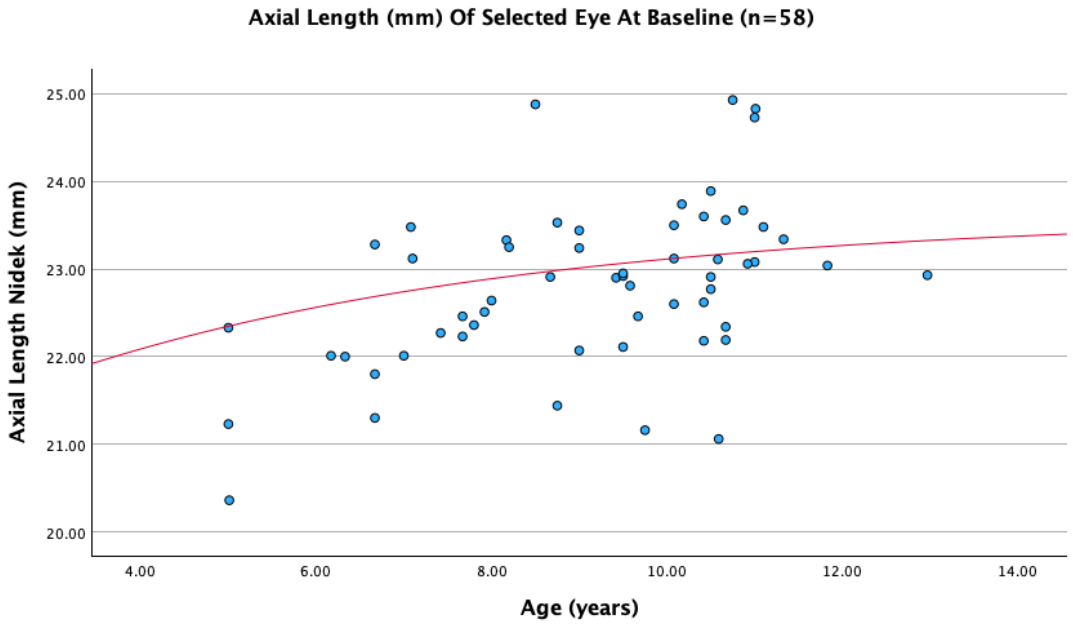

Figure 5-7 Axial length (mm) at test 1, full initial cohort (n=58). Rozema's model for axial growth is indicated by the overlaid curve $[AL = 23.61 + (-3.340 \times exp(-3.006 \times age)) + (-3.217 \times exp(-0.187 \times age))]$

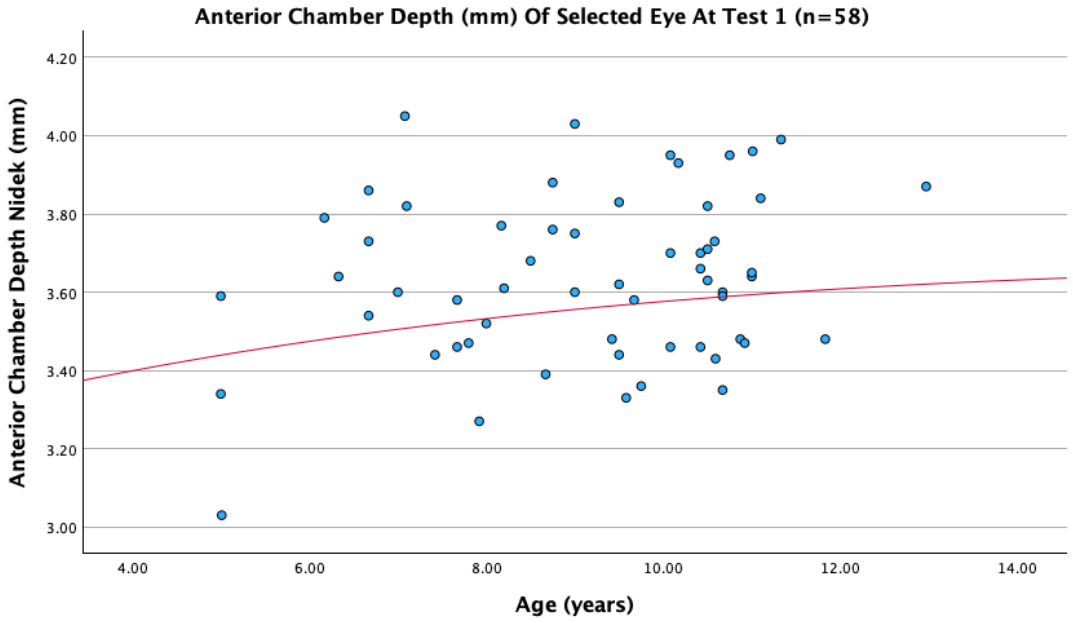

Figure 5-8 Anterior chamber depth (mm) at test 1, full initial cohort (n=58). Rozema's model for anterior chamber growth is indicated by the overlaid curve $[ACD = 3.994 + (-0.804 \times \exp(-2.965 \times age)) + (-0.812 \times \exp(-0.097 \times age)) + (-0.011 \times age)]$

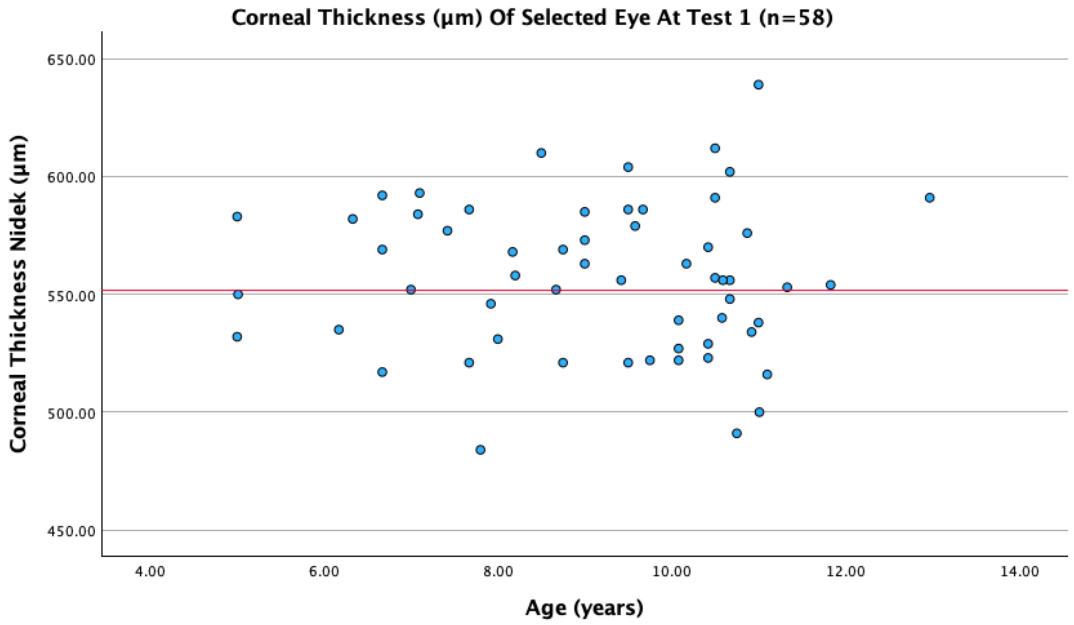

Figure 5-9 Corneal thickness (µm) at test 1, full initial cohort (n=58). Rozema's model for anterior chamber growth is indicated by the overlaid curve $[551.7 + (29.860 \times exp(-6.371 \times age))]$

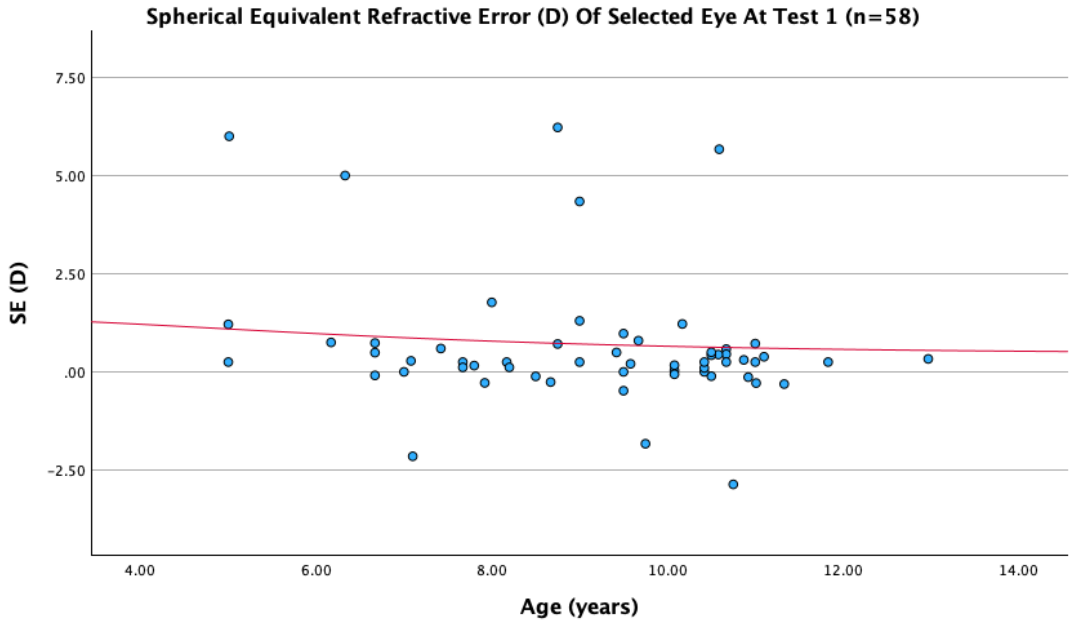

Figure 5-10 Spherical equivalent refractive error (D), full initial cohort. Rozema's model for anterior chamber growth is indicated by the overlaid curve $[(63.04 + (13.29 \times exp(-4.981 \times age)) + (15.37 \times exp(-0.351 \times age))) - (62.57 + (11.82 \times exp(-5.845 \times age)) + (14.96 \times exp(-0.399 \times age)))]$

Total sum of squares and root mean sum of squares were calculated for AL, ACD, and CCT, with the results presented in table 5-7. As with previous analysis CCT measurements did not provide useful data and have not been included.

	Mean	*Sum of Squares*	*Average Square Error /measurement*	*RMSE*
AL (mm)	-0.18	42.25	0.73	0.85
ACD (mm)	0.08	2.80	0.05	0.22

Table 5-7 - Sum of squares analysis for biometry results at test 1

5.2.4 Survey Results

The survey was divided into sections for birth conditions, developmental milestones, education results, visual environment, maternal data, and paternal data. The following represents the responses returned for the individuals included in the first test data set. Three individuals did return consent forms for inclusion in the study but failed to return surveys giving a cohort of n=55 for whom the survey and biometry was available.

Respondents indicated mean birth maturity for the cohort as +0.11 weeks (+/- 1.71, min -3, max +7). 19 individuals (34.55%) reported pre-term birth, 24 (43.64%) individuals reported on-term birth, and 12 (21.82%) reported post-term birth. The maximum value of 7 weeks was reported twice and represented the only twins in the study. Mean birth weight was 3.44kg (+/- 0.65, min 1.2, max 4.7). Mean length at birth was 50.01cm (+/- 7.34, min 18, max 59). 18 (32.73%) individuals reported complication with the birth and 37 (67.27%) reported no complication. Complication was recorded as a binary response (present/not present) due to the wide-ranging responses received making categorical definitions require a large range of options, resulting in weak statistical utility.

The average age when the participant first crawled/shuffled was 10.02 months (+/-3.08), and age at first words was 15.83 months (+/- 6.81). 45 (81.82%) of participants were right-handed and 10 (18.18%) were left-handed. 11 (20.00%)

participants reported behavioural difficulties, 32 (58.18%) wore spectacles for which the refractive error is indicated in the biometry results in the preceding section. Average age at commencement of wear was 4.94 years (+/- 3.88).

The categorical data for developmental milestones is presented in the table below.

Developmental Milestones	*Lower*	*%*	*Average*	*%*	*Higher*	*%*
Height (18 months)	6	10.91	32	5818	17	30.91
Weight (18 Months)	12	21.82	34	61.82	9	16.36
Height (24 months)	6	10.91	35	63.64	14	25.45
Weight (24 Months)	12	21.82	35	63.64	8	14.55
Height (36 months)	6	10.91	35	63.64	14	25.45
Weight (36 Months)	12	21.82	35	63.64	8	14.55
Height (48 months)	4	7.27	39	70.91	12	21.82
Weight (48 Months)	10	18.18	40	72.73	5	9.09

Table 5-8 Development Milestones reported for cohort 1

All of the participants were in primary school, with an average of grade 4 (4.24 ± 1.95 with a whole number constraint). N=36 (65.45%) of participants attended private schools, 19 (34.55%) attended schools in the public education system, no

participants were home schooled. Educational performance and related data is presented in table 5-9.

Educational Milestones	*Lower*	*%*	*Average*	*%*	*Higher*	*%*
Reading	9	16.36	20	36.36	26	47.27
Writing	10	18.18	19	34.55	26	47.27
Spelling	9	16.36	22	40	34	43.64
Mathematics	6	10.91	25	45.45	24	43.64
Behaviour	1	3.64	22	40	31	56.36

Table 5-9 – Educational milestones reported for cohort 1

In the context of this study, visual environment is taken to represent the time spent at various tasks as well as sports participation and home type. The average interruption to regular activities due to COVID-19 lockdowns was reported by this cohort as 5.48 months. 36 (65.45%) of participants performed their study in the kitchen or shared area of the family home while 19 (34.55%) had a dedicated study area set aside. Sports participation was undertaken by 46 (83.64%) individuals, 86.96% of sports played were classified as outdoors.

The geographical region for this study experiences seasonal variation in daylight, ranging from approximately 9.5 hours in winter to over 14 hours in summer. Daylight saving time, observed from early October to early April, extends evening light by one hour, potentially influencing behavioural and circadian patterns relevant to the study. These changes may affect children's exposure to outdoor light, which is a known factor in ocular growth and refractive development. It is noted, however, that these variations are less pronounced than those of other studies at greater latitudes [3]. As the average period between tests was more than 12 months, all candidates experienced the full range of seasonal variations in daylight exposure.

No participants reported living in apartments or semi-detached homes. 3 (3.64%) participants reported living in small residential homes, 35 (63.64%) lived in large

residential homes and 18 (32.73%) reported living in rural or semi-rural homes on acreage.

Table 5-10 outlines the time spent at a range of tasks pertaining to the visual environment for the participants. Time was estimated at task per day as indicated.

Visual Environment	*Nil*	*%*	*<30 min*	*%*	*30 min to 1 hour*	*%*	*Over 1 hour*	*%*
Outdoor Play (Day)	0	0	4	7.27	8	14.55	43	78.18
Outdoor Play (Night)	10	18.87	27	50.94	8	15.09	8	15.09
Study (total)	3	5.45	15	27.27	18	32.73	19	34.55
Screen Time Study	3	5.45	17	30.91	17	30.91	18	32.73
Screen Time Recreational	3	5.45	8	14.55	20	36.36	24	43.64

Table 5-10 - Visual Environment for cohort 1

Maternal demographics captured birth country, ethnicity, education, employment spectacle wear, and type of refractive error. The average age was 42.58 years (+/-6.76). 44 (80.00%) participants reported maternal country of birth as Australia, 3, (5.45%) as Vietnam, 3 (5.45%) as the U.S.A., 2 (3.64%) as the United Kingdom, 1 (1.82%) as Canada, 1 (1.82%) as the Czech Republic, and 1 (1.82%) as Hong Kong. Maternal ethnicity was 51 (92.73%) White European and 4 (7.27%) East Asian.

Highest level of maternal education was reported as 5 (9.09%) high school, 8 (14.55%) technical college (TAFE), 42 (76.36%) university level.

Maternal workforce engagement was indicated as 6 (10.91%) not employed, 32 (58.18%) part time, and 17 (30.91%) full time.

30 (54.55%) individuals reported maternal requirement of wearing correction for a visual condition. Myopia was reported for 21 (38.18%) of individuals, hyperopia for 2 (3.64%) of individuals, and astigmatism for 7 (12.73%) of individuals.

Paternal demographics also captured birth country, ethnicity, education, employment spectacle wear, and type of refractive error. The average age was 45.38 years (+/- 8.42). 49 (89.09%) participants reported paternal country of birth as Australia, 3 (5.45%) as the United Kingdom, 2 (3.64%) as South Africa, and 1 (1.82%) as Chile. Paternal ethnicity was 54 (98.18%) White European and 1 (1.82%) East Asian.

Highest level of paternal education was reported as, 8 (14.55%) high school, 10 (18.18%) technical college (TAFE), 37 (67.27%) university level.

Paternal workforce engagement was indicated as 2 (3.70%) not employed, 2 (3.70%) part time, and 50 (92.59%) full time.

19 (34.55%) individuals reported paternal requirement of wearing correction for a visual condition. Myopia was reported for 12 (21.82%) of individuals, hyperopia for 2 (3.64%) of individuals, and astigmatism for 5 (9.09%) of individuals.

5.2.5 Analysis of Baseline Data For Influence Of Environmental Factors On Biometry

In this section a Kruskal-Wallis analysis of the biometric data from the baseline examination was performed in the context of a range of developmental and environmental factors. Due to the volume of data this test produces the complete output is available as an excel file, pdf or SPSS output on request. Summary data is presented here with detail given to significant findings. Maternal and paternal country of birth was withdrawn from the data set as the number of categories for responses (n=9) indicated a larger sample size cohort size beyond that available in the study would be required.

Categories are as listed. Variables tested were axial length at test 1 (AL @ test 1), anterior chamber depth at test 1 (ACD @ test 1), corneal thickness at test 1 (CCT @ test 1), spherical equivalent refractive error at test 1 (SE @ test 1), axial length at

test 2 (AL @ test 2), anterior chamber depth at test 2 (ACD @ test 2), corneal thickness at test 2 (CCT @ test 2), spherical equivalent refractive error at test 2 (SE @ test 2), change in axial length over 12 months (AL change), change in anterior chamber depth over 12 months (ACD change), corneal thickness change over 12 months (CCT change), and spherical equivalent refractive error change over 12 months (Rx change).

	Categories	*Asymp. Sig.*
Maturity at birth	Preterm/On term/Post term	CCT = 0.017
Birth Complications	Complication/ No Complication	None
Length at 18 months	Below Average / Average/ Above Average	None
Weight at 18 months	Below Average / Average/ Above Average	None
Length at 24 months	Below Average / Average/ Above Average	ACD = 0.01
Weight at 24 months	Below Average / Average/ Above Average	None
Length at 36 months	Below Average / Average/ Above Average	ACD = 0.01
Weight at 36 months	Below Average / Average/ Above Average	None
Length at 48 months	Below Average / Average/ Above Average	None
Weight at 48 months	Below Average / Average/ Above Average	None
Handedness	Right / Left	None
Behavioural Difficulties	Yes / No	None
Spectacle Wear	Yes / No	None
School Type	Private / Public	None
School Progression	Held Back / None / Skipped	None

Reading Performance	Below Average / Average/ Above Average	AL = 0.02
Writing Performance	Below Average / Average/ Above Average	AL = 0.03
Spelling Performance	Below Average / Average/ Above Average	None
Mathematics Performance	Below Average / Average/ Above Average	SE = 0.043
Behavioural Performance	Below Average / Average/ Above Average	None
Outdoor Play Time (Day)	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Outdoor Play Time (Night)	Nil / <30 min / 30 min – 1 hr / >1 hour	AL = 0.018
Study Time Total	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Study Time (Screen)	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Recreational Screen Time	Nil / <30 min / 30 min – 1 hr / >1 hour	SE = 0.048
Study Location	Shared living space / dedicated study space	None
Sport	Yes/ No	None
Sport Type	Indoor / Outdoor	None
Home Type	Small detached house / large detached house / semi-rural or rural acreage	AL = 0.029
Maternal Ethnicity	White European / East Asian	ACD = 0.013
Maternal Education	High school / TAFE / university	None
Maternal Employment	None / Part time / Full time	AL = 0.027

Maternal Spectacle Wear	Yes / No	AL = 0.005 SE = 0.005
Maternal Visual Condition	None / Myopia / Hyperopia / Astigmatism	AL = 0.038 SE = 0.041
Paternal Ethnicity	White European / East Asian	None
Paternal Education	High school / TAFE / university	None
Paternal Employment	None / Part time / Full time	None
Paternal Spectacle Wear	Yes / No	None
Paternal Visual Condition	None / Myopia / Hyperopia / Astigmatism	None

Table 5-11 Results of Kruskal - Wallis analysis of data set

Eta squared was calculated and effect size was determined and defined according to Cohen (small = 0.01, medium = 0.06, and large = 0.14) [227].

	Asymp. Sig.	*Eta squared (effect size)*
Maturity at birth	CCT =0.017	0.150 (large)
Length at 24 months	ACD = 0.01	0.171 (large)
Length at 36 months	ACD =0.01	0.171 (large)
Reading Performance	AL = 0.02	0.145 (large)
Writing Performance	AL = 0.03	0.130 (medium)
Mathematics Performance	AL = 0.043	0.117 (medium)
Outdoor Play Time (Night)	AL = 0.018	0.186 (large)
Recreational Screen Time	SE = 0.048	0.146(large)
Home Type	AL = 0.029	0.129(medium)
Maternal Ethnicity	ACD = 0.013	0.113 (medium)
Maternal Employment	AL = 0.027	0.133 (medium)
Maternal Spectacle Wear	AL = 0.005 SE = 0.003	0.148 (large) 0.145 (large)
Maternal Visual Condition	AL = 0.038 SE = 0.041	0.156 (large) 0.153 (large)

Table 5-12 - Eta squared and effect size for Kruskal-Wallis analysis test points with statistically significant outcomes

A series of Mann-Whitney U tests were performed to ascertain the relationship between the dependent variables listed above and the categorical data. Instances where the Mann-Whitney U test have not yielded statistically significant results have been omitted. Results have been presented in the following tables detailing outcomes

between dependent variables. Each table describes statistically significant results for paired categorical data. While each sub section may contain multiple relationships for the categorical data with respect the dependent variable, this should not be taken to imply relationships other than those detailed.

5.2.6 Birth Conditions

Maturity at birth

CCT	*Median*	*Interquartile Range*	
Pre-term birth (n=19)	556µm	547 µm	574.5µm
On term birth (n=24)	573µm	537.25µm	587.25µm
Z	-2.352		
p	0.019 (2 tailed)		
Effect Size (r)	Medium = 0.42		

Table 5-13 CCT and maturity at birth – pre-term and on term births

CCT	*Median*	*Interquartile Range*	
On term birth (n=24)	573µm	537.25 µm	587.25µm
Post term birth (n=12)	530µm	522.75µm	543.25µm
Z	-1.967		
p	0.049 (2 tailed)		
Effect Size (r)	Medium = 0.43		

Table 5-14 CCT and maturity at birth – on term and post term births

5.2.7 Developmental Milestones

Length at 24 Months

ACD	*Median*	*Interquartile Range*	
Above average length (n=14)	3.73mm	3.635mm	3.852mm
Average length (n=35)	3.58mm	3.46mm	3.67mm
Z	-2.734		
p	0.006 (2 tailed)		
Effect Size (r)	Medium = 0.39		

Table 5-15 ACD and length at 24 months – above average and average responses

Length at 36 Months

ACD	*Median*	*Interquartile Range*	
Above average length (n=14)	3.73mm	3.635mm	3.852mm
Average length (n=35)	3.58mm	3.46mm	3.67mm
Z	-2.734		
p	0.006 (2 tailed)		
Effect Size (r)	Medium = 0.39		

Table 5-16 ACD and length at 36 months – above average and average responses

5.2.8 Education

Reading Performance

AL	*Median*	*Interquartile Range*	
Average (n=20)	23.12mm	22.90mm	23.59mm
Below average (n=9)	22.23mm	22.07mm	22.60mm
Z	-2.189		
p	0.029 (2 tailed)		
Effect Size (r)	Medium = 0.37		

Table 5-17 Axial length and reading performance – average and below average responses

Writing Performance

AL	*Median*	*Interquartile Range*	
Above average (n=26)	23.10mm	22.57mm	23.59mm
Below average (n=10)	22.21mm	22.10mm	22.56mm
Z	-2.402		
p	0.016 (2 tailed)		
Effect Size (r)	Medium = 0.4		

Table 5-18 Axial length and writing performance – above average and below average responses

Mathematics Performance

AL	*Median*	*Interquartile Range*	
Above average (n=25)	23.05mm	22.57mm	23.54mm
Below average (n=6)	22.18mm	22.10mm	22.40mm
Z	-2.463		
p	0.014 (2 tailed)		
Effect Size (r)	Medium = 0.45		

Table 5-19 Axial length and mathematics performance - above average and below average responses

5.2.9 Visual Environment

Outdoor Playtime (Night)

AL	*Median*	*Interquartile Range*	
<30 minutes (n=27)	23.39mm	23.04mm	23.74mm
> 1 hour (n=8)	22.35mm	21.55mm	22.83mm
Z	-2.687		
p	0.007(2 tailed)		
Effect Size (r)	Large = 0.51		

Table 5-20 Axial length and outdoor play time (night) - <30 minutes and > 1 hour responses

Recreational Screen Time

SE refraction	*Median*	*Interquartile Range*	
30min-1 hour (n=20	+0.21D	-0.17D	+0.51D
None (n=3)	+1.77D	+1.26D	+3.38D
Z	-2.008		
p	0.045 (2 tailed)		
Effect Size (r)	Medium = 0.42		

Table 5-21 SE refraction and recreational screen time – 30 minutes to 1 hour and no screen time responses

Home Type

AL	*Median*	*Interquartile Range*	
Large residential (n=35)	23.06mm	22.42mm	23.51mm
Rural/semi-rural (n=18)	22.53mm	22.10mm	23.04mm
Z	-2.132		
p	0.033 (2 tailed)		
Effect Size (r)	Small = 0.29		

Table 5-22 Axial length and home type – large residential and rural/semi-rural responses

5.2.10 Maternal Factors

Maternal Ethnicity

ACD	*Median*	*Interquartile Range*	
White European (n=51)	3.64mm	3.50mm	3.80mm
East Asian (n=4)	3.37mm	3.21mm	3.48mm
Z	-2.496		
p	0.013 (2 tailed)		
Effect Size (r)	Small = 0.34		

Table 5-23 Anterior chamber depth and maternal ethnicity – White European and East Asian responses

Maternal Employment

AL	*Median*	*Interquartile Range*	
Full time (n=17)	23.33mm	22.77mm	23.89mm
None (n=6)	22.40mm	22.04mm	22.85mm
Z	-2.100		
p	0.036 (2 tailed)		
Effect Size (r)	Medium = 0.43		

Table 5-24 Axial length and maternal employment – full time and no employment responses

AL	*Median*	*Interquartile Range*	
Full Time (n=17)	23.33mm	22.77mm	23.89mm
Part time (n=32)	22.77mm	22.16mm	22.25mm
Z	-2.463		
p	0.014 (2 tailed)		
Effect Size (r)	Medium = 0.45		

Table 5-25 Axial length and maternal employment – full time and part time responses

Maternal Spectacle Wear

AL	*Median*	*Interquartile Range*	
Corrective lenses (n=30)	23.09mm	22.67mm	23.54mm
No correction (n=25)	22.33mm	22.07mm	23.08mm
Z	-2.883		
p	0.005 (2 tailed)		
Effect Size (r)	Medium = 0.38		

Table 5-26 Axial length and maternal requirement for correction of refractive error – correction required, and no correction required responses

SE refraction	*Median*	*Interquartile Range*	
No correction (n=25)	+0.45D	+0.25D	+0.79D
Corrective lenses (n=30)	+0.21D	-0.11D	+0.46D
Z	-2.802		
p	0.005 (2 tailed)		
Effect Size (r)	Medium = 0.38		

Table 5-27 SE refractive error and maternal requirement for refractive error correction – no correction required, and correction required responses

Maternal Visual Condition

AL	*Median*	*Interquartile Range*	
Myopia (n=21)	23.33mm	22.07mm	23.08mm
Emmetropia (n=25)	22.12mm	22.77mm	23.50mm
Z	-2.669		
p	0.008 (2 tailed)		
Effect Size (r)	Medium = 0.39		

Table 5-28 Axial length and maternal visual condition – emmetropia and myopia responses

SE refraction	*Median*	*Interquartile Range*	
Emmetropia (n=25)	+0.25D	-0.13D	+0.49D
Myopia (n=21)	+0.45D	+0.25D	+0.79D
Z	-2.561		
p	0.01 (2 tailed)		
Effect Size (r)	Medium = 0.38		

Table 5-29 SE refractive error and maternal visual condition – emmetropia and myopia responses

SE refraction	*Median*	*Interquartile Range*	
Emmetropia (n=25)	+0.25D	-0.13D	+0.49D
Astigmatism (n=7)	+0.16D	-0.06D	+0.25D
Z	-2.709		
p	0.038 (2 tailed)		
Effect Size (r)	Medium = 0.37		

Table 5-30 SE refractive error and maternal visual condition – emmetropia and astigmatism responses

5.2.11 Paternal Factors

No significant relationships were detected for the initial cohort between paternal factors and biometric or refractive outcomes for the participants.

5.3 DISCUSSION

Biometric data for the cohort was found to be broadly in line with published data and models. Statistically significant associations were found between a range of environmental, lifestyle and parental factors, most notably with regards to outdoor play time at night, and maternal visual performance.

Compared to the Rozema model for emmetropisation, axial length (AL) measurements in the current dataset (n = 58) demonstrated a mean difference of -0.18 mm, indicating that the eyes in the sample were, on average, shorter than predicted by the model. The total sum of squared differences was 42.25 mm, yielding an average squared error of approximately 0.73 mm per measurement. This corresponded to a root mean square error (RMSE) of 0.85 mm, equating to an approximate dioptric prediction error of ±1.5 D per eye, based on a conversion of ~1 D per 0.56 mm of axial length change.

For anterior chamber depth (ACD), the mean difference from the model was 0.08 mm, with a total sum of squared differences of 2.80 mm^2. This resulted in an average squared error of 0.05 mm^2 per measurement and an RMSE of 0.22 mm. While the overall variation in ACD was smaller, the deviation from model expectations may still be clinically relevant in biometric-based IOL calculations or growth trajectory modelling.

This cross-sectional analysis of the cohort provides broad information about the demographics, biometric data, lifestyle and environmental factors that may influence the refractive and biometric state of the individual at the time of testing. The data presented here provides initial conditions and context for the longitudinal analysis performed in chapter 6.

5.3.1 Demographics

The age of participants covers the full extent of the cohort limits of 5 to 12 years. The negative skew was indicative of the observed tendency for parents in the area to engage in optometric care for children in later primary school ages. Sex distribution was in line with the local population as indicated by Australian Government census data performed in 2021 [221].

While ethnicity was broadly in line with census data for the region, a strong tendency towards White European ethnicity was reported which exceeded that of census data. While this level of homogeneity is problematic from the perspective of detecting the influence of ethnicity on refractive error development, it does permit the removal of ethnicity as an obfuscating effect. The relationship of ethnicity on refractive error is well established in the literature, therefore the homogenous ethnicity is beneficial in this study. Similarly, cultural effects such as external tutoring beyond the scope of regular school attendances are minimised in comparison to those seen in the major urban centres.

5.3.2 Refractive Error and Biometry

The mean spherical refractive error of $+0.63D \pm 1.67$ displayed by the cohort is indicative of a tendency to mild hyperopia (figure 5-9), as would be expected by the mean age of the participants. The strong tendency towards myopia that is being detected in other regions [239-242], particularly urban centres, is not in evidence for this cohort (5.18%). When examined in the context of the modelled refractive development the cohort was broadly in line with expected values. While ethnicity, refractive error and biometry are well established in the literature, in this study the relationships are contradictory. Prevalence of hyperopia was relatively low at 8.62%, compared to 19.3% in the Kleinstein study [63], and 22.9% in the Aston Eye Study [4].

Axial length as a function of age tended to be shorter than those indicated by published data, and emmetropisation models (figure 5-7) [14]. While the trend for eyes in the study was close to the values predicted by the model, a number of outliers were present. Of interest is the refractive error associated with the longest eyes in the study, with four eyes >24.5mm only one exhibited myopic refractive error (SE=-2.865D).

The remaining three individuals exhibited refractive error in the order of -0.25D. Two of the individuals in this groups were twins, with the cause of significant difference between refractive outcomes unclear as all developmental conditions were consistent between the two. Unlike the outlier instances of long axial length the shorter axial lengths are in line with expectations as these individuals were those with the greatest hyperopic refractive error.

Anterior chamber depth (figure 5-8) was overall greater than that indicated by the modelled and published data [14]. The contribution of the ACD to the overall refractive power of the eye is relatively low compared to the cornea. As this cohort tends to shorter axial lengths, the correlation between these two factors suggests the axial length and ACD relationship for this cohort may be a signal of favourable emmetropisation. This is supported by the tendency to low hyperopia consistent with age as indicated by the spherical equivalent refractive error (figure 5-10). Despite the wide range of axial lengths there is a tendency to refractive errors that are close to the values indicated by modelling. Furthermore, the outliers in the cohort for refractive error and axial length do not display a correlation between myopia and long axial length. The opposite is typically the case for short axial length, where hyperopic refractive error is linked to shorter axial length.

Corneal thickness (figure 5-9) has been identified as the least consistent biometric factors in this data set. Examination of data collected for bulk analysis in studies such as those by Rozema suggest that this is consistent with the results found in other studies. This result is also in keeping with other studies who have not found a relationship between corneal thickness and refractive error [243].

5.3.3 Birth Conditions

Maturity at Birth

As the bulk of corneal growth occurs prenatally the results for preterm vs on term births are logical. Research indicates that preterm births nonetheless exhibit equivalent CCT at term age [26, 244]. The values in this data are lower than that of published results and do not conform with the published research in this area. Furthermore, the relationship between post term births and on term births is

inconsistent with the established research and would warrant further examination in the context of this regional cohort.

5.3.4 Developmental Milestones

Length at 24 Months and 36 Months

These ACD results are consistent with published data linking stature with biometry [232, 245]. Of note is that these were not replicated in axial length, only ACD. It is further noted that the studies cited tend to refer to older adolescent candidates. The failure to find consistent correlations between height and weight across all categories is of interest as it implies a disconnect between these parameters and ocular biometric development. The younger (1.5 to 2 year) age bracket where significant growth occurs was not encompassed by this study, so any effect detected may be as a residual effect in biometric parameters in later life.

5.3.5 Education

Reading, Writing, and Mathematics Performance

All three of these results suggest a relationship between longer axial lengths and higher levels of performance at tasks requiring longer periods of effort at near vision, with associated accommodative demands. In all instance above average performance was associated with longer axial lengths when compared with below average performance in the listed fields. Several authors have published data showing a linkage between study time and ametropia [98, 150, 156, 177]. However, the results of this study did not replicate the same magnitude of linkage between refractive error and study habits, despite showing an association between increased axial length and study. This is noteworthy as it would be expected that an increase in axial length would indicate a tendency towards myopia, which was not found here.

This study does not provide a mechanism for the definition of near working distance in the context of the tasks performed, precluding examination of an association between vergence demands and biometry which would allow comparison to the work of Harb et al. [198]. Confounding factors such as the potential trade-off

between outdoor exposure and increased time at study for academic performance also make isolation of a causative effect in this area difficult.

5.3.6 Visual Environment

Outdoor Playtime (Night)

These results are suggestive of a relationship between more time spent at play or other tasks than at study, with an associated reduction in axial length. This aligns with the results of Jiang et al [200], with outdoor play time associated with shorter axial lengths. 15.09% of responses indicated > 1hour and 15.09% indicated 20 minutes to 1 hour, of outdoor time in the evening. The remainder indicated < 30minutes or no time outdoors in the evening. A corresponding linkage between sport and time at sport was not detected. Further investigation into correlations between this result, the type of activities undertaken and other metrics such as screen time may clarify this result.

The results found in this study associate nighttime outdoor time with shorter axial lengths. These results are also consistent with the observed tendency towards hyperopic refractive error observed in the cohort. The nighttime nature of the outdoor time contrasts with the results of Yotsokura et al. [55] which associated high luminance (100 lux) with shorter axial lengths. The suggests that the effect found in the regional cohort of this study is not related to luminance as was the case for the Yotsukura cohort and may be indicative of an optical effect as a potential mechanism [211].

Recreational Screen Time

An association between decreased screen time and hyperopia was found (nil screen time mean = +1.77D, and 30 minutes to 1 hour mean = +0.21D). While the overall SE was not myopic for the cohort, the association is of interest. Studies have thus far not drawn any meaningful correlation between screen time and refractive error [246]. This result may support the studies indicating a positive relationship between emmetropisation and time spent on a range of tasks of differing dioptric demands, including daylight exposure [210, 211, 247].

Home Type

Longer axial length was associated with large residential homes when compared with rural or semi-rural homes. Home size may be indicative of a range of factors

influencing emmetropisation. 63.64% of responses indicated larger residential style homes, 32.73% were rural or semi-rural and 3.64% were small residential homes. Rural homes by nature tend to have yards and/or significant amounts of surrounding property which permit greater outdoor exposure time compared with more dense urban environments. This again relates to the potential for a protective optical mechanism related to the dioptric complexity of the visual environment as a factor in emmetropisation [55, 159, 248]. From this data it is not immediately apparent how much time is spent by the participants outdoors at home compared to during the school day. Analysis of the relationship between outdoor play, home size as well as exploration of the time spent outdoors at school may clarify this aspect.

5.3.7 Maternal Factors

Maternal Ethnicity

The small effect size and small number of participants in the East Asian category render this result showing an association between ethnicity and shorter axial lengths, while significant in this study, difficult to contextualise. Two of the participants were siblings in this category with one candidate representing an outlier hyperopic data point. Consequently, this outcome may represent an anomaly rather than be indicative of the broader population. Further study with a larger representation from East Asian ethnicity may provide better insight into this result.

Maternal Employment

Maternal employment was associated with axial length, the children of mothers in full time employment (30.91%) having larger AL values than those in part time (54.55%) or with no employment outside the home (10.91%). It is speculated that this may be linked with increased time spent in school and after school care environments. From this perspective these results may be linked those of academic performance where the effect is due to decreased time outdoors as a function of increased time indoors or in supervised care [177]. Further examination of the nature of childcare and time spent outdoors may be beneficial for exploring this relationship.

Maternal Spectacle Wear

The relationship between parental refractive error and childhood ametropia is established in the literature [139, 140]. In this study 54.55% of responses indicated a maternal requirement for spectacles or vision correction. This data from this study supports the general association of maternal ametropia with presentation in their child, indicating that maternal refractive error, regardless of magnitude or type, is associated with more myopic SE refractive error and longer AL.

Maternal Visual Condition

The linkage between maternal myopia and axial length for their child's incidence of myopia and associated biometry is consistent with the literature [139, 140], with children of maternal myopes displaying longer AL than those with maternal emmetropia. In this study myopia (54.55%) and emmetropia (45.45%) represented the bulk of responses for visual condition, with hyperopia (3.64%) and astigmatism (12.73%) only weakly represented. Further study examining the relationship between the magnitude of maternal myopia and that of the participants may provide insight into the nature of emmetropisation in the rural environment. Of note is the relationship between the presence of maternal myopia, which indicated more hyperopic refractive error in the child (0.45D) than when no maternal refractive error was present (0.25D). This contradicts the published data in which the presence of a myopic parent is indicative of elevated risk for myopia in the child [80]. The scope of this study did not permit inclusion of maternal magnitude of refractive error.

5.3.8 Paternal Factors

No significant relationships were detected for the initial cohort between paternal factors and biometric or refractive outcomes for the participants. This is not necessarily indicative of no possible correlations but is indicative that the cohort size was perhaps insufficient to detect and effects. This is noteworthy given the number of relationships between maternal refractive error and the biometry of the participants shown above.

5.3.9 Summary

A range of associations between lifestyle, environmental and developmental influences were found in this cross-sectional baseline component of the study. Many

were in line with published results of other studies indicating the importance of managing the emmetropisation of individuals in the context of their larger environment.

The demographics of the cohort were consistent with the data presented by the most recent census. Biometry and refractive error were in line with the normative models presented by Rozema [14]. It is noted that this cohort is not necessarily representative of the general population from an ophthalmic perspective as all of the individuals were engaged in optometric care, a feature which is not true for the general population.

Significant relationships were detected between CCT and maturity at birth, with results lower than those from the literature. Developmental milestones for length (height) at 24 and 36 months indicated a relationship between size of the child at these ages and biometry at the time of their examination in this study, suggesting a long-term effect. The educational environment and performance was observed to have an impact on the axial length of the individuals, with better performance associated with longer AL values.

An expected relationship between outdoor play time during the day and biometry was not detected. However, a similar effect was found in the cohort between nighttime play outdoors and axial length, with greater time spent outdoors in the evening associated with shorter axial lengths. No exposure to recreational screen usage was associated with more hyperopic refractive error. Size of domicile and associated land was associated with axial length. Individuals on rural or semi-rural blocks displayed shorter axial lengths.

Parental influence on refractive and biometric outcomes was restricted to maternal factors. Ethnicity of the cohort was almost completely homogenous, making meaningful results difficult to ascertain. Maternal spectacle wear and visual condition both exhibited significant associations, with the presence of ametropia and myopia indicative of the presence of refractive error and longer axial lengths in the cohort.
Of note is the association between more hyperopic refractive error for the children of myopes compared to the children of emmetropes. As the cohort is self-selected and already undertaking optometric management it is suggested that the children of myopes are subject to heightened care levels due to parental concern borne of their own refractive error.

Chapter 6: Longitudinal Data – A Study of Lifestyle Factors on the Biometric Development of Children in a Regional Australian Population

A longitudinal analysis of the data was undertaken to determine the influence of lifestyle factors on the growth and changes to biometry of the eye over a 12-month period. While the cross-sectional analysis provided insight into the features of the cohort in a broad sense, it did not provide information on the behaviour of the cohort over a period of time, with the attendant data on growth over a period, and potential insight into trends, that longitudinal analysis provides.

6.1 METHODS

The cohort of participants for whom the second (subsequent) consultation took place was reduced from the initial cohort (test1 baseline). This is primarily due to non-compliance with scheduled review appointments. This section presents the data for the cohort who returned for their subsequent consultation at the practice. The study design called for an interval of 12 months between attendances. The average time between data points for the cohort was 13.60 months (+/- 5.32). Data in this section are presented again as a cross-sectional study for the first and second test in isolation due to the change in cohort size, and as a longitudinal study for the examination of change between attendances (test 1 and test 2) in the context of environmental factors. In this section only the eye selected for study is discussed.

38 of the 58 participants (65.52%) included in the study had two or more consultations for which biometry was collected during the timescale of the study. This was in excess of the number of participants required as indicated by the G*Power calculations performed during the study design phase (n=28). Of these 38, 36 (62.07%) completed and returned the questionnaire. Of the range of data collected, some elements, such as wavefront aberrometry, did not return significant results and were not reported upon in the following chapter.

6.2 RESULTS - LONGITUDINAL COHORT (TEST 1 AND TEST 2 DATA)

6.2.1 Demographics of Participants

The total number of participants for whom an initial data and subsequent point was extracted was 38. This represents 50% of the candidates who initially expressed interest in participation, and 65.5% of the cohort represented in the cross-sectional analysis performed in chapter 5. There were 18 (47.37%) female participants and 20 (52.63%) male participants. The mean age of the participants from this second group at their first consultation was 9.35 (±1.62) years, ranging from 5 to 11.1 The mean age for this group at their second attendance was 10.48 (±1.74) years, ranging from 5.95 to 12.33 years of age (Figures 6-1 & 6-2). Using the Shapiro-Wilk Test, the age data appear to not be normally distributed for either attendance.

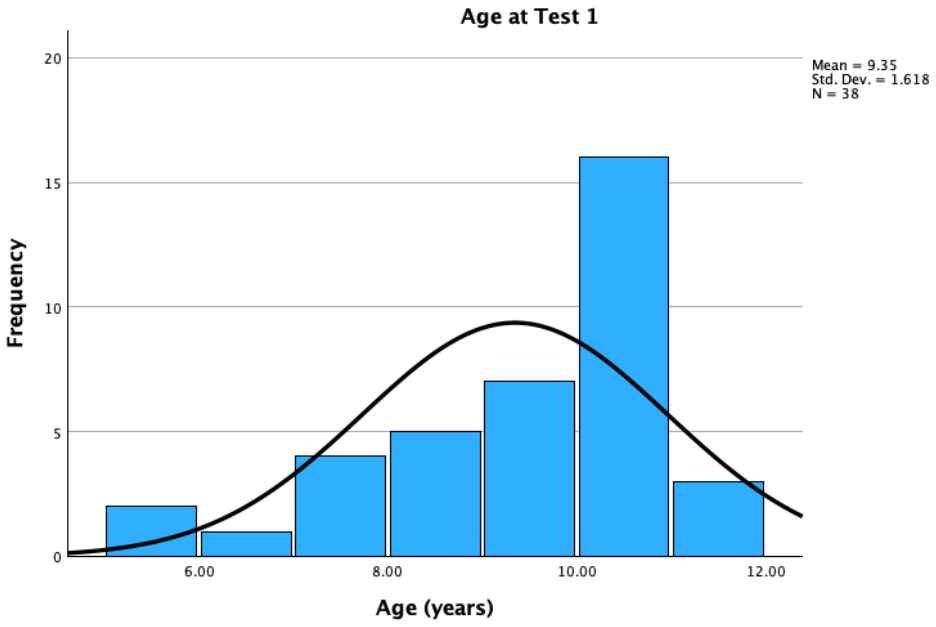

Figure 6-1 Age at which first consultation for inclusion in the study occurred for the cohort with two attendances

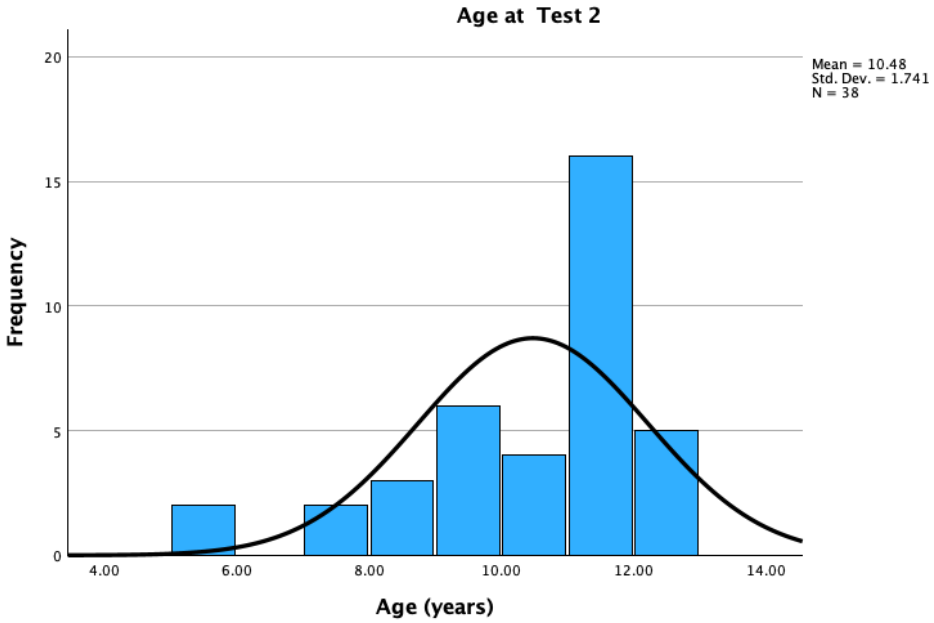

Figure 6-2 Age at which second consultation for inclusion in the study occurred for the cohort with two attendances

Compared with the cohort for whom there was either one or two data points, 2 respondents (5.26%) did not complete or return the questionnaire. This indicates a drop out of one of the candidates who had failed to return a questionnaire. Of those who did complete the questionnaire, the majority of parental respondents were of white European ethnicity (94.29%), with the rest being of East Asian ethnicity (5.71%). The children were also predominantly of White European ethnicity (91.67% both parents), maternal East Asian ethnicity and paternal White European ethnicity (5.55%), and one of both parents with East Asian ethnicity (2.78%).

A comparison of the demographics of the total cohorts for test1 and test 2 is presented in Table 6-1.

	Test 1 n=58	*Test 2 n=38*
Female	30 (51.72%)	18 (47.37%)
Male	28 (48.28%)	20 (52.63%)
Age (years)	9.13 ±1.83	10.48 ±1.74

Table 6-1 - Demographics of total cohorts at test 1 and test 2

6.2.2 Refractive Error

Refractive error data for the longitudinal cohort is presented in Table 6-2 and Table 6-3. As indicated, the cohort is reduced due to noncompliance with normal attendance schedules. Data in this section is for the eye selected for inclusion in the study only, this is the same eye as that used for each candidate in the cross-sectional analysis. Results were determined by autorefraction using the Rodenstock DNEye unit.

	Test 1			*Test 2*		
Refractive Error	Mean	Min	Max	Mean	Min	Max
Mean spherical equivalent power	$+0.60D \pm 1.76$	$-2.87D$	$+6.23D$	$+0.47D \pm 1.84$	$-3.72D$	$+6.34D$
Mean spherical power	$+0.79D \pm 1.96$	$-2.68D$	$+6.60D$	$+0.70D \pm 1.84$	$-3.53D$	$+6.93D$
Mean cylindrical power	$-0.39D \pm 0.47$	$-2.26D$	$0.00D$	$-0.46D \pm 0.42$	$-2.36D$	$0.00D$

Table 6-2 Refractive error of selected eyes in cohort for longitudinal study n=38

Refractive Error Definition	*Test 1*	*Test 2*
Hyperopia $(\geq +2.00D)$	3 (7.89%)	3 (7.89%)
Myopia $(\leq -0.50D)$	2 (5.26%)	3 (7.89%)
Astigmatism $\geq 0.75D)$	7 (18.42%)	5 (13.16%)

Table 6-3 Refractive error defined by type for selected eyes n=38

6.2.3 Biometry

Normality tests were performed on the data for test 1 in the longitudinal cohort using the Shapiro – Wilk test as shown in Table 6-4. The null hypothesis is that the data are normally distributed indicating that only the spherical equivalent refraction is not normally distributed in this case.

	Statistic	*df*	*Sig.*
Axial length	0.953	38	0.116
Anterior Chamber Depth	0.974	38	0.509
Corneal Thickness	0.978	38	0.660
Spherical Equivalent Refraction	0.667	38	<0.001

Table 6-4 Tests of Normality for data from first data collection for longitudinal cohort (test 1)

Additionally, normality tests were performed on the data for test 2 in the longitudinal cohort using the Shapiro – Wilk test as shown in Table 6-5.

	Statistic	**df**	**Sig.**
Axial length	0.953	38	0.108
Anterior Chamber Depth	0.969	38	.371
Corneal Thickness	0.978	38	0.656
Spherical Equivalent Refraction	0.666	38	<0.001

Table 6-5 - Tests of Normality for data from first data collection for longitudinal cohort (test 2)

The biometry of the selected eye as measured using the Nidek AL-Scan is presented in Table 6-6 and following figures.

	Test 1			*Test 2*		
Biometry	Mean	Min	Max	Mean	Min	Max
Axial length	$22.93mm \pm 0.96$	$20.36mm$	$24.93mm$	$23.03mm \pm 0.94$	$20.60mm$	$25.08mm$
Anterior chamber depth	$3.65mm \pm 0.2$	$3.03mm$	$4.05mm$	$3.68mm \pm 0.23$	$3.09mm$	$4.10mm$
Central Corneal Thickness	$557\mu m \pm 32.42$	$484\mu m$	$612\mu m$	$557\mu m \pm 31.08$	$486\mu m$t	$612\mu m$

Table 6-6 Biometry data of cohort for selected eye n=38

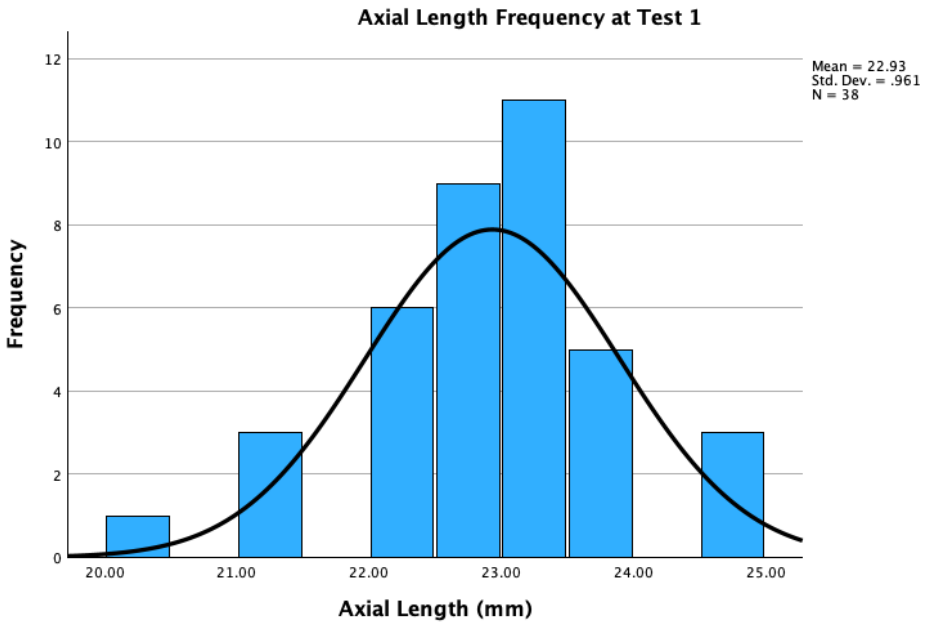

Figure 6-3 Axial length (mm) distribution for initial data collection point (test 1) for the longitudinal cohort

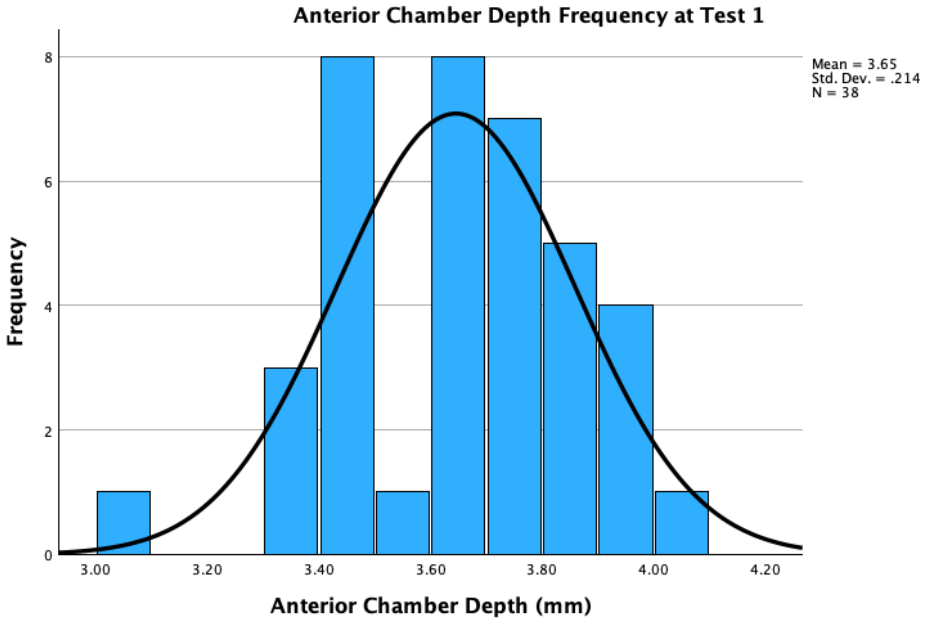

Figure 6-4 Anterior chamber depth (mm) distribution for initial data collection point (test 1) for the longitudinal cohort

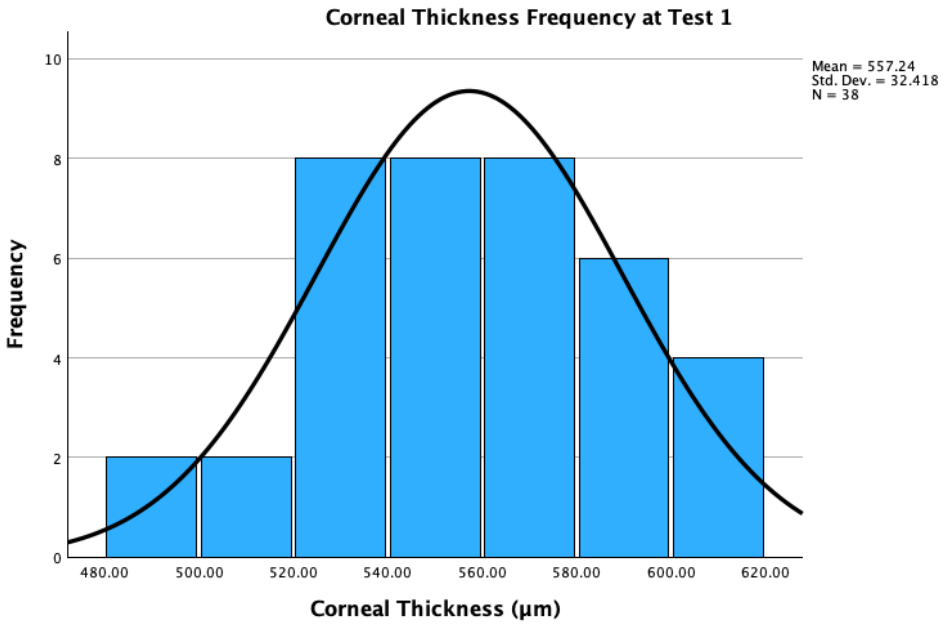

Figure 6-5 Corneal thickness (µm) for initial data collection point (test 1) for the longitudinal cohort

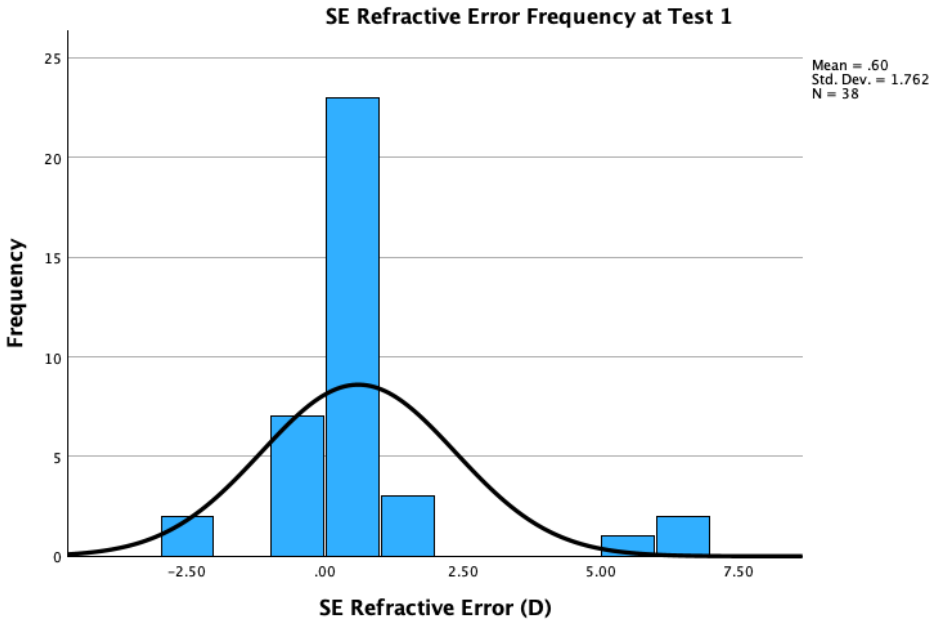

Figure 6-6 Spherical equivalent refractive error (D) distribution for initial data collection point (test 1) for the longitudinal cohort

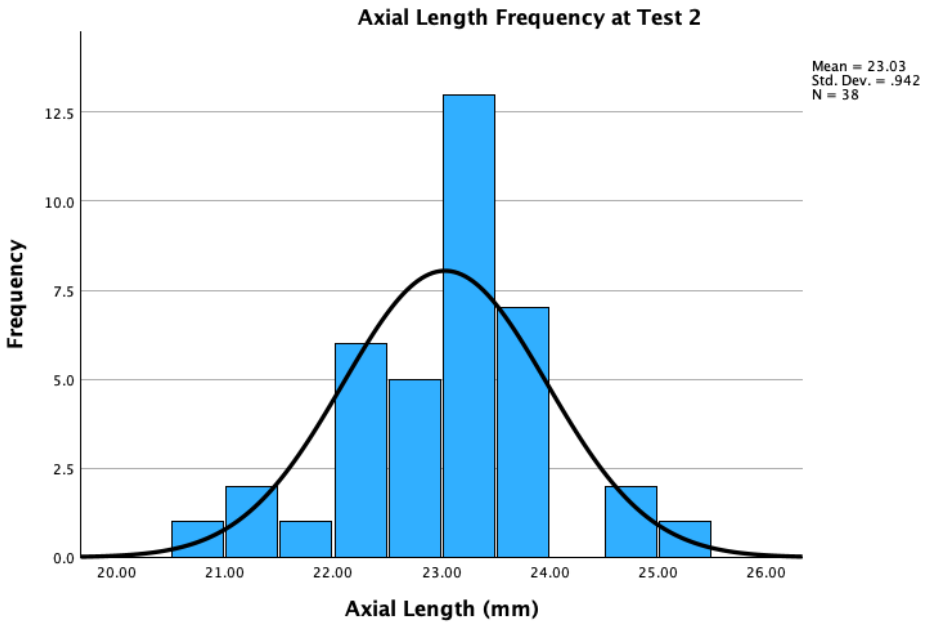

Figure 6-7 Axial length (mm) distribution for second data collection point (test 2) for the longitudinal cohort

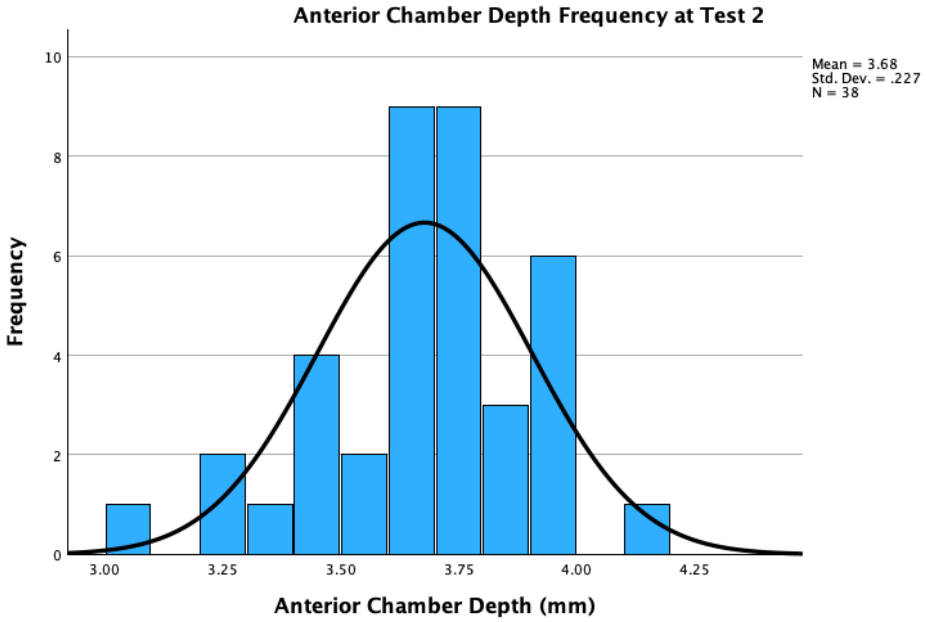

Figure 6-8 Anterior chamber depth (mm) distribution for second data collection point (test 2) for the longitudinal cohort

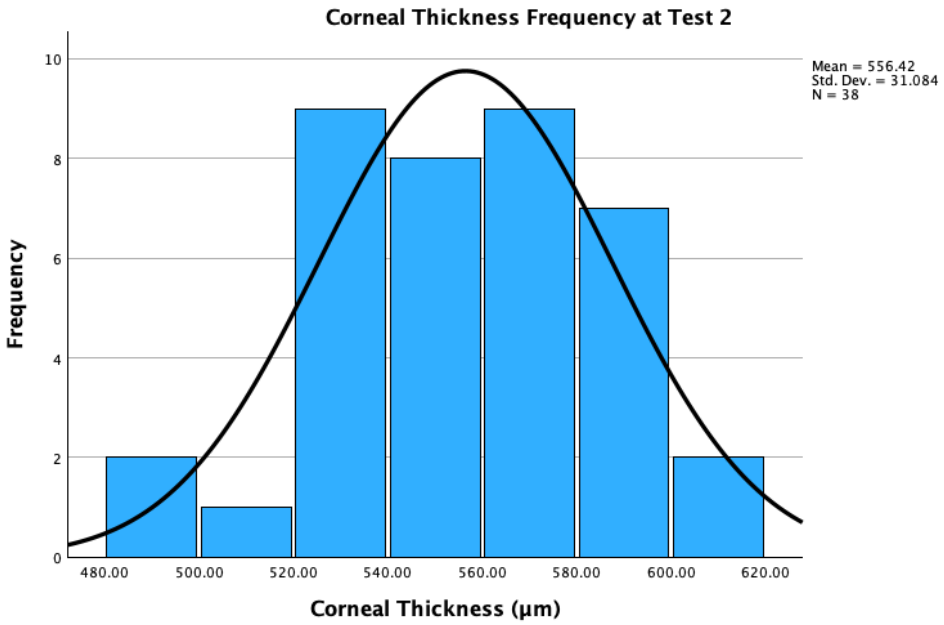

Figure 6-9 Corneal thickness (µm) for second data collection point (test 2) for the longitudinal cohort

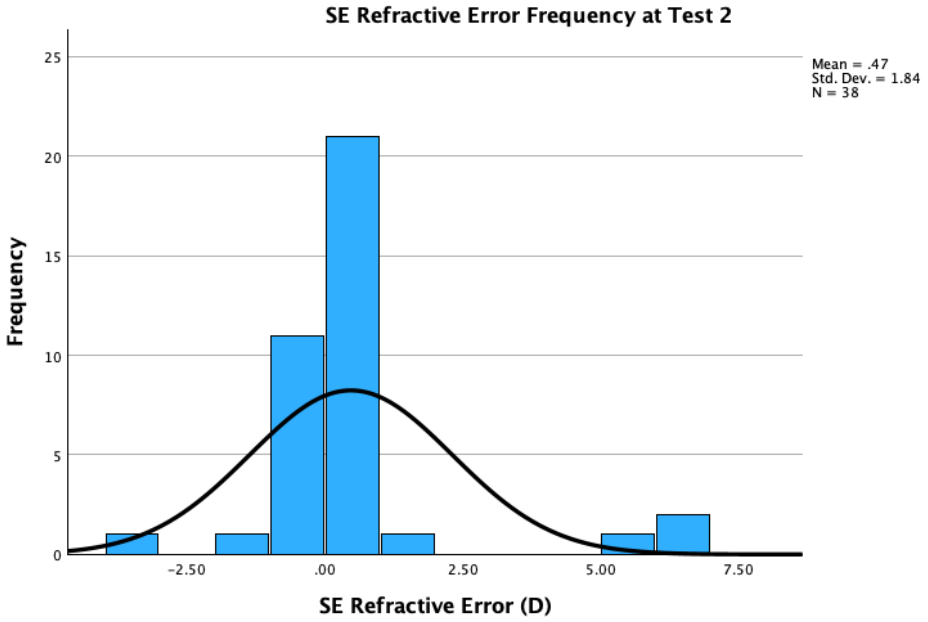

Figure 6-10 Spherical equivalent refractive error (D) distribution for second data collection point (test 2) for the longitudinal cohort

As the SE data is not normally distributed (Shapiro-Wilk p = <0.001) a Spearman Rank Correlation was again performed to examine the relationship between refractive error and biometry. SE and axial length for test 1 showed a negative correlation

(Pearson correlation = -0.690, sig 2 tailed = <0.001, Spearman's rho = -0.381, sig 2 tailed = 0.018) with a medium effect size (>0.30). This is in line with the established negative correlation between refractive error and axial length. Figure 6-11 shows the scatter plots for the above tests and linear regression lines. G*Power was used to confirm the sample size for future studies using the Pearsons coefficient for effect size, which indicated a total sample size of 14 candidates are required to confirm the results found for the Pearsons correlation and 51 for the Spearman's rho.

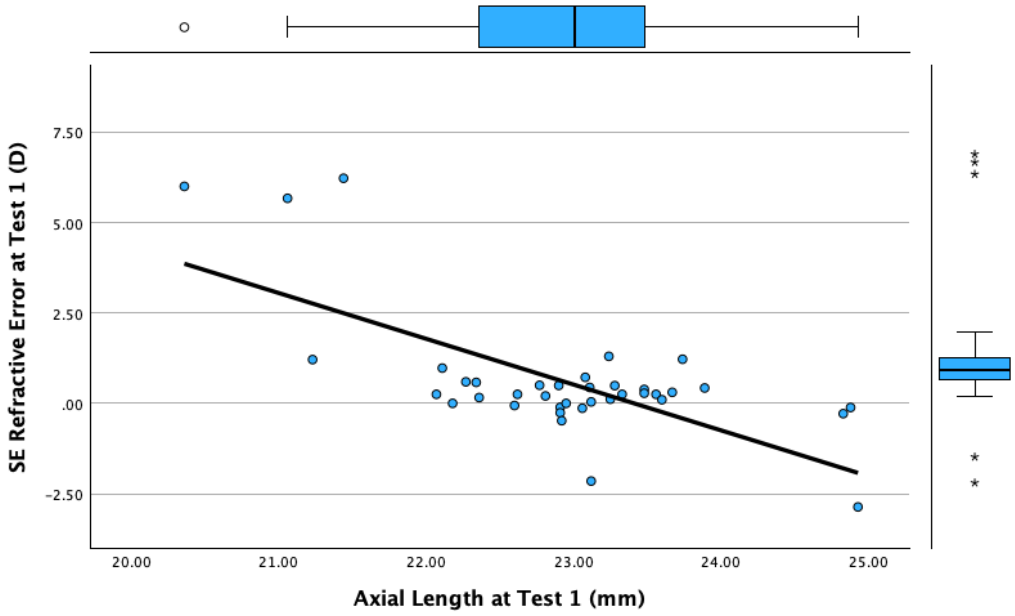

Figure 6-11 Linear regression plot of Spherical Equivalent Refraction (SE) in dioptres and Axial Length (AL) in mm. Test 1 data in cohort with two attendances.

This test was again repeated for ACD and CCT. SE and ACD results yielded a Pearson Correlation of -0.384 (sig. 2 tailed =0.017) and Spearman's rho = -0.176 (sig 2 tailed = 0.291). SE and CCT results were Pearson Correlation of 0.068 (sig. 2 tailed =0.685) and Spearman's rho = 0.037 (sig 2 tailed = 0.827). ACD and AL Pearsons correlation was 0.580 (sig. 2 tailed = <0.001) with a Spearman's rho of 0.500 (sig. 2 tailed = 0.001).

SE and axial length for test 2 also showed a negative correlation (figure 6-12). Pearson correlation was -0.686 (sig 2 tailed = <0.001), Spearman's rho = -0.275 (sig 2 tailed = 0.094) with a medium effect size (>0.30). This test was again repeated for ACD and CCT. SE and ACD results yielded a Pearson Correlation of -0.233 (sig. 2

tailed =0.038) and Spearman's rho = -0.233 (sig 2 tailed = 0.159). CCT results were a Pearson Correlation of 0.125 (sig. 2 tailed =0.453) and Spearman's rho = 0.098 (sig 2 tailed = 0.557). ACD and AL Pearsons correlation was 0.562 (sig. 2 tailed = <0.001) with a Spearman's rho of 0.500 (sig. 2 tailed = 0.001) as with the data from the first collection point for the longitudinal cohort.

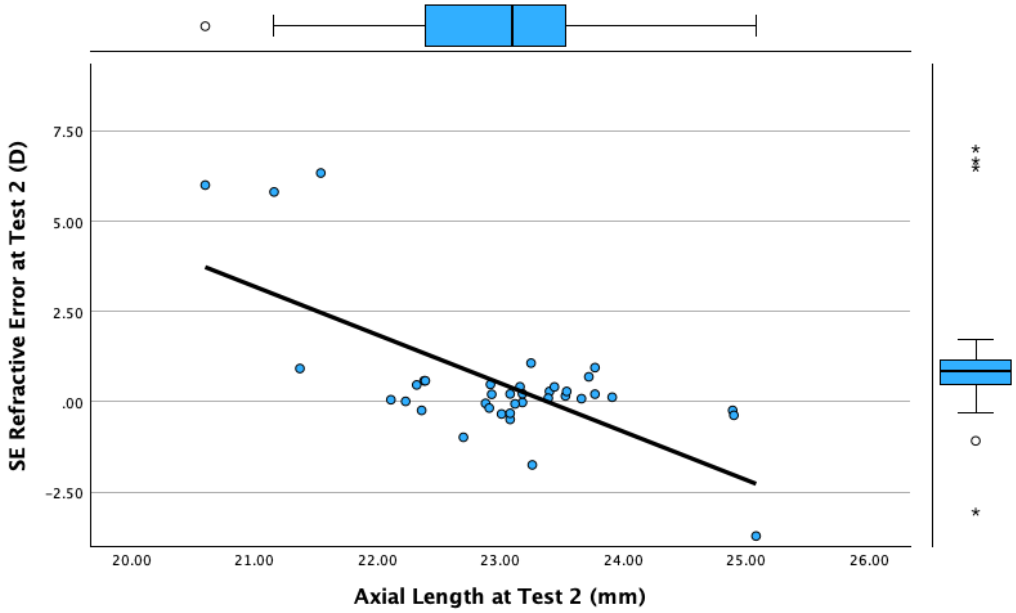

Figure 6-12 - Linear regression plot of Spherical Equivalent Refraction (SE) in dioptres and Axial Length (AL) in mm. Test 2 data in cohort with two attendances.

These results are in line with those from test one and indicate a measure of consistency between the cohort across the testing time interval.

In the same manner as in chapter 5, scatter plots of axial length of the selected eye as a function of age were produced to examine the relationship between age and overall eye length. Normative lines for growth were overlaid to examine the age and axial length relationships in the context of publish normative models. This process was repeated for ACD, CCT, and SE refractive error at both test 1 and test 2 (Figure 6-15 to Figure 6-20). These models were drawn from Rozema's bi exponential functions describing emmetropisation and applied to figures where appropriate [14]. Longitudinal changes are presented in chapter 6.2.4.

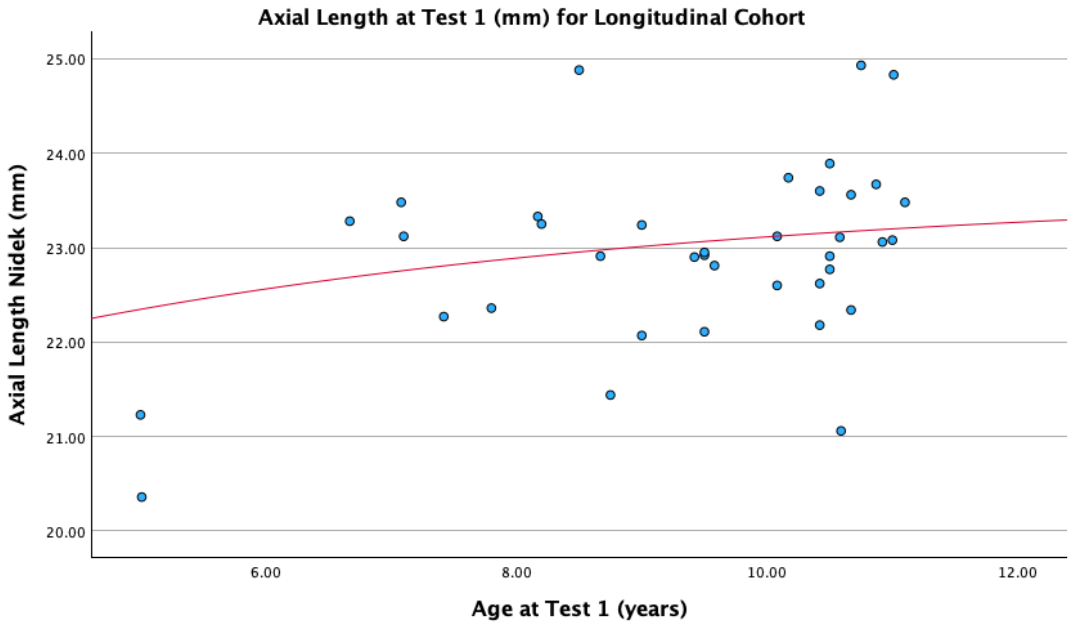

Figure 6-13 Axial length (mm) at test 1, longitudinal cohort (n=38). Rozema's model for axial growth is indicated by the overlaid curve.

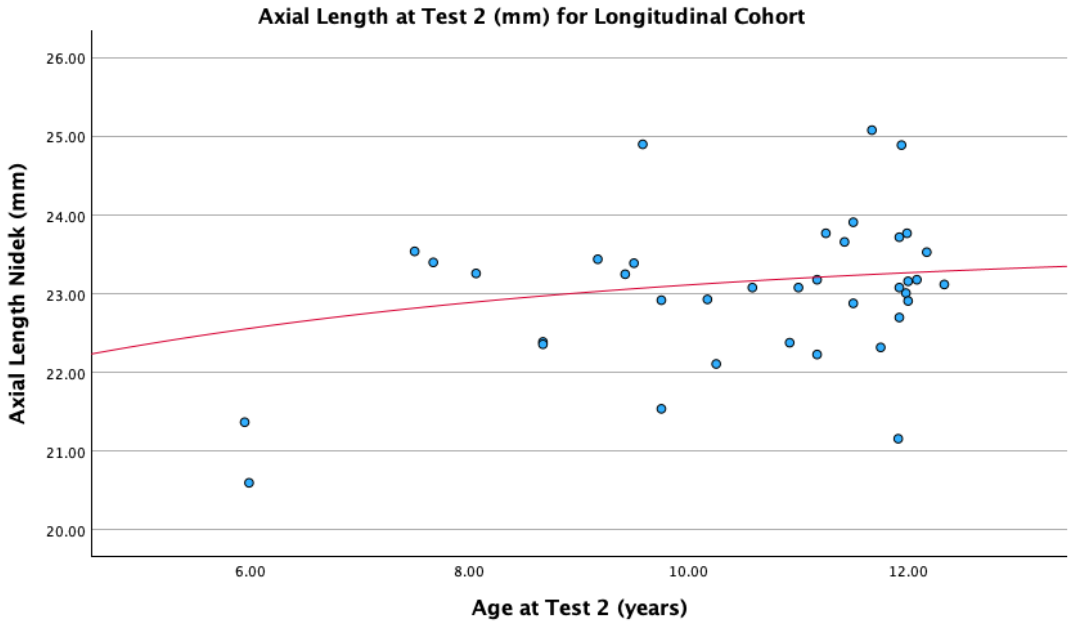

Figure 6-14 Axial length (mm) at test 2, longitudinal cohort (n=38). Rozema's model for axial growth is indicated by the overlaid curve.

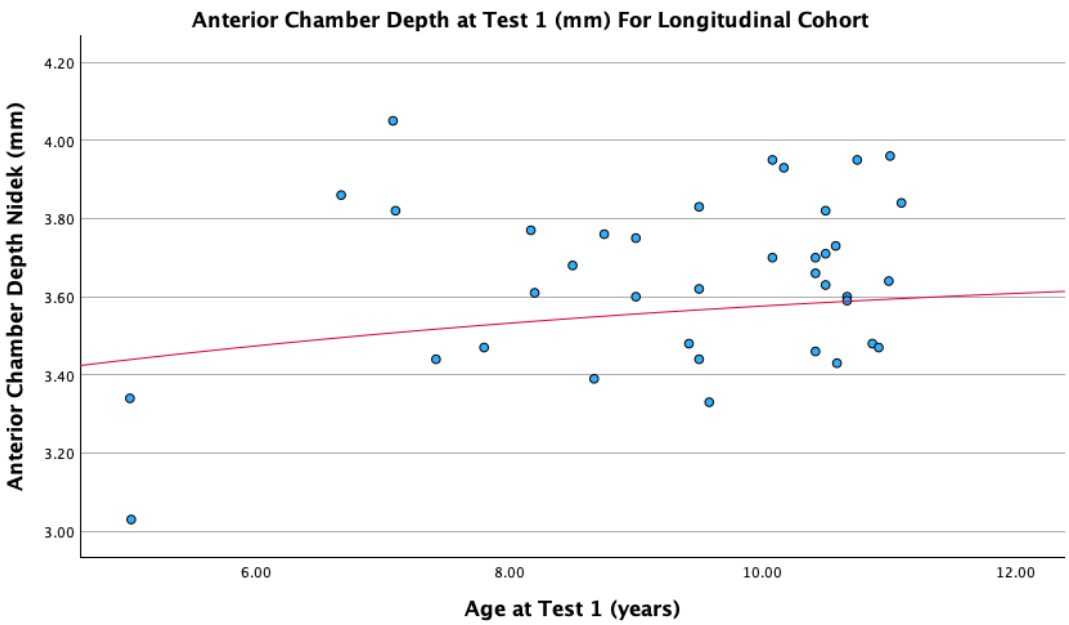

Figure 6-15 Anterior chamber depth (mm) at test 1, longitudinal cohort (n=38). Rozema's model for anterior chamber growth is indicated by the overlaid curve.

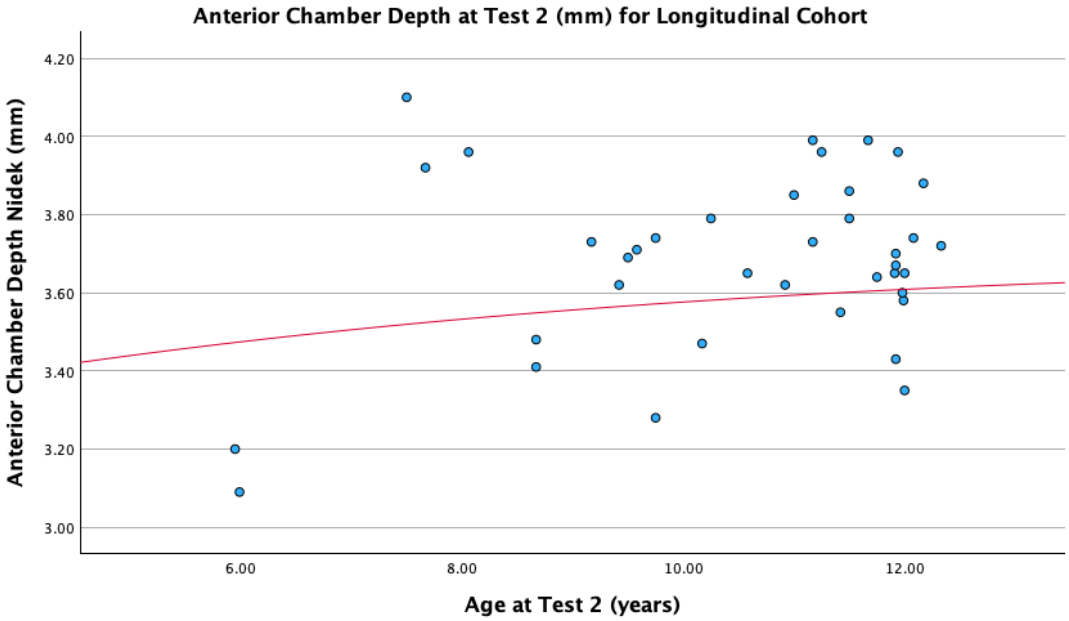

Figure 6-16 Anterior chamber depth (mm) at test 2, longitudinal cohort (n=38). Rozema's model for anterior chamber growth is indicated by the overlaid curve.

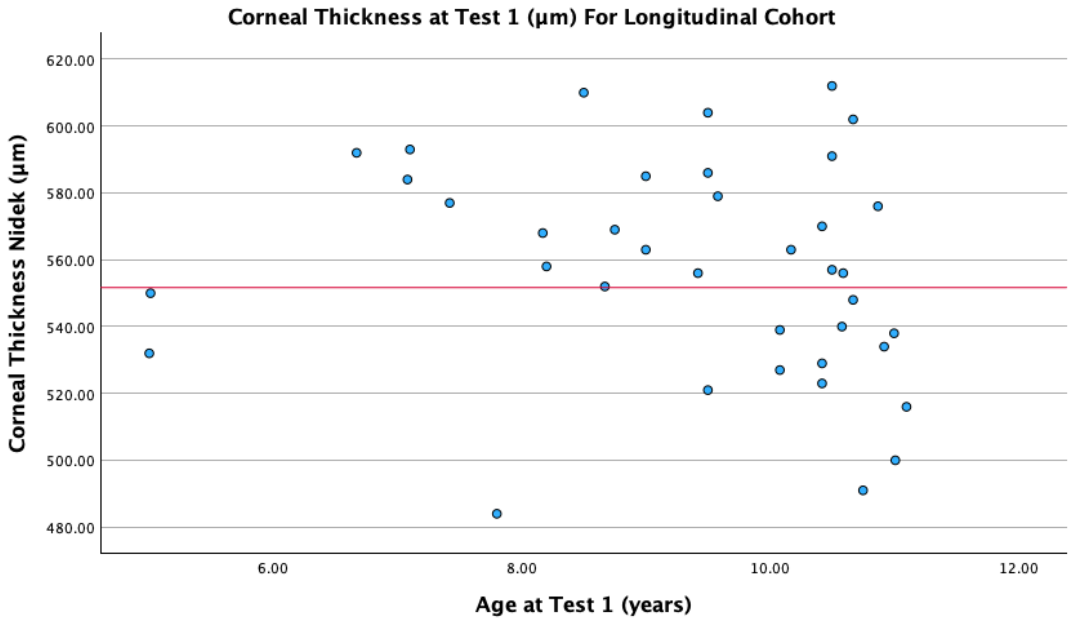

Figure 6-17 Corneal thickness (µm) at test 1, longitudinal cohort (n=38). Rozema's model for CCT growth is indicated by the overlaid curve.

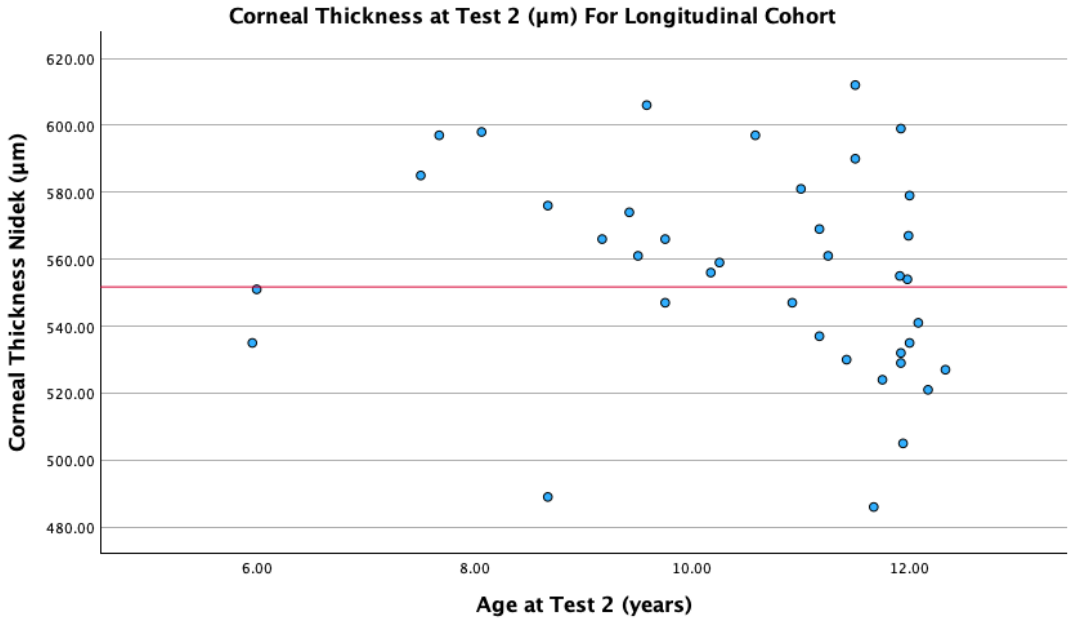

Figure 6-18 Corneal thickness (µm) at test 2, longitudinal cohort (n=38). Rozema's model for CCT growth is indicated by the overlaid curve.

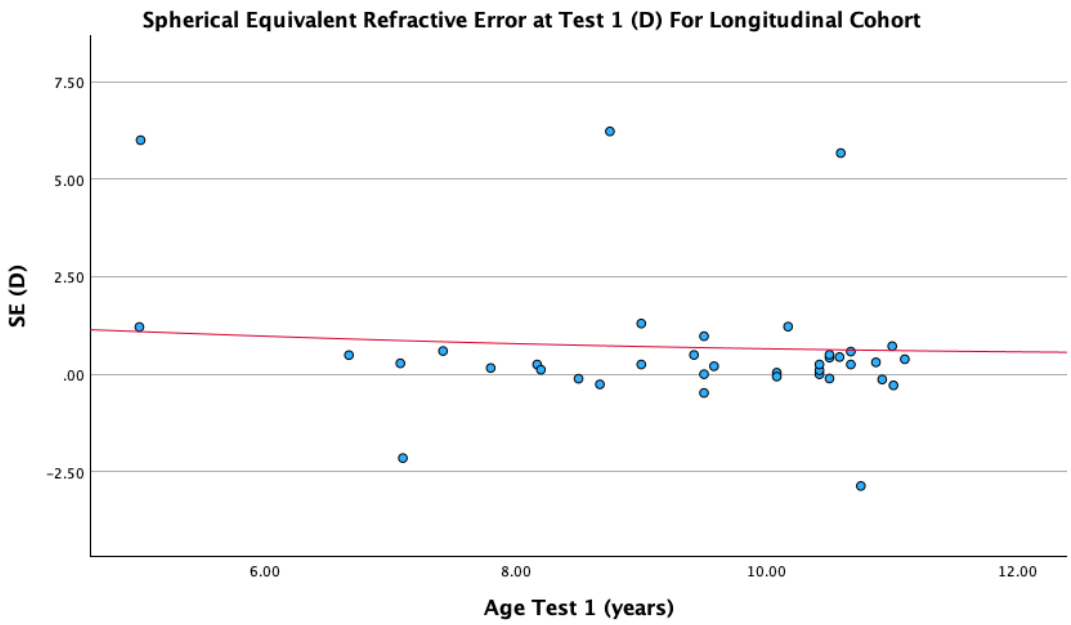

Figure 6-19 SE refractive error (D) at test 1, longitudinal cohort (n=38). Rozema's model for SE development is indicated by the overlaid curve.

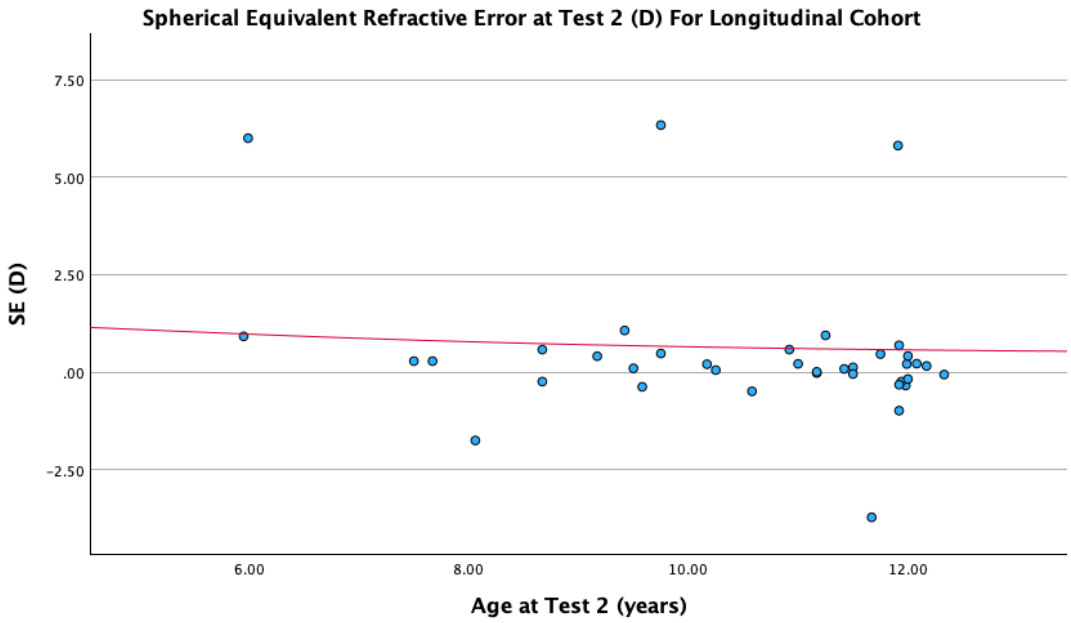

Figure 6-20 SE refractive error (D) at test 2, longitudinal cohort (n=38). Rozema's model for SE development is indicated by the overlaid curve.

Total sum of squares and root mean sum of squares were calculated for AL, ACD, and CCT, with the results presented in Table 6-7. As with previous analysis CCT measurements did not provide useful data.

	Mean	*Sum of Squares*	*Average Square Error /measurement*	*RMSE*
AL (mm)	-0.10	29.22	0.77	0.88
ACD (mm)	0.06	2.12	0.06	0.24

Table 6-7 - Sum of squares analysis for biometry results at test 2

6.2.4 Biometry and Refractive Error Change

The average interval between data collection points was 13.60 (± 5.32) months. While it is understood that growth of the eye is nonlinear and best modelled via bi exponential functions during emmetropisation, in order to provide consistency with time scales for analysis the average values for each variable across a 12-month period were determined. This was achieved by dividing the variable by the interval in months to determine the monthly rate of change, this was then multiplied by 12 to yield an annual value.

Mean axial length change for the 12-month period was $0.09mm$ (± 0.06), ACD change for 12 months was $0.03mm$ (± 0.06) , and CCT was $-1.18\mu m$ (± 5.36).

Mean change in SE refractive error was $-0.12D$ $(\pm 0.33D)$ with a minimum of $-0.93D$ and maximum of $+0.69D$.

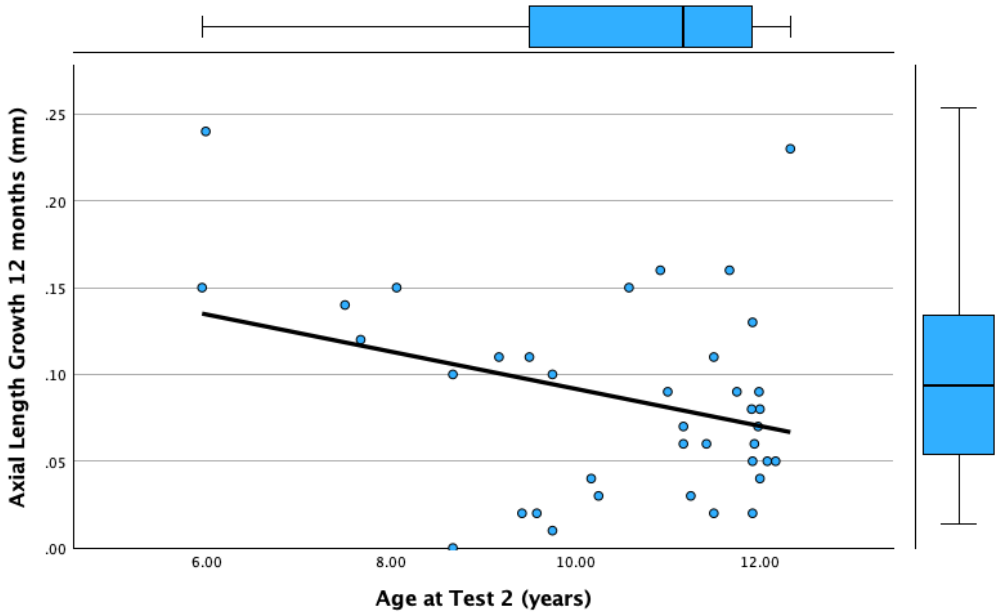

Figure 6-21 Axial length (mm) growth across 12 months, longitudinal cohort (n=38). Trend for axial growth is indicated by the black line

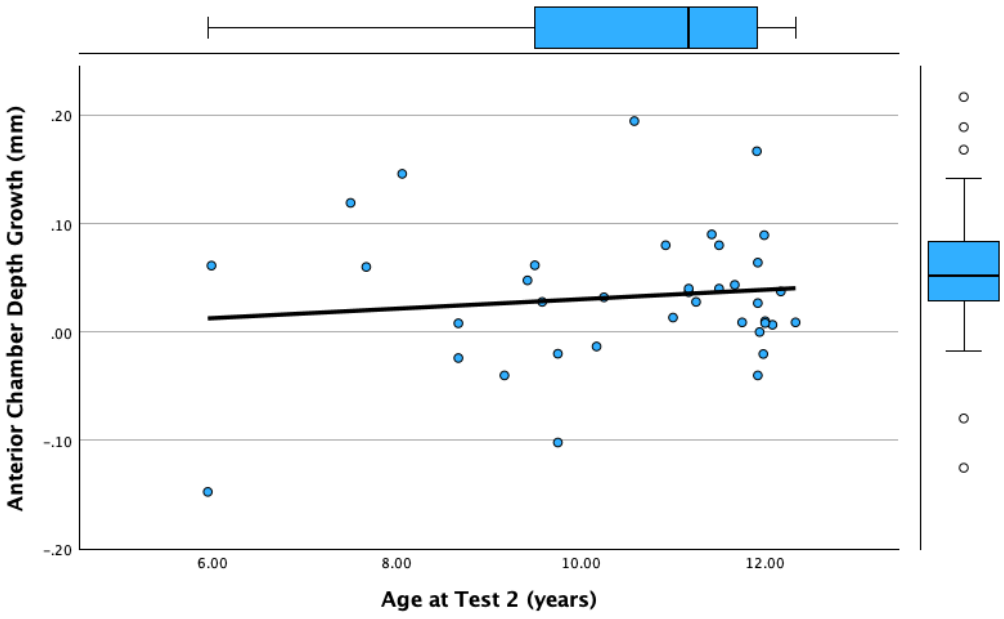

Figure 6-22 Anterior chamber depth (mm) growth across 12 months, longitudinal cohort (n=38). Trend for ACD growth is indicated by the black line.

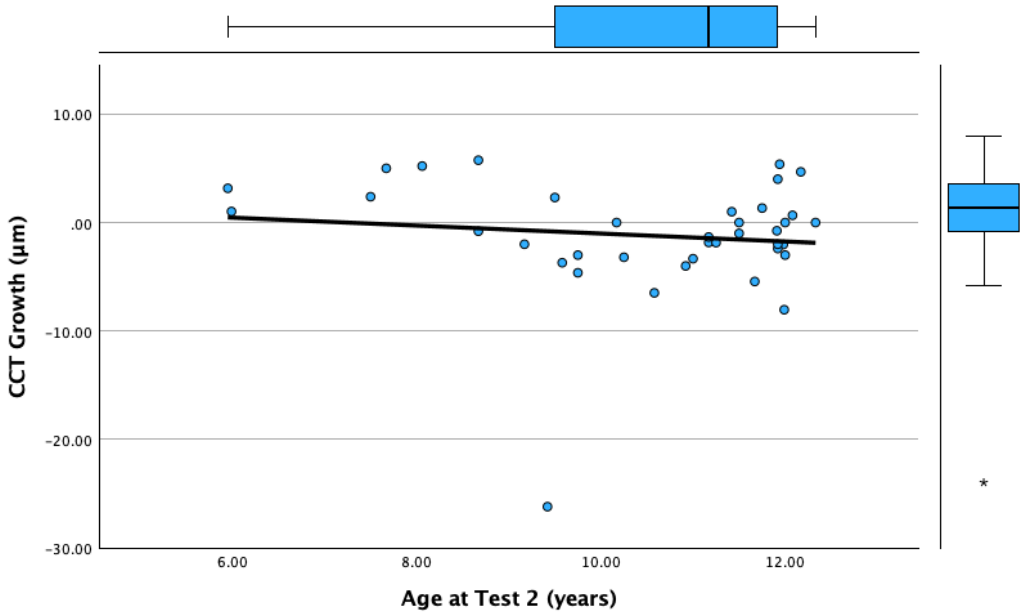

Figure 6-23 Corneal thickness (µm) growth across 12 months, longitudinal cohort (n=38). Trend for CCT growth is indicated by the black line

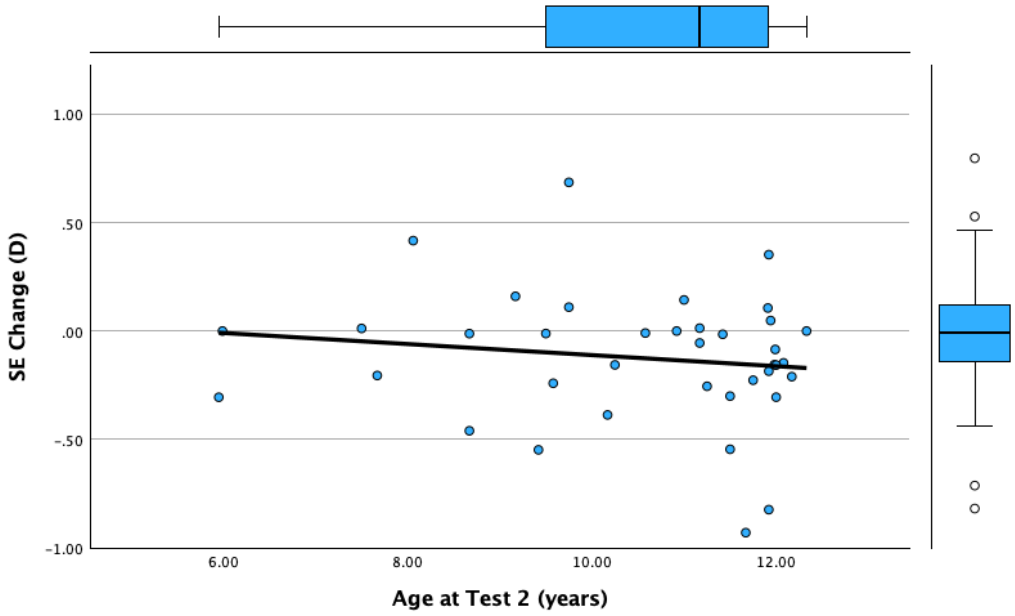

Figure 6-24 SE refractive error (D) change over 12 months, longitudinal cohort (n=38). Trend for SE development is indicated by the black line.

Total sum of squares and root mean sum of squares were calculated for longitudinal changes AL, ACD, and CCT, with the results presented in Table 6-8. As with previous analysis CCT measurements did not provide useful data.

N=38	*Mean*	*Sum of Squares*	*Average Square Error /measurement*	*RMSE*
AL (mm)	-0.01	0.21	0.01	0.08
ACD (mm)	0.01	0.18	0.00	0.07

Table 6-8- Sum of squares analysis for longitudinal change in biometry results

6.2.5 Survey Results

As with the data set for the initial test point containing individual who did not return for the subsequent test, the survey was divided into sections for birth conditions, developmental milestones, education results, visual environment, maternal data, and paternal data. The following represents the responses returned for the individuals included in the first test data set. Two individuals did return consent forms for inclusion in the study but failed to return surveys giving a cohort of n=36 for whom the survey and biometry was available.

Respondents indicated mean birth maturity for the cohort as +0.25 weeks (+/- 1.99, min -3, max +7). 14 individuals (38.89%) reported pre-term birth, 13 (36.11%) individuals reported on-term birth, and 9 (25.00%) reported post-term birth. Mean birth weight was 3.07kg (+/- 0.65, min 1.2, max 4.7). Mean length at birth was 49.22cm (+/- 8.58, min 18, max 56). 14 (38.89%) individuals reported complication with the birth and 22 (61.11%) reported no complication.

The average age when the participant first crawled/shuffled was 9.45 months (+/-3.43), and age at first words was 16.16 months (+/- 7.99). 29 (80.56%) of participants were right-handed and 7 (19.44%) were left-handed. 7 (19.44%) participants reported behavioural difficulties, 21 (58.33%) wore spectacles for which the refractive error is indicated in the biometry results in the preceding section. Average age at commencement of wear was 4.47 years (+/- 3.71).

The categorical data for developmental milestones is presented in the table below.

Developmental Milestones	**Lower**	**%**	**Average**	**%**	**Higher**	**%**
Height (18 months)	5	13.89	19	52.78	12	33.33
Weight (18 Months)	10	27.78	21	58.33	5	13.89
Height (24 months)	5	13.89	21	58.33	10	27.78
Weight (24 Months)	10	27.78	21	58.33	5	13.89
Height (36 months)	5	13.89	21	58.33	10	27.78
Weight (36 Months)	10	27.78	21	58.33	5	13.89
Height (48 months)	3	8.33	23	63.89	10	27.78
Weight (48 Months)	8	22.22	23	63.89	5	13.79

Table 6-9 Development Milestones reported for cohort 2

All of the participants were in primary school, with an average school grade of 4.42 (+/- 2.06). 22 (62.86%) of participants attended private schools, 13 (37.14%) attended schools in the public education system, no participants were home schooled. One student was advanced ahead (‘skipped a year’) of the normal school grade progression. Educational performance and related data is presented in Table 6-10.

Educational Milestones	*Lower*	*%*	*Average*	*%*	*Higher*	*%*
Reading	4	11.11	11	30.56	21	58.33
Writing	4	11.11	12	33.33	20	55.56
Spelling	4	11.11	11	30.56	21	58.33
Mathematics	3	8.33	14	38.89	19	52.78
Behaviour	2	5.56	11	30.56	23	63.89

Table 6-10 – Educational milestones reported for cohort 2

The average interruption to regular activities due to COVID-19 lockdowns was reported by this cohort as 4.06 months. 23 (63.89%) of participants performed their study in the kitchen or shared area of the family home while 13 (36.11%) had a dedicated study area set aside. Sports participation was undertaken by 32 (91.43%) individuals, 91.67% of sports played were classified as outdoors.

No participants reported living in apartments or semi-detached homes. 2 (5.56%) participants reported living in small residential homes, 23 (63.89%) lived in large residential homes and 11 (30.56%) reported living in rural or semi-rural homes on acreage.

Table 6-11 outlines the time spent at a range of tasks pertaining to the visual environment for the participants. Time was estimated at task per day as indicated.

Visual Environment	*Nil*	*%*	*<30 min*	*%*	*30 min to 1 hour*	*%*	*Over 1 hour*	*%*
Outdoor Play (Day)	0	0	4	11.11	4	11.11	28	77.78
Outdoor Play (Night)	15	42.86	7	20.00	6	17.14	7	20.00
Study (total)	3	8.33	9	25.00	10	27.78	14	39.89
Screen Time Study	3	8.33	10	27.78	9	25	14	38.89
Screen Time Recreational	0	0	6	16.67	14	38.89	16	44.44

Table 6-11 - Visual Environment for cohort 2

Maternal demographics

The average age was 43.67 years (+/-6.84). 29 (26.61%) participants reported maternal country of birth as Australia, 3 (2.75%) as Vietnam, 2 (1.83%) as the United Kingdom, 1 (2.78%) as Canada, and 1 (2.78%) as the Czech Republic. Maternal ethnicity was 33 (91.67%) White European and 3 (8.33%) East Asian.

Highest level of maternal education was reported as, 1 (2.78%) high school, 4 (11.11%) technical college (TAFE), 31 (86.11%) university level.

Maternal workforce engagement was indicated as 1 (2.78%) not employed, 20 (55.56%) part time, and 15 (41.67%) full time.

23 (63.89%) individuals reported maternal requirement of wearing correction for a visual condition. Myopia was reported for 15 (41.67%) of individuals, hyperopia for 2 (5.56%) of individuals, and astigmatism for 6 (16.67%) of individuals.

Paternal demographics

The average age was 46.67 years (+/- 7.49). 32 (88.89%) participants reported paternal country of birth as Australia, 2 (5.56%) as the United Kingdom, and 2 (3.64%)

as South Africa. Paternal ethnicity was 32 (97.22%) White European and 1 (2.78%) East Asian.

Highest level of paternal education was reported as, 2 (5.56%) high school, 7 (19.44%) technical college (TAFE), 7 (75.00%) university level.

Paternal workforce engagement was indicated as 1 (2.86%) not employed, 2 (5.71%) part time, and 32 (91.43%) full time.

15 (41.67%) individuals reported paternal requirement of wearing correction for a visual condition. Myopia was reported for 9 (25.00%) of individuals, hyperopia for 2 (5.56%) of individuals, and astigmatism for 4 (11.11%) of individuals.

6.2.6 Analysis Of Longitudinal Data For Influence Of Environmental Factors On Biometry

In this section a Kruskal-Wallis analysis of the biometric data is performed in the context of a range of developmental and environmental factors. Due to the volume of data this test produces the complete output is available as an excel file, pdf or SPSS output on request. Summary data is presented here with detail given to significant findings. Maternal and paternal country of birth was withdrawn from the data set as the number of categories for responses (n=9) indicated a larger sample size cohort size beyond that available in the study would be required.

Categories are as listed. Variables tested were axial length at test 1 (AL @ test 1), anterior chamber depth at test 1 (ACD @ test 1), corneal thickness at test 1 (CCT @ test 1), spherical equivalent refractive error at test 1 (SE @ test 1), axial length at test 2 (AL @ test 2), anterior chamber depth at test 2 (ACD @ test 2), corneal thickness at test 2 (CCT @ test 2), spherical equivalent refractive error at test 2 (SE @ test 2), change in axial length over 12 months (AL change), change in anterior chamber depth over 12 months (ACD change), corneal thickness change over 12 months (CCT change), and spherical equivalent refractive error change over 12 months (Rx change).

	Categories	*Asymp. Sig.*
Maturity at birth	Preterm/On term/Post term	CCT @ test 1 = 0.007 CCT @ test 2 = 0.008
Birth Complications	Complication/ No Complication	None
Length at 18 months	Below Average / Average/ Above Average	None
Weight at 18 months	Below Average / Average/ Above Average	None
Length at 24 months	Below Average / Average/ Above Average	None
Weight at 24 months	Below Average / Average/ Above Average	None
Length at 36 months	Below Average / Average/ Above Average	None
Weight at 36 months	Below Average / Average/ Above Average	None
Length at 48 months	Below Average / Average/ Above Average	AL @ test 2 = 0.044
Weight at 48 months	Below Average / Average/ Above Average	None
Handedness	Right / Left	None
Behavioural Difficulties	Yes / No	ACD growth = 0.036 Rx change = 0.014
Spectacle Wear	Yes / No	SE @ Test 2 = 0.007 Rx change = 0.045
School Type	Private / Public	None
School Progression	Held Back / None / Skipped	None
Reading Performance	Below Average / Average/ Above Average	None
Writing Performance	Below Average / Average/ Above Average	None

Spelling Performance	Below Average / Average/ Above Average	None
Mathematics Performance	Below Average / Average/ Above Average	SE @ test 2 = 0.014
Behavioural Performance	Below Average / Average/ Above Average	SE @ test 2 = 0.014
Outdoor Play Time (Day)	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Outdoor Play Time (Night)	Nil / <30 min / 30 min – 1 hr / >1 hour	AL test 1 = 0.039 AL test 2 = 0.035
Study Time Total	Nil / <30 min / 30 min – 1 hr / >1 hour	AL test 1 = 0.039 AL test 2 = 0.031
Study Time (Screen)	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Recreational Screen Time	Nil / <30 min / 30 min – 1 hr / >1 hour	None
Study Location	Shared living space / dedicated study space	None
Sport	Yes/ No	None
Sport Type	Indoor / Outdoor	None
Home Type	Small detached house / large detached house / semi-rural or rural acreage	AL @ test 1 = 0.035 AL @ test 2 = 0.036
Maternal Ethnicity	White European / East Asian	ACD @ test 2 = 0.024
Maternal Education	High school / TAFE / university	None
Maternal Employment	None / Part time / Full time	None
Maternal Spectacle Wear	Yes / No	AL @ test 1 = 0.035 SE @ test 1 = 0.035 AL @ test 2 = 0.041 SE @ test 2 = 0.036

Maternal Visual Condition	None / Myopia / Hyperopia / Astigmatism	AL growth = 0.045
Paternal Ethnicity	White European / East Asian	None
Paternal Education	High school / TAFE / university	None
Paternal Employment	None / Part time / Full time	None
Paternal Spectacle Wear	Yes / No	ACD growth = 0.043
Paternal Visual Condition	None / Myopia / Hyperopia / Astigmatism	None

Table 6-12 Results of Kruskal - Wallis analysis of data set

Eta squared was calculated and effect size was determined and defined according to Cohen (small = 0.01, medium = 0.06, and large = 0.14) [227]

	Asymp. Sig.	*Eta squared (effect size)*
Maturity at birth	CCT @ test 1 = 0.007	0.287 (large)
	CCT @ test 2 = 0.008	0.275 (large)
Length at 48 months	AL @ test 2 = 0.044	0.178 (large)
Behavioural Difficulties	ACD growth = 0.036	0.126 (medium)
	Rx change = 0.014	0.173 (large)
Spectacle Wear	SE @ Test 2 = 0.007	0.210 (large)
	Rx change = 0.045	0.115 (medium)
Mathematics Performance	SE @ test 2 = 0.014	0.243 (large)
Behavioural Performance	SE @ test 2 = 0.014	0.245 (large)
Outdoor Play Time (Night)	AL test 1 = 0.039	0.238 (large)
	AL test 2 = 0.035	0.246 (large)
Study Time Total	AL test 1 = 0.039	0.239 (large)
	AL test 2 = 0.031	0.254 (large)
Home Type	AL @ test 1 = 0.035	0.191 (large)
	AL @ test 2 = 0.036	0.190 (large)
Maternal Ethnicity	ACD @ test 2 = 0.024	0.146 (large)
Maternal Spectacle Wear	AL @ test 1 = 0.035	0.127 (medium)
	SE @ test 1 = 0.035	0.127 (medium)
	AL @ test 2 = 0.041	0.119 (medium)
	SE @ test 2 = 0.036	0.125 (medium)
Maternal Visual Condition	AL growth = 0.045	0.230 (large)
Paternal Spectacle Wear	ACD growth = 0.043	0.117 (medium)

Table 6-13 - Eta squared and effect size for Kruskal-Wallis analysis test points with statistically significant outcomes

A series of Mann-Whitney U tests were performed to ascertain the relationship between the dependent variables listed above and the categorical data. Instances where the Mann-Whitney U test have not yielded statistically significant results have been omitted.

6.2.7 Birth Conditions

Maturity at Birth

CCT test 1	*Median*	*Interquartile Range*	
On term birth (n=13)	584µm	563µm	561µm
Post term birth (n=9)	532µm	527µm	539µm
Z	-2.972		
p	0.003 (2 tailed)		
Effect Size (r)	Large = 0.63		

Table 6-14 Corneal thickness at test 1 and birth maturity - on term and post term birth responses

CCT test 2	*Median*	*Interquartile Range*	
On term birth (n=13)	576µm	561µm	590µm
Preterm birth (n=14)	552.5µm	542.5µm	564.25µm
Z	-1.967		
p	0.049 (2 tailed)		
Effect Size (r)	Large = 0.8		

Table 6-15 Corneal thickness at test 2 and birth maturity - on term and preterm birth responses

CCT test 2	*Median*	*Interquartile Range*	
On term birth (n=13)	576µm	561µm	590µm
Post term birth (n=9)	532µm	529µm	537µm
Z	-2.941		
p	0.003 (2 tailed)		
Effect Size (r)	Large = 0.63		

Table 6-16 Corneal thickness at test 2 and birth maturity - on term and post term birth responses

6.2.8 Developmental Milestones

Length at 48 Months

AL test 2	*Median*	*Interquartile Range*	
Average length (n=23)	23.08mm	22.79mm	23.6mm
Below average (n=3)	21.11mm	21.35mm	22.17mm
Z	-2.449		
p	0.008 (2 tailed)		
Effect Size (r)	Medium = 0.48		

Table 6-17 Axial length and length(height) at 48 months – average and below average responses

AL test 2	*Median*	*Interquartile Range*	
Above average (n=10)	23.18mm	23.05mm	23.39mm
Below average (n=3)	21.11mm	21.35mm	22.17mm
Z	-2.200		
p	0.028 (2 tailed)		
Effect Size (r)	Medium = 0.43		

Table 6-18 Axial length and length(height) at 48 months – above average and below average responses

Behavioural Difficulties

ACD growth	*Median*	*Interquartile Range*	
No difficulties (n=29)	0.037mm	0.009mm	0.064mm
Difficulties (n=7)	-0.022mm	-0.022mm	0.020mm
Z	-2.009		
p	0.036 (2 tailed)		
Effect Size (r)	Medium = 0.35		

Table 6-19 Anterior chamber depth growth over 12 months and behavioural difficulties – no reported difficulties and reported difficulties

SE change	*Median*	*Interquartile Range*	
No difficulties (n=29)	-0.19D	-0.31D	+0.01D
Difficulties (n=7)	+0.01D	-0.01D	+0.08D
Z	-2.459		
p	0.014 (2 tailed)		
Effect Size (r)	Medium = 0.41		

Table 6-20 SE refractive error change over 12 months and behavioural difficulties - no reported difficulties and reported difficulties

Spectacle Wear

SE test 2	*Median*	*Interquartile Range*	
Spectacle wear (n=15)	+0.41D	+0.16D	+0.69D
No spectacle wear (n=21)	-0.02D	-0.29D	+0.17D
Z	-2.712		
p	0.007 (2 tailed)		
Effect Size (r)	Medium = 0.45		

Table 6-21 SE refractive error at test 2 and spectacle wear- wear and no wear

SE change	*Median*	*Interquartile Range*	
No spectacle wear (n=15)	-0.16D	-0.31D	-0.04D
Spectacle wear (n=21)	+0.01D	-0.01D	+0.08D
Z	-2.006		
p	0.045 (2 tailed)		
Effect Size (r)	Medium = 0.33		

Table 6-22 SE refractive error change over 12 months and spectacle wear- wear and no wear

6.2.9 Education

Mathematics Performance

SE test 2	*Median*	*Interquartile Range*	
Average (n=14)	+0.44D	+0.29D	+0.66D
Below average (n=3)	-0.01D	-0.02D	+0.03D
Z	-2.269		
p	0.025 (2 tailed)		
Effect Size (r)	Large = 0.55		

Table 6-23 SE refractive error at test 2 and mathematics performance – average and below average reported

SE test 2	*Median*	*Interquartile Range*	
Average (n=14)	+0.44D	+0.28D	+0.66D
Above average (n=19)	+0.1D	-0.28D	+0.21D
Z	-2.569		
p	0.01 (2 tailed)		
Effect Size (r)	Large = 0.62		

Table 6-24 SE refractive error at test 2 and mathematics performance – average and above average reported

Behavioural Performance

SE test 2	*Median*	*Interquartile Range*	
Average (n=11)	+0.48D	+0.25D	+1.01D
Below average (n=2)	0.00D	-0.03D	+0.03D
Z	-1.974		
p	0.048 (2 tailed)		
Effect Size (r)	Large = 0.55		

Table 6-25 SE refractive error at test 2 and behavioural performance – average and below average reported

6.2.10 Visual Environment

Outdoor Playtime (Night)

AL test 1	*Median*	*Interquartile Range*	
< 30 min (n=15)	23.25mm	22.93mm	23.61mm
> 1 hour (n=6)	22.17mm	21.44mm	22.37mm
Z	-2.649		
p	0.008 (2 tailed)		
Effect Size (r)	Large = 0.56		

Table 6-26 Axial length at test 1 and outdoor play time (night) - < 30min and > 1 hour reported

AL test 2	*Median*	*Interquartile Range*	
< 30 min (n=15)	23.39mm	23.05mm	23.75mm
> 1 hour (n=6)	22.35mm	21.56mm	22.38mm
Z	-2.687		
p	0.007 (2 tailed)		
Effect Size (r)	Large = 0.57		

Table 6-27 Axial length at test 2 and outdoor play time (night) - < 30min and > 1 hour reported

Study Time

AL test 1	*Median*	*Interquartile Range*	
30 min – 1 hour (n=10)	23.62mm	23.30mm	24.56mm
< 30 min (n=9)	22.90mm	22.62mm	23.08mm
Z	-2.368		
p	0.018 (2 tailed)		
Effect Size (r)	Large = 0.54		

Table 6-28 Axial length at test 1 and study time – 30 min to 1 hour and < 30 min reported

AL test 1	*Median*	*Interquartile Range*	
<30 min (n=9)	22.90mm	23.30mm	24.56mm
> 1 hour (n=14)	22.99mm	22.13mm	23.24mm
Z	-2.431		
p	0.015 (2 tailed)		
Effect Size (r)	Large = 0.56		

Table 6-29 Axial length at test 1 and study time – <30 min and > 1 hour reported

AL test 2	*Median*	*Interquartile Range*	
30 min – 1 hour (n=10)	23.75mm	23.33mm	24.61mm
< 30 min (n=9)	22.93mm	22.70mm	23.16mm
Z	-2.369		
p	0.018 (2 tailed)		
Effect Size (r)	Large = 0.54		

Table 6-30 Axial length at test 2 and study time – 30 min to 1 hour and < 30 min reported

AL test 2	*Median*	*Interquartile Range*	
<30 min (n=9)	23.75mm	23.32mm	24.61mm
> 1 hour (n=14)	23.08mm	22.25mm	23.35mm
Z	-2.519		
p	0.012 (2 tailed)		
Effect Size (r)	Large = 0.58		

Table 6-31 Axial length at test 2 and study time – <30 min and > 1 hour reported

Home Type

AL test 2	*Median*	*Interquartile Range*	
Large residential (n=23)	23.18mm	22.93mm	23.69mm
Small residential (n=2)	21.48mm	21.04mm	21.92mm
Z	-2.106		
p	0.035 (2 tailed)		
Effect Size (r)	Medium = 0.42		

Table 6-32 Axial length at test 2 and home type – large and small residential reported

6.2.11 Maternal Factors

Maternal Spectacle Wear

AL test 1	*Median*	*Interquartile Range*	
Corrective lenses (n=23)	23.12mm	22.84mm	23.58mm
No correction (n=13)	22.27mm	22.07mm	23.11mm
Z	-2.108		
p	0.035 (2 tailed)		
Effect Size (r)	Medium = 0.35		

Table 6-33 Axial length at test 1 and maternal requirement for correction

SE test 1	*Median*	*Interquartile Range*	
No correction (n=13)	+0.44D	+0.25D	+0.98D
Corrective lenses (n=23)	+0.25D	-0.11D	+0.49D
Z	-2.109		
p	0.035 (2 tailed)		
Effect Size (r)	Medium = 0.35		

Table 6-34 SE refractive error at test 1 and maternal requirement for correction

AL test 2	*Median*	*Interquartile Range*	
Corrective lenses (n=23)	23.18mm	22.93mm	23.69mm
No correction (n=13)	22.39mm	22.11mm	23.18mm
Z	-2.043		
p	0.041 (2 tailed)		
Effect Size (r)	Medium = 0.34		

Table 6-35 Axial length at test 2 and maternal requirement for correction

SE test 1	*Median*	*Interquartile Range*	
No correction (n=13)	+0.29D	+0.13D	+0.98D
Corrective lenses (n=23)	+0.09D	-0.28D	+0.46D
Z	-2.092		
p	0.037 (2 tailed)		
Effect Size (r)	Medium = 0.35		

Table 6-36 SE refractive error at test 2 and maternal requirement for correction

Maternal Visual Condition

AL growth	*Median*	*Interquartile Range*	
Emmetropia (n=13)	0.09mm	0.07mm	0.10mm
Astigmatism (n=6)	0.02mm	0.01mm	0.05mm
Z	-2.156		
p	0.031 (2 tailed)		
Effect Size (r)	Medium = 0.49		

Table 6-37 Axial length growth over 12 months and maternal visual condition – emmetropia and astigmatism reported

AL growth	*Median*	*Interquartile Range*	
Myopia (n=15)	0.11mm	0.06mm	0.15mm
Astigmatism (n=6)	0.02mm	0.01mm	0.05mm
Z	-2.156		
p	0.031 (2 tailed)		
Effect Size (r)	Medium = 0.49		

Table 6-38 Axial length growth over 12 months and maternal visual condition – myopia and astigmatism reported

6.2.12 Paternal Factors

Paternal Spectacle Wear

ACD growth	*Median*	*Interquartile Range*	
Corrective lenses (n=15)	0.04mm	0.03mm	0.07mm
No correction (n=21)	0.01mm	-0.02mm	0.04mm
Z	-2.022		
p	0.043 (2 tailed)		
Effect Size (r)	Medium = 0.34		

Table 6-39 ACD growth and paternal requirement for correction

6.3 DISCUSSION

As in chapter 5 biometric data for the cohort was found to be broadly in line with published data and models. Statistically significant associations were found between a range of environmental, lifestyle and parental factors, most notably with regards to outdoor play time at night, and maternal visual performance.

This cross-sectional and longitudinal analysis of the cohort refines the information about the demographics, biometric data, lifestyle and environmental factors from chapter 5 in the context of the smaller cohort, as well as providing longitudinal analysis.

6.3.1 Demographics

The demographics of the cohort remain broadly unchanged for the longitudinal group, despite the reduction in cohort size. The ratio of female to male participants changed from female dominated (51.72% in cohort for chapter 5) to male dominated (53.63% in cohort for this chapter) indicating female participants dominated the dropout group. It is noted that school year is a problematic measure in the longitudinal analysis. As the questionnaire was only completed once, school year would reasonably be expected to change over the study period, making the response a poor indicator of year at school.

Ethnicity remained in line with the initial cohort analysis. One candidate with both East Asian and White European ethnicity dropped out with the remaining of the remaining dropout candidates (n=19) being of White European ethnicity. This ratio is broadly in holding with the overall ratios from the initial cohort.

Consequently, it may be expected that the overall results of analysis would be similar, however this was proven not to be the case. This suggests that there are either some features of the dropout candidates that were not representative of the overall cohort or that there are candidates remaining in the longitudinal cohort that are introducing outlier effects that are not readily apparent via the statistical tests implemented in this study.

6.3.2 Longitudinal Refractive Error and Biometry

Axial length for the cohort in the longitudinal cohort exhibited the same trends as the larger cross-sectional cohort in section 5.1, despite the removal of some outliers. The data were again clustered towards the normative growth line indicated in Figure 6-13 and Figure 6-14. The consistency between groups from the larger cohort of n=58 and this cohort of n=38 again suggests the likelihood of this cohort being representative of the broader patient base of the practice, although the relatively small sample size does make the cohort more sensitive to outliers.

Mean axial length growth was 0.09mm. As the mean age of the cohort is 10.48 years, there is an expectation that the individuals will be nearing the point where the rate of axial growth will be slowing. This is reflected in the data in Figure 6-21 where the trend is towards lower rates of axial length growth with increasing ages.

Mean anterior chamber depth was higher than modelled by Rozema [14] for the cohort at both the baseline and subsequent consultations. ACD exhibited increasing rates of growth with age, contradicting the published data suggesting growth rates decline at 10 to 14 years of age [14]. It is noted that the trend is weakly positive and the presence of significant outliers in this data set may influence this. Of note is the persistence of the lack of association between refractive error development and the longest eyes in the cohort.

Corneal thickness measurements remained consistent across with period of the study and the flat growth pattern was in line with published data.

As with the results from chapter 5 the mean spherical refractive error of the cohort (test 1 = $+0.60D \pm 1.76$, test 2 = $+0.47D \pm 1.84$)is indicative of a tendency to mild hyperopia (table 6-1), as would be expected by the mean age of the participants. The strong tendency towards myopia that is being detected in other regions [239-242], particularly urban centres, is again not in evidence for this cohort (test 1 = 5.26%, test 2 = 7.89%), although prevalence did increase across the study period. Prevalence of hyperopia was stable across the duration of the study and was relatively low (7.89%,), compared to 19.3% in the Kleinstein study [63], and 22.9% in the Aston Eye Study [4].

At the second test point, axial length (AL) continued to differ from the Rozema emmetropisation model. The mean difference was -0.10 mm, with a total sum of squared differences of 29.22 mm². This corresponded to an average squared error of 0.77 mm² per measurement and a root mean square error (RMSE) of 0.88 mm, suggesting a persistently high level of deviation from the model and potential refractive prediction error of approximately ±1.6 D per eye.

Anterior chamber depth (ACD) at the second test point showed a mean difference of 0.10 mm compared to the model, with a sum of squared differences of 2.12 mm². The average squared error per measurement was 0.06 mm², and the RMSE was 0.24 mm, indicating a slightly larger deviation than observed at the initial time point.

When evaluating longitudinal changes across the 12-month period, the mean change in axial length was minimal at -0.01 mm. The total sum of squared differences was 0.22 mm², with an average squared error per measurement of 0.01 mm² and an RMSE of 0.08 mm, reflecting high consistency in AL measurements over time relative to the model. Similarly, the longitudinal change in ACD showed a mean increase of 0.01 mm, with a total squared deviation of 0.18 mm², an average squared error of 0.00 mm², and an RMSE of 0.07 mm. These results indicate minimal biometric changes across the study period, with low variance and strong repeatability.

Of note in this data is the stability of the hyperopic presentation between tests. While myopisation is reported widely in the literature, this cohort does not exhibit the strong trend observed elsewhere. Mean spherical equivalent refractive error was mildly hyperopic in line with expected values for age. However, on the removal of significant outliers the mean shifted to effectively 0.00D. While not necessarily indicative of the strong myopic tendency shown in other studies, it does suggest the shift of SE to effective emmetropia is occurring earlier than the models would suggest for the bulk of the cohort. The overall trend of myopic shift during the course of

emmetropisation is in keeping with established data, however in this cohort the existence of two strong myopic shifts by individuals close to 12 years of age is grounds for further investigation.

6.3.3 Birth Conditions

Maturity at Birth

CCT was found to be greater for on term births at both test 1 and test 2 when compared to post term births. CCT at test 2 was also found to be greater for on term births compared to preterm births.

These results differ from the cross-sectional data for the initial cohort through the omission of a significant difference between CCT for preterm and on term births at test 1. This may be indicative of the statistical influence of candidates who did not return for their second consultation. However, the presentation of an effect between preterm birth an on term births at test 2 obfuscates these results. Given the stability of CCT reported in the literature post birth [249], the nature of these relationships found in this study is unclear. As the data for CCT was the most unreliable of the data set collected it is posited that these results may not have significance in the context of this study.

6.3.4 Developmental Milestones

Length at 48 Months

AL was found to be greater for individuals reporting average length at 48 months compared below average length at the same age. This result is consistent with the results from the cross-sectional analysis of the initial cohort, however the effect due to length is at a greater age than that of the cross-sectional group (24 and 36 months). It also corresponds to published literature relating to biometry and stature [232] while further corresponding to a significant overall growth period. This suggests that ACD is sensitive to significant growth phases with a long residual effect.

Behavioural Difficulties

ACD growth was greater for individuals with no reported behavioural difficulties compared to those with reported difficulties. Individuals reporting

behavioural difficulties also reported negative ACD growth (-0.022mm). The relationship between ACD, SE, and behavioural difficulties suggests that growth and associated SE development for children is attenuated in the presence of behavioural difficulties. Participants in the cohort who indicated the presence of behavioural difficulties (19.44%) did not display the typical myopic shift associated with emmetropisation and had no overall change in axial length across the time span of the study. The nature of this is unclear but may be associated with the relationship between high academic performance and longer AL.

Spectacle Wear

The prevalence of spectacle wear in the cohort was 58.33% spectacle wear compared to 41.67% not reporting spectacle wear. The change in refractive error was less pronounced (less negative) for those individuals wearing spectacles than those who did not. As this study took place within the context of individuals undertaking regular management of emmetropisation it would suggest that intervention in emmetropisation is effective in minimising myopic shift in this cohort. This is consistent with the practice in the location in which the study occurred of fully correcting refractive error, which is in keeping with published findings [85]. Furthermore, individuals engaged in spectacle wear exhibited more hyperopic refractive error (+0.41D versus -0.02D) at test 2. It is noted that the outliers for hyperopic refractive error were of a larger magnitude than myopes (max = +6.34D versus min -3.72), which may skew the results towards hyperopia. Nonetheless, this effect was not present at test 1, so this result may be suggestive of a protective effect found by implementing spectacle correction. This result is again in keeping with the published literature [85].

6.3.5 Education

Mathematics and Behavioural Performance

A statistically significant difference was found between SE refraction at test 2 for performance in mathematics and behaviour. No significant effect in change in SE over 12 months was detected, however these results also suggest the presence of a similar relationship between performance to that found in the cross-sectional analysis of the baseline data (chapter 5.3.5). In this case more hyperopic SE results were

associated with average performance (mathematics 38.89% and behavioural 30.56%), with the most myopic results for those individuals with below average performance (mathematics 8.33% and behavioural 5.56%), whereas the cross-sectional data indicated a relationship between AL and academic performance. Performance at academic tasks is indicative of greater time spent at study, although this is not a feature of the questionnaire used here. As mentioned in section 5.3.6 the interplay between time spent at near tasks, outdoor time, and the associated trade-off between tasks is a confounding element in isolating the effects of these factors. It is of interest that the baseline cross-sectional study presented an AL relationship, while the reduced data set for longitudinal analysis found SE relationships. These two elements are linked, with AL being a reasonable indicator of SE refractive error [250]. The reason why both elements did not return a significant relationship in both the cross-sectional and longitudinal analysis is unclear.

6.3.6 Visual Environment

Outdoor Playtime (Night)

A statistically significant relationship between extended play time outdoors at night and shorter axial lengths was found at both test 1 and test 2. In both instances it was found that increased outdoor play at night was associated with shorter axial length, although there was not a significant link detected with SE as may have been expected given the AL association. 17.14% of respondents indicated spending > 1 hour outside after dark, compared with 20% (30min to 1 hour) and 42.86% (<30min). The nature of this relationship is unclear as it does not relate to daylight exposure as discussed in the literature and therefore may be related to time spent on activities with a wider range of dioptric demands rather than light conditions [9, 12, 251]. The questionnaire did not differentiate between time spent outdoors pre dusk, and those under lights such as sports training, as such it is not possible to determine the effect of light type or intensity [210, 211]. There was no significant effect on SE change over the 12-month period of the study.

Study Time

At both test 1 and test 2 shorter AL values were consistently associated with both the shortest and longest daily study periods, with the longest AL associated with

the 30 minutes to 1 hour group in both cases. Each of the categories was represented similarly, with the exception of no study time (nil = 8.33%, < 30 min = 27.78%, 30 min to 1 hour = 25%, and > 1 hour = 38.89%). This is somewhat inconsistent with published data indicating that increased study time and the associated visual environment are related to myopisation [97, 98, 156, 176, 178, 252]. The results presented here indicate that for this cohort there is some disconnect between AL lengthening and study time beyond a given threshold. Further study of this relationship is indicated to ascertain the nature of the interaction and isolate confounding factors such as visual hygiene management (i.e. rest periods) in this area.

Home Type

As previously discussed, home size may be indicative of a range of factors influencing emmetropisation. The cross-sectional results in the reduced data set used for the longitudinal analysis set appear to contradict those of the larger cross-sectional baseline set. It is notable that the number of instances of large (n=23) to small domiciles (n=2) is problematic, as both the instances of small domiciles represent AL values that are shorter than the mean. One is the extreme outlier for short AL values (over twice the SD) which may indicate unreliability of this result as an effect of the reduction in individuals in the cohort, despite the outcome of the analysis. Larger domiciles tend to have yards or significant amounts of surrounding property which permit greater outdoor exposure time compared with more dense urban environments. Similarly, they are indicative of a level of affluence that suggests better access to health care, and a higher level of health care. From this data it is not immediately apparent how these may interrelate. More detailed questionnaires may aid in the separation of variables, however this would come at the cost of more complex analysis.

6.3.7 Maternal Factors

In contrast to the cross-sectional baseline analysis of chapter 5, there were no detected effects for the influence of maternal ethnicity and employment on the cohort data.

Maternal Spectacle Wear

As with the cross-sectional analysis in chapter 5.3.7, the maternal requirement for the correction of refractive error was associated with longer AL and tendency to

lower (more negative) SE refractive error. 63.89% of responses indicated maternal spectacle wear. The longitudinal SE trend for refractive error was negative. Despite this, in all instances the mean SE remained hyperopic although the mean SE for test 2 may be considered effectively zero (0.085D).

The published data indicate that there is a relationship between maternal refractive error and the refractive outcomes of their children [139, 140], which is supported by this data. A response of no requirement for refractive correction was associated with less negative SE and shorter AL values. There was no detected effect on longitudinal change for these elements. Future study of this relationship would benefit from inclusion of parental biometry and magnitude of SE data for the parent.

Maternal Visual Condition

Axial length growth was greatest in the case of maternal myopia (mean 0.110mm) compared to emmetropia (mean 0.087mm), and astigmatism (mean 0.021mm). Reported maternal visual conditions were predominantly emmetropia and myopia (emmetropia = 36.11%, myopia = 41.67%, hyperopia = 5.56%, and astigmatism = 16.67%). These prevalences of refractive error differ significantly from those of their children, particularly with regards to the decreased prevalence of myopia withing the children in the cohort. Maternal visual condition is also one of the few areas in this study that exhibited significant relationships between influencing factors and longitudinal change. The relationship between presence of maternal astigmatism and change in AL during emmetropisation of their child is not known to have been reported in the literature. The relationship between astigmatism and myopia has been researched, with the suggestion that meridionally specific blur may have a similar effect to radial blur as a myopogenetic trigger [145, 253], however this effect was not detected in this cohort. The relationship found in the cross-sectional study of chapter 5 between more hyperopic refractive error in the children of myopic mothers was not detected in this part of the study. Given the optical complexity of astigmatic refractive error, the range of variables to be examined would require significantly greater sample size that that which is available here. The relatively high prevalence of astigmatism among the cohort suggests that this is an area for future investigation.

6.3.8 Paternal Factors

The only paternal effect detected indicates that anterior chamber depth growth over the period of the study was higher for the children of fathers with a requirement for correction of refractive error (0.043 compared to 0.010). This effect was not detected in either of the test points when examined as a cross-sectional data set. In conjunction with the data relating to maternal influence on a child's biometry they support the published research on parental influence on biometric outcomes. The difference in the number and significance of the maternal compared to paternal influences is of interest.

6.3.9 Summary

The results of the cross-sectional analysis of the reduced cohort for both test 1 and test 2 displayed consistency across most areas with those of the cross-sectional analysis performed on the larger cohort in chapter 5. Despite the reduction in cohort the demographics and biometry remained largely unchanged, which is represented in the consistency across sets of analysis.

Notable differences occurred in the developmental milestones, with the influence of height being more pronounced in the larger initial cohort at an earlier age than that of the smaller longitudinal cohort. The influence of educational performance was more broadly apparent in the larger cohort than in the smaller longitudinal set, the impact of cohort size being a potential confounding factor in the exclusion of some results from the longitudinal analysis.

The presence of significant relationships between evening outdoor play time and shorter axial lengths is not present in the literature to the best of the authors knowledge. While the nature of this relationship is unclear from the data available, the visual environment and light exposure represent candidates for future examination.

Significant longitudinal effects were relatively rare in this study. The relationship between spectacle wear and SE change was expected, however the nature of the relationship suggests that intervention through optometric management may have a protective effect during emmetropisation. Behavioural difficulties and ACD development suggest an interaction between a disengagement with study and slower ACD growth. Hereditary influences on childhood refractive error have been

documented in other studies and are present in this instance. Maternal myopia was observed to be linked to faster growth, suggesting an increased risk of myopia in the child. Less clear was the relationship between paternal refractive error and greater ACD growth across the duration of the study. While significant, it was not linked to a particular paternal refractive error, precluding meaningful conclusions to be drawn.

Chapter 7: Conclusions

The research program presented in this work was the first to examine the impact of environmental factors on the biometric development of children in a rural Australian population. The prevalence of myopia was lower than reported by other sources (5.26% and 7.89%) at both the baseline and subsequent test points, with the trend towards myopisation observed in the cohort across the timescale of the study. Prevalence of hyperopia was consistently above that reported by other sources (7.89% at both tests) Mean SE refractive error remained hyperopic while displaying the negative trend associated with emmetropisation. This is likely a result of the cohort being comprised entirely of self-selected individuals who are under optometric care, hence a degree of overrepresentation of ametropia may be expected. Nonetheless, if the prevalence of ametropia were entirely in line with reported population values, there may be an expectation of higher rates of myopia. This indicates that the cohort displays a tendency towards hyperopia that is not in line with reported global trends towards myopisation [2, 8]. The rate of power change (-0.12 per annum) across the cohort was in line with those provided by large scale population models [14], suggesting that among this cohort, emmetropisation was progressing normally. Axial length and anterior chamber depth growth patterns were also in keeping with modelled data [14].

Birth conditions were not observed to have an effect on biometric development, with the exception of CCT. As corneal development is effectively complete at birth, with reported CCT normalised for preterm births at equivalent term, the nature of this relationship between CCT and birth conditions at >4 years is unclear. Further obfuscating the results is the inconsistent presentation of lower CCT for both pre and post terms births.

While this cohort did not display the trend towards strong myopisation reported in other studies [23, 254], indeed the prevalence of myopia in the children of the cohort was greatly reduced with regards to maternal prevalence (41.67% maternal myopia versus 7.89% at test 2 in the cohort), the nature and relationship of the factors causing this are unclear. Outdoor daylight exposure was not observed to have a statistically significant effect on either longitudinal biometric development or as an effect in cross sectional analysis despite noted effects in the literature [159]. However, as the entire

cohort is of a rural population, there is the possibility that their normal exposure through regular activities is in excess of the ideal minimum. Of note is the persistent presentation of a relationship between increased nighttime outdoor play time and shorter axial length. The nature of this relationship is also unclear and may warrant further investigation with a more detailed separation of variables to permit better identification of relationships.

The education performance of the participants did not show a significant effect in change in SE over 12 months, however the results indicate the presence of a relationship between performance in mathematics and refractive error at the end of the study at test 2. In this case more hyperopic results were associated with average performance, with the most myopic results for those individuals with below average performance. This contradicts the results from other studies where correlations between elevated academic performance and myopisation were reported [182]. Performance at academic tasks may indicate greater time spent at study, although this is not a feature of the tests used here it is an area that may warrant further investigations. Furthermore, this is not necessarily a causative relationship, as there may be a predisposition to near tasks due to myopisation. The interplay between time spent at near tasks, outdoor time, and the associated trade-off between tasks is a confounding element in isolating the effects of these factors.

Participants reporting behavioural difficulties (19.44%) displayed less myopic shift across the period of the study. There was no apparent linkage between this effect and study time or performance in academic pursuits, with the majority indicating average study time and generally performing at average or higher levels in assessments.

Spectacle wear was also identified as a factor in reducing the magnitude of myopic SE shift during emmetropisation. As all patients are in managed care under supervision of an optometrist, this may influence the results and in terms of SE change suggests that optometric management has an effect. The magnitude of this effect is difficult to ascertain across a population as the cohort in this study is not indicative of the general population, which would include individuals receiving no optometric care.

This study supports published research pertaining to parental factors with regards to maternal influence to a limited extent, although the influence on rates of change during emmetropisation was not observed in this data set. This suggests that

for this cohort the initial biometric and refractive conditions are not as strongly linked with refractive outcomes as those for other populations. Paternal influence was either not detected, or weakly present in the data which is not consistent with results from other studies [255].

The cohort displayed significant homogeneity with regards to ethnicity. While a relationship between ACD and ethnicity initially indicated greater ACD values for White European ancestry, these data were not replicated in the longitudinal study. Given the very low percentage of participants with non-White European ancestry, it is suggested that this data be approached as a cohort with a relative absence of obfuscating effects due to ethnicity.

The axial length results obtained from the DNEye (Visionix) device in this study (mean $23.80 \pm 0.72\,mm$) were statistically consistent with those reported by Hessler et al. ($24.74 \pm 1.22\,mm$), though the mean difference likely reflects age variation between cohorts. Comparison with the results of a known device, the Nidek AL-Scan ($22.96 \pm 0.73mm$) indicated a statically significant difference, which raised questions around the validity of the DNEye measurements for use in clinical practice. Since DNEye axial length is partially derived from normative data and calculated values, some deviation is expected. Across all test sets, axial lengths were significantly shorter than the Gullstrand model, with none falling within one standard deviation of the model's value. This suggests that fixed adult eye models may not be appropriate for paediatric populations and highlights the potential value of age-specific biometric models. Although the DNEye data differ from traditional biometers, they reflect a step toward individualized modelling, which may benefit lens design, particularly in myopia management. While DNEye data may not be ideal for clinical axial length monitoring, it presents opportunities in lens optimisation. The consistent deviation from the Gullstrand model reinforces the need for population-specific biometry in both research and clinical practice, especially for predictive modelling, custom lens designs, and optical simulation based on real eye anatomy.

This study served to identify relationships between biometry and the emmetropisation of a rural population. While the data found here offers limited opportunities for the modification of patient management strategies during emmetropisation, some elements, such as outdoor play and the relationship between spectacle wear and SE development may provide strengthening of established patient

advice. Future study in this area would benefit greatly from a tightening of scope to permit detection of more detailed relationships to develop future patient management strategies.

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Appendices

Appendix A

Ethics Application and Approval

Aston University Ethics Application Form

Please note that if your research involves NHS patients, staff, or their data, you will need to complete an IRAS application form instead of this form. This also applies if you are recruiting adults who lack capacity to consent. Please visit our Sponsorship webpage for further information.

Section 0: Ethics Application Triage

Does your research involve <u>any</u> of the following?	*Delete as applicable*
Human participants *(Including all types of interviews, questionnaires, focus groups, records relating to humans, use of online datasets or other secondary data, observations, etc.)*	Yes
Human tissue or cells *(Please contact Becky Case via research_governance@aston.ac.uk – your research cannot commence until ethics approval and Designated Individual approval is in place.)*	No
Risk to members of the research team such as:	No
lone working during data collection	No
travel to areas where researchers may be at risk *(Any request for research requiring international travel should be accompanied by a University travel risk assessment form)*	No
risk of emotional distress	No
other: *please outline*	No
Any risk to the environment	No

Any conflict of interest	No
Research that could be considered controversial or be of reputational risk to Aston University	No
Social media data and/or data from internet sources that could be regarded as private	No
Any other ethical considerations *(Please state here or contact the Research Ethics Officer via your College Ethics inbox if there are any substantial ethical considerations you are aware of and would like to flag for the reviewer.)*	No

If you have answered YES to any of the above, you need to take the following steps in applying to your College Research Ethics Committee (CREC) in order to seek approval to commence your research:

1. Complete this application form and all necessary accompanying materials such as but not limited to:
    - Advertising materials (posters, recruitment e-mails);
    - Letters of invitation to participate;
    - Participant information sheets;
    - Consent forms;
    - Questionnaires, surveys, demographic data collection sheets, etc.;
    - Interview schedules, interview question guides, focus group materials/scripts, etc.;
    - Debriefing sheets (if applicable);
    - Risk assessment; and
    - Standard Operating Procedure (if applicable, as agreed with Health & Safety) – *an example of when this is required may be for Covid-19 safe working, when undertaking Phlebotomy work, a distress protocol etc.*
2. Create a zip file containing all application materials (i.e., application form and all of the applicable documents noted above).
3. Submit the zip file to your dedicated CREC e-mail address:
    - College of Engineering and Physical Sciences: eps_ethics@aston.ac.uk
    - College of Health and Life Sciences: hls_ethics@aston.ac.uk
    - College of Business and Social Sciences: bss_ethics@aston.ac.uk
4. If required by invitation, be available to attend a CREC meeting to present and answer questions on your application (this is mostly for complex proposals).

Please note, you must obtain ethical approval from your College REC prior to your research commencing (including recruitment of participants). Failure to do so could amount to research misconduct.

Section 1: Ethics Application Form

Research Team Details	
Title of research project:	A longitudinal study of lifestyle factors and biometric development in children of a regional population
Principal Applicant Details:	Name: Mr Grant Hannaford Email: [student ID no. removed]@aston.ac.uk Contact Telephone Number: +[no. removed]
College: *(Delete as applicable)*	Health & Life Sciences (HLS)
Supervisor(s) Name(s): *(If the principal applicant is a PhD/MPhil/MSc by Research student, please provide details of the supervisory team; expand as required)*	Name: Prof Nicola Logan Email: n.s.logan@aston.ac.uk Contact Telephone Number:01212044128 Name: Email: Contact Telephone Number:
Details of Other Research Team Members: *(If applicable, expand as required to accommodate all research team members)*	Name: Email: Contact Telephone Number: Name: Email: Contact Telephone Number: Name: Email: Contact Telephone Number:
Anticipated Start Date for the Research: *(Please note that the start date must fall after ethics approval has been granted so please allow a reasonable time after the date of submission for ethical approval)*	1/3/2023
Anticipated End Date for the Research: *(Please give yourself enough time to complete your data collection)*	February 2024
If this application is linked to previously submitted/approved ethics applications, please list the respective CREC reference number(s): *(For example if this application is for a follow-on study)*	Number unknown
Please provide a *brief* overview (summary) of your research, clearly outlining your objectives/aims and rationale in language suitable for a generalist/lay audience.	

Refractive and biometric development for myopes (short-sightedness) is an area of significant research. However, normal developmental pathways for biometry and refractive development are relatively poorly studied.
Hyperopic (long-sighted) and emmetropic (requiring no spectacle correction) children have demonstrated a successful cessation of coordinated growth in the eye, albeit prematurely for hyperopes. This provides an opportunity to identify and isolate the factors which promote cessation of emmetropisation (the co-ordinated growth of the eye towards the state of not needing a spectacle correction).
In this study, we propose to examine relationships between ocular biometry development and the natural progression of refractive development in the context of lifestyle and environmental factors for children in the emmetropisation phase of development, that is between 5 and 12 years of age. While biometric and refractive data provide objective measurements of refractive conditions, context will be given through family history and the social and environmental conditions present during
emmetropisation. Data will be retrospective and is to be extracted from existing patient records with candidates identified through examination of the patient database at Hannaford Eyewear, Bowral, NSW.

Secondary and tertiary questions that will be addressed using the data are:
• Correlations between DNEye & Nidek AL-Scan data. The DNEye aberrometer from Rodenstock uses a proprietary algorithm to determine overall axial length from measured anterior biometric
data. Comparison of measurements from this device and the measurements taken with a Nidek AL-scan will assess the usefulness of determined (as opposed to directly measured) biometry for patient management.
• Calculate the magnitude of peripheral blur (hyperopic or myopic) based on the Gullstrand eye model with individual participant data to determine the magnitude of improvement in image formation that may be available through the implementation of customised lens design based on biometry. This is of interest in looking at manipulating rate of eye growth in children.

Section 1.A: Secondary Human Data

Secondary Human Data: Existing Documents/Data Only ***This section needs to be completed if your study proposes to use data from existing datasets/documents OR if the data will be collected from social media or other online spaces where privacy and anonymity are contentious. Typically, no recruitment of human participants will take place if you are only using secondary data.*** **Is this section applicable to this application: Yes (if no, skip to section 1.B)**	
1.	What data will be studied and what evaluation will be undertaken? *(Please provide a clear outline of your research protocol, including the data sources you will be accessing and what evaluation will be conducted with that data; be mindful of the fact that it is not necessarily the case that just because online data is "out there" it can be used without due consideration of consent and legal implications. Please be as detailed as possible here and*

	be aware that permission to use data may require specific levels of assessment).

Data that have been captured as part of a child's eye historical examinations will be studied in the context of a survey presented to their primary carer.
Biometric and refractive data will include:

1. Refraction – both non-cycloplegic (indicating functional refractive power) & cycloplegic (to remove accommodative influence)
2. Axial Length (AL)
3. Corneal Radius (CR)
4. Central Corneal Thickness (CCT)
5. Anterior Chamber Depth (ACD)

All these data are captured as part of a child's routine eye examination at the applicant's optometry practice. Devices used and referenced in the study are part of a routine eye examination and do not constitute addition testing.

The survey presented to the primary carer will be used to determine additional data that may not already exist in the clinical record. This will require no additional clinical interaction with the child.

Environmental factors:
1. Parental ethnicity
2. Birth country – parental and child
3. Health care access
4. Birth conditions – weight and maturity
5. Visual environment– near work duration, dioptric composition of home environment, outdoor exposure duration/regularity
6. Developmental milestones

Data will be used to model the emmetropisation process in this cohort of children and also will be used to model type of peripheral blur they would be expected to have based on their individual biometry. This information is of interest in assisting with most appropriate interventions to alter rate of growth of the eye for future work.

Exclusion criteria is age based with patients older than 12 years of age considered unsuitable for inclusion.

2.	How will data or records be obtained? *(Please indicate how you will obtain the data/records and what permissions are in place for you to do so).*

Informed consent will be obtained from the parents/guardians of the children after their identification as a candidate or after attendance for routine care. The applicant is the practice owner and thus has access to the data already obtained as part of standard eye examinations. Included on the patient entrance forms is an option to be contacted for inclusion in research or marketing. Patients who have not indicated their consent to be contacted in this context will not be considered

for inclusion. Once informed consent has been obtained the applicant will access the data electronically. Source data is drawn from patient records which are accessible to all practice staff. Data pertaining to the study is limited to Grant Hannaford once inclusion is confirmed. Practice support staff will not necessarily be aware of the inclusion status of any individual in the study unless this is divulged by the individual themselves. Other practitioners in the practice may be aware of the identity of candidates for inclusion as they may refer candidates for inclusion to the study during the course of a consultation. All practice staff are bound by and adhere to the privacy laws of the Commonwealth of Australia.		
3.	Is the secondary data you will be using in the public domain? *(Please indicate the original purpose for which the data was collected, and comment on whether consent was gathered for additional later use of the data and/or how your use of the data falls within the scope of the consent originally given)*	NO
The data was collected as part of standard eye examinations and is held electronically in the applicant's optometry practice. Consent will be obtained to use this data for research purposes.		
4.	If your study involves re-analysis and potential publication of existing data which was gathered as part of a previous project involving direct contact with human participants, how will you ensure that your re-analysis of this data maintains confidentiality and anonymity as guaranteed in the original study? *(Please indicate what the original agreement was and how you will observe confidentiality and anonymity of data going forward)*	
N/A		
5.	How will you store the data and who will have access to it? *(Please indicate how you will store the data – ideally this will be on an encrypted storage facility provided by Aston; you should ensure that any storage complies with stipulations of the dataset (if applicable) such as geographical location of physical servers; please also outline who will be accessing it for analysis)*	
The optometry practice and research student are both based in Australia thus as per Australian privacy legislation the patient database is secured using practice management software encryption (SUNIX Vision software platform). Databases are encrypted and password protected. Data analysis and manipulation is performed once cases are deidentified with case references in the data handling software pointing to numerical file references inside the encrypted database rather than identifiable patient data. Once data are extracted from the practice management software the individual cases are not identifiable by any other means than the reference number which is only linked to the patient specific information from inside the encrypted practice management software. Grant Hannaford as the principal applicant will have access to the data. The supervisor, Prof Nicola Logan, will only have access to anonymous data relevant to the research.		
6.	How will the findings of your research be disseminated?	

	(Please indicate how you will publish your work, including any revisions to the dataset itself)	
The results of this study are planned to be published in scientific journals and/or presented at conferences. A lay summary of the results of the study can be forwarded to participants (if they wish) when the study has been completed. The results of the study will also be used in Grant Hannaford's Doctor of Ophthalmic Science thesis.		
7.	What other ethical considerations (if any), not previously noted on this application, do you think there are in your proposed study? How will these issues be addressed? *(Please indicate if there are any ethical considerations that need factored in terms of your access, use and publishing of the data and, if so, how you will address them)*	
This study will use data that has already been measured as part of standard clinical care. It will be anonymized, but there is a slight risk that participants could be 'recognised' from their eye data.		
8.	Will you be gathering data from discussion forums, online 'chat rooms', and similar online spaces where privacy and anonymity are contentious? *(Please note that if, for example, a forum/chat room/etc. requires membership for access, the use of data from such sources needs careful consideration and you MUST therefore complete Section 1.B of this application form; you should justify your response to this question here)*	NO
Please include here any other comments/information in relation to the use/analysis of this proposed data that will assist in the ethics application approval review process: *(For example, if you have an existing data sharing agreement or other supporting documents that demonstrate your permissions to use any data, please state this here and attach those documents to your e-mail submission for your application)*		

Section 1.B: Involvement of Human Participants

Human Participants Involved: Data Collected Directly or Indirectly from Human Participants

This section needs to be completed if your study proposes to involve human participants, either directly or indirectly. This includes observation of people in public spaces/at public events where consent is not feasible/appropriate and/or necessary; where questions in this section don't apply to your study on these

grounds, please just indicate this. Please note, this section should be completed in addition to section 1.A if the data will be collected from social media or other online spaces where privacy and anonymity are contentious. **Is this section applicable to this application: Yes (if no, skip to section 1.C)**		
9.	Please describe briefly the intended human participants (including number, age, gender, and any other relevant characteristics): *(Please provide a clear outline of your participant pool, paying particular attention to inclusion/exclusion criteria for your study and the inclusion of any vulnerable groups. Please remember that inclusion/exclusion criteria should also be reflected in study advertisements and participant information sheet as appropriate)*	
The intended participants are children aged between 5 and 12 years of age both males and females. It is expected that up to 50 children will be recruited. Inclusion criteria are existing patients at Hannaford Eyewear, Bowral, Australia.		
10.	How will participants be recruited and from where? *(Please indicate how you will recruit your participants and provide evidence of any applicable permissions you must do so (e.g., if you are recruiting via organisations, what permission do you have to contact prospective participants); please remember that your submission package should include all relevant recruitment material)*	
After identification of candidates from the patient database at Hannaford Eyewear, Bowral, NSW, Australia, they will be contacted as follows: Initial contact by phone followed by email/mail of relevant documents. In the event of unsuccessful contact by phone email/mail of invitation will be sent.		
11.	Please describe your data collection methods, drawing particular attention to any potential ethical issues: *(Please provide an outline of the problem you are trying to solve, the goals of your study, how you are structuring your study and how the data collection relates to that, what you are asking participants to do on which basis to collect data (or how you are collecting data if indirectly) and the data you will be collecting, your proposed analysis, etc.; please also indicate where the research will be taking place – e.g., online, in-person in the UK or abroad, etc.)*	
Data have already been collected as part of an eye examination. The current study will use that data in terms of defining patterns in eye growth and associated risk indicators. The research will take place in Australia.		
12.	Will you take all necessary steps to obtain, *before participation*, the voluntary and informed consent of the prospective participants or, in the case of individuals not capable of giving informed consent, the permission of a legally authorised representative in accordance with applicable law?	YES
*Voluntary, informed consent is at the heart of ethical research conduct, but it is acknowledged that at times this cannot be obtained before participation for several reasons. If you answer **YES**, please jump to **Question 15**; if you answer **NO**, please **continue to Question 13**.*		
13.	If it will be necessary for participants to take part in the study without their knowledge and/or full informed consent *at the time*, please explain why (**if you intend to recruit adult participants who lack capacity to consent,**	

	please contact ethics@aston.ac.uk before proceeding with this application). *(Covert observations, for example, may be necessary in some settings/contexts and some studies may need to use deception or partial deception upfront to avoid influencing the findings; if these situations apply to your study, please explain them carefully and justify why this approach is necessary)*
N/A	
14.	If your study involves withholding information about the aims of the research beyond the final debriefing and/or deliberate deception of the participant that is not clarified in a debriefing session, please justify and provide details here. You may then skip to Question 16. *(Please explain and justify if it will not be possible to achieve full disclosure, even after participation)*
15.	Please explain the procedure you will use for obtaining informed consent from your participants. If applicable, please explain the procedures you intend to use to gain permission on behalf of participants who are unable to give informed consent (e.g. children). Where partial deception is required before participation, please explain your debrief and final consenting process at the end of participants' involvement. If your study runs over a long period or where reconsenting is advisable for other reasons, please explain your process here. *(Please explain in detail your process for informed consent; your submission package should include appropriately constructed Participant Information Sheets and Consent Forms for this purpose (this may necessitate bespoke forms for different participant cohorts as well as debriefing content and re-consenting forms where applicable))*
As the study concerns data from children, parental/guardian informed consent will be obtained in all cases. As the data have already been collected as part of an eye examination, there is no deception involved.	
16.	How will you protect participants' confidentiality and/or anonymity in data collection (e.g., interviews, focus groups, video surveillance, etc.), data storage, data analysis, presentation of findings and publications? *(It is important to protect the confidentiality and/or anonymity of participants; consider carefully how their data will be handled to protect this, including in settings such as focus groups where disclosure is to more than just the research team; care should also be taken in terms of ensuring the data will not be delivered into the hands of, for example, employers when interviewing employees)*
As per Australian privacy legislation the patient database is secured using practice management software encryption (SUNIX Vision software platform) Databases are encrypted and password protected. Data analysis and manipulation is performed once cases are deidentified with case references in the data handling software pointing to numerical file references inside the encrypted database rather than identifiable patient data. Once data is extracted from the practice management software the individual cases are not	

identifiable by any other means than the reference number which is only linked to the patient specific information from inside the encrypted practice management software.	
17.	Could participation cause discomfort (physical and/or psychological – e.g., distressing, sensitive or embarrassing topics), inconvenience and/or danger beyond the risks encountered in normal life? Please indicate the level of risk and plans to address these potential risks. *(Please consider if the study might cause a participant physical discomfort (e.g., use of devices/sensors, physical exertion, application of substances, etc.) or require any limitations to activity before/after their participation, psychological discomfort (e.g., questions about mood, mental or physical health, personal behaviours/experiences, etc.) or if by participating in your study an individual could be placed in a compromising position – e.g., an employee could risk their job by participating; please ensure appropriate measures are in place to mitigate such risks – e.g., risk assessment of physical devices/substances, support resources in place for psychological distress, avoiding running interviews with employees in their workplace and suitable measures to mitigate employer coercion; finally, please document how you will handle disclosures during data collection that would require action on your part – e.g., indication of risk to the individual or someone else)*
The data have already been collected as part of an eye examination so there is no additional discomfort or inconvenience.	
18.	State the timescales within which participants may withdraw from the study, noting your reasons. *(Where data has been collected completely anonymously – e.g., fully anonymised online surveys – it will not typically be possible for participants to withdraw after submission and this needs to be made clear in the PIS; where participants have contributed to the likes of a focus group, they can withdraw their participation and no quotes from them should be used but their data up to the point of withdrawal cannot be fully withdrawn as it has influenced the direction of the group discussion and this needs to be made clear in the PIS; for most other studies, participants should be given a reasonable window within which to withdraw their research data – e.g., 2 weeks from the date of their participation – but if you are holding any personal data (e.g. e-mail addresses of participants for future contact) this should be deleted if the participant requests at any time.*
The data are secondary data and thus only extracted anonymised. Therefore it will not be possible to withdraw after data extraction. This is stated on the PIS.	
19.	Do you anticipate any power imbalances or dependent relationships, either with participants or with/within the research team? If yes, please explain how you intend to address these? *(Power imbalances can lead to coercion or perceived coercion and so it is best to avoid these where possible; examples of such relationships include staff recruiting to studies students they teach/supervise, employers recruiting employees to a study on behalf of a researcher, etc.; as such, consider how you could recruit your participants in such a way as to remove this imbalance or avoid dependent relationships in the recruitment process)*

Grant Hannaford is both the main researcher on this project and an owner of the clinical practice where the data are currently held. To avoid any conflicts of interest, the participants have time to decide on participation and it clearly states on the PIS that there will be no impact on clinical care if they do not wish to participate. This point will also be verbally discussed with potential participants.	
20.	Please give details of any conflicts of interest which need to be considered for your project? *(Such conflicts could include power imbalances as noted above, where research is funded by an external, commercial entity which stands to gain directly from the research, where members of the team have vested interest in the outcome of the research, etc; these should be clearly declared and mitigating measures outlined where applicable/possible)*
Grant Hannaford is both the main researcher on this project and an owner of the clinical practice where the data are currently held. To avoid any conflicts of interest, the participants have time to decide on participation and it clearly states on the PIS that there will be no impact on clinical care if they do not wish to participate. There is no direct gain to Grant Hannaford's practice.	
21.	What potential risks may exist for the researcher and/or research team? Please indicate plans to address such risks? *(Just as it is important to protect study participants, we need to ensure the safety of our researchers; to this end, please consider where there is potential for risk to members of your research team – such risks might include lone working, exposure to distressing subject matter, conducting the research in some international research locations; support for researchers would include lone worker considerations which should be covered by a risk assessment, access to support networks related to the topic of study and, in extreme cases, regular professional/psychological assessment to monitor the researchers' wellbeing, submission of travel risk assessment and suitable approval for international travel, etc.)*
There are minimal risks as the data have already been collected as part of a regular eye examination. In terms of data extraction and analysis, the researchers are aware of risks of lone worker as this would apply to clinical practice as well as for research.	
22.	Whilst there may not be any significant *direct* benefits to participants because of this research, please state here any (including indirect) benefits that may result from participation in the study. *(It is appropriate to state in the PIS that there is no direct benefit but to then explain the wider benefit of the work)*
There are not any direct benefits to participating in the study however, indirect benefits may give the parent and child better insight into their eye development and better knowledge that may be beneficial should their child develop myopia and need an intervention for this. This type of knowledge could help the decision making in that instance.	
23.	Depending on the nature of your study, there may be scope for *incidental findings* to emerge from the data collection. Please outline where this may occur in your study and the measures you will include to handle such findings.

	(For example, if your study involves the recording of physiological data (e.g., brain scan) it may highlight potential cause for concern; you need to consider where this could happen and what protocol you will have in place if it does, placing duty of care to your participants at the centre of any such protocol)
The data will already have been reviewed by an optometrist as part of clinical care therefore it is unlikely that any incidental findings relevant to clinical care will emerge.	
24.	Please provide details of any incentives/payments (including out-of-pocket expenses), and the rationale for these, that will be made to participants. *(it is entirely reasonable to cover participants' expenses – e.g., modest travel and parking costs – associated with their participation in your study; it is also reasonable to compensate participants for their time but the rate of compensation needs to be carefully considered to avoid the compensation becoming a potentially coercive incentive; a rule of thumb is often £10/hr paid in gift tokens but exceptions can be made where specialist participants are required – e.g., clinicians – and the level of compensation needs to reflect the value of their time)*
None.	
25.	What are your plans for the storage of data (electronic, digital, paper, etc.)? Please ensure that your plans comply with the General Data Protection Regulation (GDPR) and the (UK) Data Protection Act 2018. *(Please outline how you will store your data, its security and who will have access to it, ensuring that any data sharing is in line with GDPR; please also describe your plans for data erasure/deletion)*
As per Australian privacy legislation the patient database is secured using practice management software encryption (SUNIX Vision software platform) Databases are encrypted and password protected. Computers used in the analysis of data are password and biometrically protected. Data is to be de-identified prior to inclusion in sets that will be subject to analysis. Data will be stored on BOX. Data sets containing identifiable material will be stored on password protected drives (x2) stored in secure safes (one at the practice location and one at the researchers home). The source material (patient records) is subject to storage and security in line with the Commonwealth Privacy Act 1988 (Australia). All storage plans also comply with General Data Protection Regulation (GDPR) and the (UK) Data Protection Act 2018. I confirm that GDPR training is current and up to date, completed as a requirement of Grant Hannaford's continued engagement as a lecturer at the University of New South Wales.	
26.	How will you make your data available to meet your funders open access requirements (if applicable)? *(Please note the open access requirements that apply to your data based on funding provider and how you plan to meet those requirements)*
N/A as the study is self-funded by Grant Hannaford.	
27.	Are there any restrictions on sharing your data for open access purposes (if applicable)?

	(Please note any restrictions on sharing your data – including for patent application purposes – and how this can be addressed considering funding provider requirements)	
N/A		
28.	Will audio or video recording of participants take place? *(Please delete as applicable; if you answer **NO**, please proceed to **Question 33**)*	NO
29.	Please confirm that portable devices (laptop, USB drive, etc) will be encrypted where they are used to store identifiable data, especially audio/video recordings. If it is not possible to encrypt your portable devices, please comment on the steps you will take to protect the data. *(Ideally audio/video will be kept on encrypted portable storage for as short a time as possible before being transferred to an encrypted storage facility provided by Aston; please provide a clear outline of your handling of personally identifiable data of this nature, including who will have access to it)*	
Data is stored on encrypted drives, access to drives is controlled by password and/or biometric protection.		
30.	If your study includes audio/video recordings, what are the implications for participants' anonymity? If participants are identifiable on/via the recordings, how will you explain to them what you will do with the recordings? *(consider what you will advise participants in the PIS in terms of the audio/video recordings and how they will be handled; ideally audio/video recordings will be transcribed and anonymised as soon as possible after data collection and, once the anonymised transcripts are verified, the original recordings securely destroyed; if any still images are to be retained for use from videos, participant consent should have been obtained and the images anonymised before use; similarly, if alternative mechanisms are to be used to anonymise the data, please explain the measures clearly here)*	
N/A		
31.	What arrangements have been made for audio/video data storage? At what point in the research will tapes/digital recordings/files be destroyed? *(As noted above, anonymisation of audio/video recordings is really important and this is typically done via the creation of anonymised transcripts; if an external transcription service is to be used, this should be outlined here and reassurances provided that the service has been approved by Aston)*	
N/A		
32.	What are the plans for dissemination of findings from the research? Please also include any impact activities and potential ethical issues these may raise. *(In addition to expected research publications, please consider how results might be effectively shared with the participants and the wider community, as applicable; this could include a lay summary that is made available on*	

	request, via community groups, etc or could include dissemination workshops, etc; please consult with the RKE impact team in terms of any planned impact activities and associated ethical issues and outline those here)
The findings will be published in the Doctor of Ophthalmic Science Thesis. Findings will be published in peer revied journals as appropriate for the subject matter. Finding will also be published through conference abstracts Findings will placed into a lay summary for dissemination through the practice to the candidates/carers.	
33.	Do you wish to highlight any ethical considerations, not previously noted on this application, that you think are applicable proposed study? Are there any matters about which you wish to seek guidance from the CREC? *(This application form has attempted to guide you to consider the standard ethical concerns intrinsic in most human participant studies; there may, however, be additional or alternative concerns that have not been mentioned – in which case, please outline these below for discussion with the CREC)*
None arising.	

Section 1.C: Involvement of Human Tissue

Human Tissue: Samples Collected Directly or Indirectly Obtained from Human Participants ***This section needs to be completed if your study proposes to involve human tissue samples. Please also complete Section 1.B if you are collecting tissue directly from human participants.*** **Is this section applicable to this application: No**	
34.	What tissue are you collecting? Does this fall under the definition of relevant material? *(Please refer to the Human Tissue Authority guidance -* https://www.hta.gov.uk/guidance-professionals/hta-legislation/relevant-material-under-human-tissue-act-2004/list-materials *- to determine whether your tissue falls under the definition of relevant material. If yes, you will require Designated Individual approval as well as ethics approval. Please confirm the nature and quantity of tissue you wish to use.)*
35.	From where will tissue samples be obtained? *(Indicate from where you will source your samples, either directly from participants or from which organisation, and any licensing or use restrictions that apply)*

36.	Will a Material Transfer Agreement (MTA) be required prior to, during, or after the study? *(Please outline the need for any such agreement and who will be responsible for this)*
37.	Where will the tissue samples be stored? Please confirm whether this is an already approved location listed in the Quality Manual. *(Human tissue samples need to be appropriately logged and stored – including for protection against damage during an adverse event – so please ensure that the storage arrangements and information provided here are clear and appropriate)*
38.	How long will the samples be stored at Aston University? *(Please indicate the duration of storage at Aston)*
39.	What will happen to the tissue once the project has finished? *(Please indicate the arrangements for handover or disposal of the tissue samples, including responsibility)*
Please include here any other comments/information in relation to your application that will assist in the ethics application approval review process:	

Section 2: Supervisor Comments

Is this section applicable to this application: Yes/No

Please include comments from supervisor(s) here:
Supervisors should be involved in and guide student applications. Supervisors should comment on the proposal and outline any discussion that has taken place in the drafting of this application.

Section 3: Declarations

The following declaration should be acknowledged and signed before submission to the CREC for approval	
I understand that as Principal Investigator/Researcher/PhD candidate I have overall responsibility for the ethical management of the project and confirm the following: • I have read the Research Integrity Policy and will abide by it in relation to the current proposal; • I will manage the project in an ethically appropriate manner according to: (a) the subject matter involved; (b) any applicable funder requirements and associated codes of conduct; and (c) the Research Integrity Policy; • On behalf of the University I accept responsibility for the project in relation to promoting good research practice and the prevention of misconduct; • If applicable, I will give all staff and students involved in the project guidance on the good practice and ethical standards expected in the project in accordance with the Research Integrity Policy; • If applicable, I will take steps to ensure that no students or staff involved in the project will be exposed to inappropriate situations; and • I confirm that I have completed all risk assessments and other Health and Safety requirements as advised by my College/Departmental Safety Officer and appropriate controls are in place for the hazards and/or risks identified.	
All research team members (including supervisors where the principal applicant is a student) should sign* and date below:	
Signatures: Grant Hannaford Nicola Logan	Date: 24/11/2022 24/11/2022

** note, typed/e-signatures are acceptable, but students must copy their supervisor(s) into the email when submitting their applications. Feedback will be cc'd to supervisor(s).*

Aston University
Aston Triangle
Birmingham
B4 7ET
0121 204 3000

Date: 20th February 2023

Grant Hannaford
Copy: Prof Nicola Logan
College of Health & Life Sciences

Dear <applicant name>,

Study title:	A longitudinal study of lifestyle factors and biometric development in children of a regional population
REC REF:	#HLS21030

Confirmation of Ethical Opinion

On behalf of the Committee, I am pleased to confirm a favourable opinion for the above research on the basis described in the application form, protocol and supporting documentation listed below.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	***Version***	***Date***
Aston University Research Ethics Application Form_Oct 22_Hannaford v5.docx	5	19/02/2023
AstonUniversity_Consent_Guidance and Template secondary data Hannaford v4.docx	4	16/02/2023
AstonUniversity_PIS_Guidance and Template secondary data Hannaford v4.docx	4	16/02/2023
REC ID 1838 RiskAssessmentForm V4.docx	4	20/02/2023

With the Committee's best wishes for the success of this project.

Yours sincerely,

Dr Claire Stocker
Deputy Chair of the Health & Life Sciences Research Ethics Committee

Appendix B

Project Proposal Form

ASTON DOptom/ DOphSc PROJECT PROPOSAL FORM

Please return to Dr Preeti Bhogal-Bhamra g.bhogal-bhamra@aston.ac.uk

SECTION A – DETAILS OF SUPERVISOR

Surname:	Logan
Forename:	Professor Nicola S.

Has the proposed supervisor developed the project outline with you? Yes. Professor Nicola Logan

*****delete as appropriate

SECTION B – DETAILS OF RESEARCH PROJECT

Title of study:

A longitudinal study of lifestyle factors and biometric development in children of a regional population.

Abstract of research to be undertaken – please identify the research question and demonstrate the appropriateness of the study design. Where appropriate, please include references central to the project [suggested word count 250]:

The prevalence of myopia is increasing worldwide however, current research is still trying to understand the mechanisms behind the development of myopia and its progression[8, 9]. When considering causal links it is important to understand the optical components involved in contributing to the refractive error. Emmetropisation is the active matching of the optical power of the cornea and crystalline lens to the eye's axial length, which minimises the residual refractive error. As this emmetropisation occurs, the optical components balance in order to create an image on the fovea that is in focus. Myopia is the result of an imbalance between these optical components, where the refractive power of the cornea and lens does not offset the axial length growth[10]. With axial growth occurring during childhood, myopia generally occurs in school-age children and adolescents, typically emerging between the ages of 7-14 with possible further progression up to late teenage to early adulthood years[11]. Given variations with different populations and lifestyles in relation to myopia development refractive and biometric development for myopes is an area of significant research. Normal developmental pathways for biometry and refractive development are not fully understood. Emmetropic children have demonstrated a successful cessation of coordinated growth in the eye, whereas this process has ceased prematurely for hyperopes whereas in myopes eye grow continues beyond the normal. This provides

an opportunity to identify and isolate the factors which promote cessation of emmetropisation.
In this longitudinal study, relationships between ocular biometry development and the natural progression of refractive development in the context of lifestyle and environmental factors for children in the emmetropisation phase of development, that is, less than 12 years of age, will be examined. The minimum age for candidates is 4 years of age to allow for the inclusion of school and educational environmental factors for all candidates. While biometric and refractive data provide objective measurements of refractive conditions, context will be given through a survey of family history and the social and environmental conditions present during emmetropisation and comparison of biometric and refractive development between individuals. In particular aspects of lifestyle involving time spent outside in daylight hours along with time spent on near work and digital devices will be examined given the emerging evidence with links to myopia in this field[2, 220]. No contemporary data exist for the particular population that will be studied and the findings will help address management of myopia in children in the researcher's own clinical practice.
Biometric and refractive data will include:

6. Refraction – non-cycloplegic indicating habitual refractive power & cycloplegic refraction to remove accommodative influence. Autorefraction will also be conducted as part of the biometric assessment to provide an objective measure of refractive error.
7. Axial Length (AL)
8. Corneal Radius (CR)
9. Central Corneal Thickness (CCT)
10. Anterior Chamber Depth (ACD)

Environmental factors surveyed via questionnaire:

7. Parental ethnicity
8. Birth country
9. Health care access
10. Birth conditions – weight and maturity
11. Visual environment– near work duration and type, dioptric composition of home environment, outdoor exposure duration/regularity
12. Developmental milestones

Secondary and tertiary questions that will be addressed are:

Correlations between DNEye & Nidek AL-Scan data. The DNEye aberrometer from Rodenstock uses a proprietary algorithm to determine overall axial length from measured anterior biometric data. Comparison of measurements from this device and the measurements taken with a Nidek AL-scan will assess the usefulness of determined (as opposed to directly measured) biometry for patient management.

Calculate the magnitude of peripheral blur (hyperopic or myopic) caused by the use of Gullstrand eye model for the patients examined in this cohort to determine the magnitude of improvement in image formation that may be available through the implementation of customised lens design based on biometry.

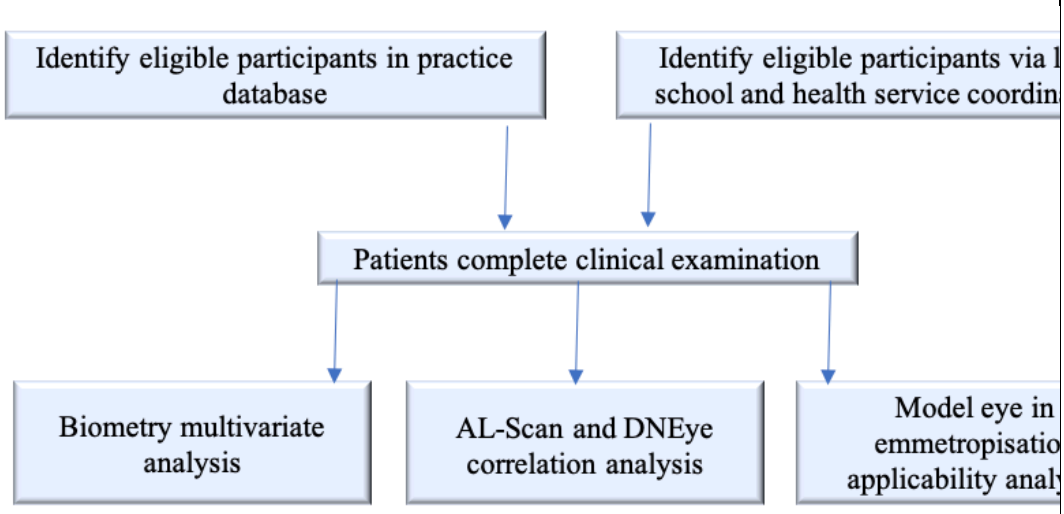


Figure 1 Participant flowchart

Brief summary of proposed programme of work; this must include an outline timetable, chapter summary, whether the work is to be carried out in collaboration with others, availability of facilities, equipment and provision of patients [suggested word count 1,000]:

This longitudinal study will determine rates of refractive and biometric development and will provide cross sectional snapshots for candidates at similar developmental points.

Chapter 1 Provides the reader with pertinent background information on the current understanding of factors that influence emmetropisation.

Chapter 2 A survey to determine correlations between lifestyle factors, refractive error and emmetropisation in a cohort of approximately 50, children, aged 4 to 12 years, in a semi-rural population. These children will be assessed at baseline, at 6 months and at 12 months. The cohort size is based on G*Power calculations (using ANOVA: repeated measures, within-between interaction, effect size f^2 =0.35 (large), α err prob=0.05, Power (1-β err prob)=0.8 and number of groups = 6, number of measurements = 3) yield a total sample size of 30. The survey will be an elaboration on that used by the Joint Writing committee for the Multi-Ethnic Pediatric Eye Diseases Study[5] and the Aston Eye Study [4] with additional questions pertaining to visual environment and developmental milestones.

Prevalence of refractive error and biometric development in the presence of environmental factors will be determined. A comparison of rates of biometric and refractive change will be performed between individuals as well as published normative data in the presence of environmental influences. The Kruskal - Wallis test is the likely candidate for checking the distribution of variables as the data will be non-parametric. Categorical variables may be defined as a percentage with quantitative variables described as a mean +/- standard deviation. Multiple linear regression analyses will be performed to evaluate independent influence of the individual risk factors.
As an extension a cross-sectional study based on the results of the resultant study data will allow comparison with normative data for similar populations which are geographically displaced from this cohort. These will include comparison with meta-analysis of published data for European and North American populations[24, 53, 190]. This comparison will serve to further isolate effects due to physical environment and social conditions.

Chapter 3 A cross sectional examination of biometric measurements and determinations in a Nidek AL Scan and Rodenstock DNEye biometers in both adults and children to determine applicability of Rodenstock's implemented algorithms [124] for determination of biometric parameters in children. These algorithms are based on the integration of three sources of biometric data;

1. Direct measurement
2. A priori values (i.e. published values in literature)
3. Calculation from consistency conditions (known relationships between refractive conditions and biometric values)

Currently the data used for development of the model are limited to adult populations indicating scope for improvement of the model with regards to juvenile biometry. It is currently unclear if the model currently used is able to successfully accommodate the biometry of an eye undergoing emmetropisation.

Preliminary ad hoc investigations using SPSS into the correlations between axial length, anterior chamber depth and corneal thickness by direct measurement of biometric parameters (Nidek) and determination (Rodenstock) have been undertaken in practice using existing databases using SPSS. For N=88 candidates aged 6.74 to 76.30 years of age yielded a mean of differences of 0.61mm and a standard deviation of 0.67mm. These values were used with MedCalc to determine the minimum number of measurements pairs required for a Bland Altman analysis to be 25 (type I error Alpha, Significance = 0.05, type II error Beta, 1-Power = 0.20). This would suggest that the proposed cohort of 50 individuals in chapter 2 would suffice for this analysis. However, as this is cross sectional study, retrospective data is available from the practice which will allow much larger sample sizes to be included.

Chapter 4 Calculate the peripheral blur (hyperopic or myopic) for parafoveal rays (~6 degrees) and marginal rays (~20 degrees) caused by the use of Gullstrand eye models in spectacle lenses for the patients examined in this cohort. These zones correspond to the centre of the treatment zones in current DIMS and HAL spectacle lens designs for myopia control. By extension an examination of the

applicability of customised biometric models for the correction of refractive error in children through application of individualised areas of defocus based upon the specific biometric parameters of the eye. The magnitude of deviation from the Gullstrand model eye may be determined through the use of the same sources of biometric data as in Chapter 3:

1. Direct measurement
2. A priori values (i.e. published values in literature)
3. Calculation from consistency conditions (known relationships between refractive conditions and biometric values)

The data provided by direct measurement and calculation enable the difference between far point spheres for the model eye and the individual eye to be determined and expressed as a function of radial distance from the shared apical points of the two relative planes (Gullstrand vs individual). The individual eyes will be compared to the Gullstrand model eye in terms of axial length, anterior biometry and refraction. While it is acknowledged that the posterior surface of the eye is not rotationally symmetric, it is possible to develop a basic model of the individual eye using biometric data to determine radial curvature of the posterior surface. As the Gullstrand eye also uses a radially symmetric assumption the individual eye and the Gullstrand model may be compared. As a secondary exercise the data will be examined for correlations between refractive errors and biometry and compared to published research. Using G Power and Cohens suggested large effect size of 0.5, a sample size of 28 individuals was indicated (Wilcoxon signed rank test (one sample case), One tail, effect size d =0.5, α err prob=0.05, Power (1-β err prob)=0.8) to determine the difference from a single constant (i.e. variation of individual from Gulstrand eye model). To address the secondary exercise of examining correlations between refractive error and biometry (i.e. axial length) a sample size of 29 individuals was indicated (G Power, Correlation: Bivariate normal modal, two tailed, Correlation ρ H1=0.5 (large), α err prob=0.05, Power (1-β err prob)=0.8, Correlation ρ H0=0). Both of these calculations indicate a sample size for the cohort of 50 individuals is sufficient.
As manipulation of the radial power profile of lenses is a developing area of intervention for refractive development, the ability to quantify the deviation of an individual eye model to the standard models used in lens design may prove beneficial in refractive interventions.

Note on calculation of cohort/sample sizes
The sensitivity of the effect size may be increased by the modification of the effect size from large to medium. The same calculations then yielded sample sizes in the range of 80 to 100 which may be too large given the scope of the study proposed and the need to refract each individual on several occasions.

Overall timetable

Month

- 0-3 recruitment of candidates and literature review

- 3-15 data collection and analysis, optimally 12 months (52 weeks) engagement from individual candidates
- 15-20 drafting of thesis

Data collection phase timetable

Week

- 0 Baseline and eligibility. Subjects attend practice for an initial assessment, orientation to the study and measurements. Provision of initial questionnaire
- 26 to 28 Subjects return for interim follow up and measurements. Provision of questionnaire to determine any changes to influencing factors
- 52 to 54 Subjects return for fourth follow up and measurements. Provision of questionnaire to determine any changes to influencing factors

Collaboration Not applicable, although reliant upon staff optometrists at the practice for refraction of subjects in conjunction with auto refraction to mitigate practitioner bias.

Availability of Facilities consultations will occur at Hannaford Eyewear, these facilities are available without any requirement for permissions or remuneration.

Availability of Equipment:

- Nidek AL-Scan located at Hannaford Eyewear, Bowral. Provides direct measurement of anterior ocular biometry and axial length. No provision for direct measurement of crystalline lens biometry in this unit.
- Rodenstock DNEye wavefront Analyser and biometer. Provides direct measurement of anterior ocular biometry. Axial length is determined mathematically. No provision for direct measurement of crystalline lens biometry in this unit.

Examination Procedure

1. Focimetry of existing spectacles (if any).
2. Autorefraction performed using the Rodenstock DNEye autorefractor and aberrometer (a development of the Visionix VX120 https://luneautech.com). Additionally, anterior chamber depth, corneal radius of curvature, corneal thickness and wavefront aberrometry will be taken with this instrument in addition to distance and near refraction. The DNEye software also provides a calculated value for axial length.
3. Ocular biometry using the Nidek AL-Scan optical biometer (http://www.nidek.com) to measure axial length, anterior chamber depth, corneal radius of curvature and corneal thickness.
4. Monocular distance visual acuities measured at 6 metres using a computerised logMAR test chart (http://www.openoptometry.com).
5. Heterophoria/tropia to be assessed at distance (6 metres using the smallest discernible letter) and near (using a fixation target at 33cm) using the cover/uncover test both aided and unaided.

6. Subjective refraction, performed at 6 metres.
7. Parental questionnaires given to carer.

Provision of Patients The practice has approximately 35 000 patients on record. It is possible to sort these records by age, gender, refractive error, prescribed lens solution, symptoms, history and consultation item number. Item numbers provide an insight into the type of consultations conducted for a given patient and enable isolation of patients as groups by treatment. Australian privacy laws permit contact to be made with existing patients of a practice to present opportunities to participate in research. Currently 564 patients on record meet initial eligibility of 4 to 12 years of age.
Patients will not be reimbursed for participation. Should refractive error be detected participants will be offered a pair of spectacles at no charge from a predetermined range of frames and lenses.
Additional candidates may be recruited through inclusion of local schools via the school health services coordinators. The most recent census indicates approximately 3400 children of primary school age in the immediate region.
Due to the age of candidates, direct parental consent for participation is necessary as are Working With Children Checks (WWC) for practice staff. These are checks are mandatory in Australia and thus are already in place for Hannaford Eyewear.
COVID-19 may present a complication with access to patients as the state is currently in lockdown with no indications of relief until October. Should the lockdown inhibit patient access there is sufficient data (>300 records) containing measurements from both the Nidek and DNEye instruments. This will enable those proposed secondary questions to be addressed until patient access is restored.

Place or places where the research work is to be undertaken:

Research work will be undertaken at Hannaford Eyewear, 1/310 Bong Bong Street, Bowral, NSW, Australia. This practice is owned by the candidate.

Appendix C

Ethics Modification 2024 Approval – Digital collection of data

Aston University
BIRMINGHAM UK

College of
Health and
Life Sciences

Aston University
Birmingham B4 7ET
United Kingdom

+44 (0)121 204 3000
aston.ac.uk

Grant Hannaford
Copy: Prof Nicola Logan

13th August 2024

Study title:	A longitudinal study of lifestyle factors and biometric development in children of a regional population
REC ID:	HLS21030 Amendment 1

Confirmation of Ethical Opinion

Dear Grant Hannaford,

On behalf of the College of Health and Life Sciences Research Ethics Committee, I am pleased to confirm a favourable opinion for the above research on the basis described in the application form and supporting documentation listed below.

Please note that as Principal Investigator you are responsible for ensuring that (where applicable) all the necessary legal and regulatory requirements to conduct the research are met, and the necessary licenses and approvals have been obtained prior to commencing your research. You are also responsible for reporting any ethics-related issues that occur during the course of the research, or arising from the research, to the Research Ethics Officer at hls_ethics@aston.ac.uk (e.g. unforeseen ethical issues, complaints about the conduct of the research, adverse reactions such as extreme distress).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	***Version***	***Date***
Amendment to REC HLS21030 ethics approval_02092024.docx	1	09/02/2024
Aston University Research Ethics Application Form_Oct 22_Hannaford v6.docx	6	09/02/2024
AstonUniversity_PIS_Guidance and Template secondary data Hannaford v5.docx	5	09/02/2024
Invitation to Participate in Research.docx	1	09/02/2024
Patient Survey.pdf	1	09/02/2024

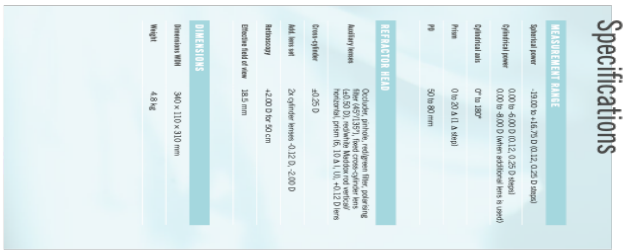
With the Committee's best wishes for the success of this project.

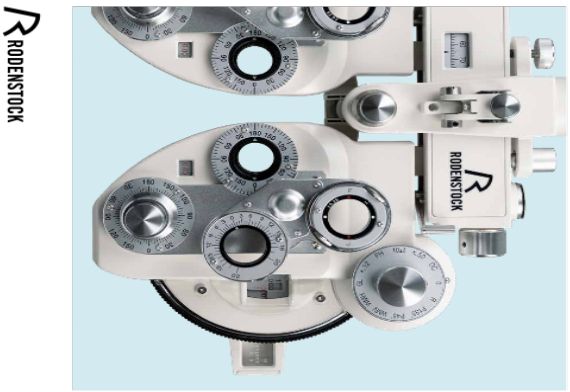
Yours sincerely,

Dr Claire Stocker
Chair of the Life and Health Sciences Research Ethics Committee

Appendix D

Rodenstock Phorovist 800 Phoropter Head





Appendix E

Nidek AL-Scan Sample Output

ID: 14997
Name: Hannaford, Grant
Sex: Male
DOB: 16/Feb/1976
Exam Date: 29/Sep/2020 11:41
Operator: Default

NIDEK

AL

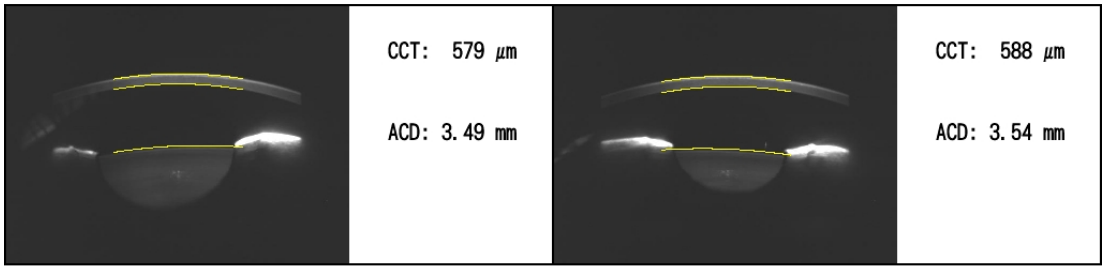
Right				Left			
Eye Type: Phakic				Eye Type: Phakic			
AL	SNR	AL	SNR	AL	SNR	AL	SNR
24.23 mm	19.8			24.37 mm	25.7		
24.23 mm	16.6			24.14 mm	22.5		
24.25 mm	21.4			24.37 mm	19.4		
24.25 mm	16.6			Error	1.3		
24.25 mm	18.0			24.36 mm	12.9		
24.24 mm	17.0			24.38 mm	21.3		
Addition:	24.24 mm	18.9		Addition:	24.38 mm	26.9	

KM

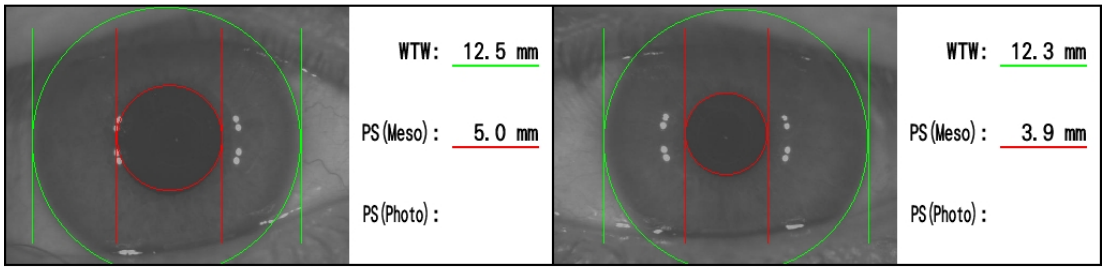
Ref. Index: 1.3375

φ2.4 mm	R1:	8.19 mm @ 87°	AVG K: 42.07 D	φ2.4 mm	R1:	8.10 mm @128°	AVG K: 42.17 D
	R2:	7.86 mm @177°	CYL: - 1.73 D @ 87°		R2:	7.91 mm @ 38°	CYL: - 1.00 D @128°
φ3.3 mm	R1:	8.21 mm @ 91°	AVG K: 41.97 D	φ3.3 mm	R1:	8.12 mm @131°	AVG K: 42.09 D
	R2:	7.88 mm @ 1°	CYL: - 1.72 D @ 91°		R2:	7.92 mm @ 41°	CYL: - 1.05 D @131°

ACD/CCT



WTW/PS



NIDEK AL-Scan OPTICAL BIOMETER V1.12.02 Report:29/Sep/2020

Appendix F

Rodenstock DNEye Sample Output

Customer	Grant Hannaford
Session	Sihouette 5567
Date	2024 Aug 20

RODENSTOCK

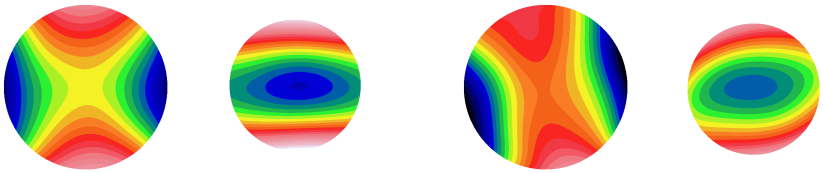
DNEye® Summary

Aberrometric data

Right		Sph [D]	Cyl [D]	A [°]
Far	Meso	1.83	-3.85	92
	Photo	1.83	-3.85	92
Near	Photo	4.32	-3.86	91

Left		Sph [D]	Cyl [D]	A [°]
Far	Meso	0.48	-2.17	105
	Photo	0.52	-2.22	104
Near	Photo	2.82	-2.04	101

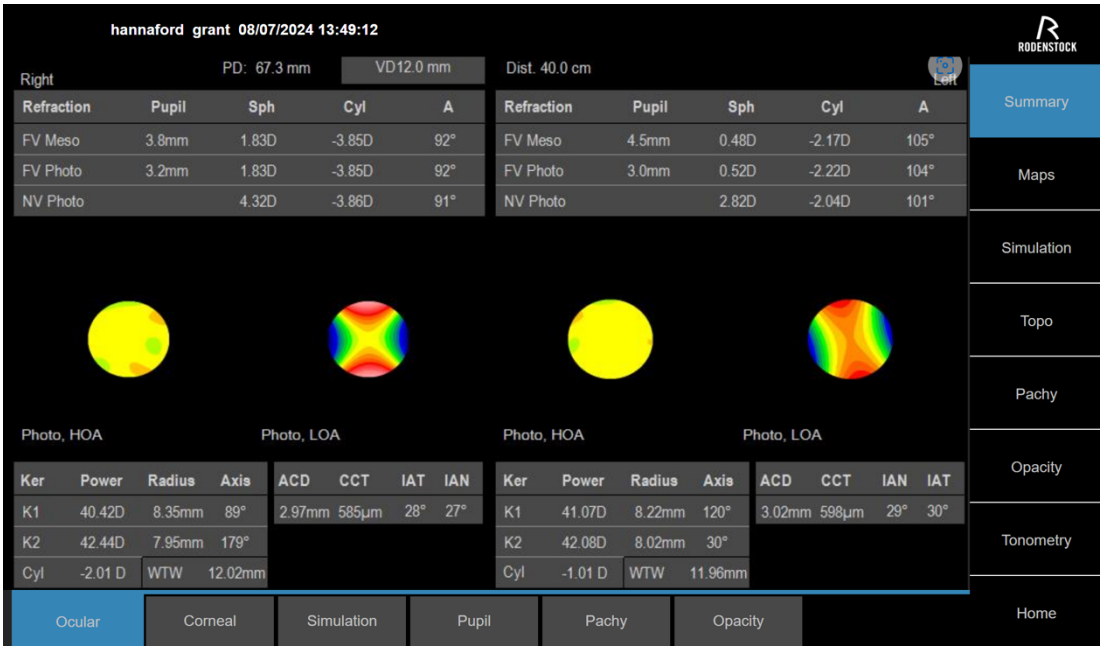
Far mesopic **Near photopic** **Far mesopic** **Near photopic**



Biometrics

Right				
Cornea	**Ker**	**r [mm]**	**P [D]**	**A [°]**
	K1	8.35	40.42	89
	K2	7.95	42.43	179
	Cyl		-2.01	89
Anterior chamber depth [mm]				2.97
Axial eye length [mm]				24.37

Left				
Cornea	**Ker**	**r [mm]**	**P [D]**	**A [°]**
	K1	8.22	41.07	120
	K2	8.02	42.08	30
	Cyl		-1.01	120
Anterior chamber depth [mm]				3.02
Axial eye length [mm]				24.43




hannaford grant 08/07/2024 13:49:12
RODENSTOCK
Both Eyes
Meso Photo
Photo
Meso
Near
Summary
Maps
Simulation
Topo
Pachy
Opacity
Tonometry
Home
Aberration
Right 2.9mm
Left 3.0mm
Defocus Z(2,0) 0.02µm 0.18µm
Astigm. Z(2,±2) 0.80µm @ 2° 0.50µm @ 14°
LOA 0.80µm 0.53µm
HOA 0.07µm 0.06µm
RMS 0.80µm 0.53µm
Coma Z(3,±1) 0.03µm @ 147° 0.02µm @ 146°
Sph. Aber. Z(4,0) 0.02µm 0.01µm
Astigm. II Z(4,±2) 0.02µm @ 93° 0.02µm @ 77°
Trefoil Z(3,±3) 0.05µm @ 103° 0.04µm @ 75°
Tetrafoil Z(4,±4) 0.01µm @ 66° 0.02µm @ 18°
PSF
Acuity
MTF
Zernike
Ocular

Appendix G

Questionnaire

A Longitudinal Study of Lifestyle Factors and Biometric Development In Children of a Regional Population.

Patient Survey

Thank you for agreeing to take part in this study REC ID HLS21030, [Version2], [3rd February, 2023]. Please find the survey questions below. We would like to remind you that participation is voluntary and should you wish to decline to answer any questions you may do so at your discretion.

Personal Details

Child's Surname ..... Male☐ Female ☐

Child's Given Name (s) ..... Date of Birth ...../...../.....

Parent/Guardian's Surname ..... Given Name .....

Parent/Guardian's Email .....

Parent/Guardians Phone Number .....

Birth Conditions

Relative to due date, when was your child born? ..... Week(s) Pre ☐ Post ☐

What was their birth weight? ..... Kg ..... What was their birth length? ..... cm

Were there complications at birth? ..... Yes ☐, No ☐

If you answered 'yes' to this question, what was the nature of the complication? .....

.....

.....

.....

.....

Developmental Milestones

To the best of your recollection, how did their development relate to growth charts (percentiles) at various ages?

18 months Height: Lower than average ☐ Average ☐ Higher than average ☐

18 months Weight: Lower than average ☐ Average ☐ Higher than average ☐

24 months Height: Lower than average ☐ Average ☐ Higher than average ☐

24 months Weight: Lower than average ☐ Average ☐ Higher than average ☐

36 months Height: Lower than average ☐ Average ☐ Higher than average ☐

36 months Weight: Lower than average ☐ Average ☐ Higher than average ☐

48 months Height: Lower than average ☐ Average ☐ Higher than average ☐

48 months Weight: Lower than average ☐ Average ☐ Higher than average ☐

At what age did your child start to crawl or move by shuffling on bottom? Years

At what age did your child start to talk? Years

Is your child right or left handed? Left ☐ Right ☐

Has your child been diagnosed with any behavioural or learning difficulties? Yes ☐ No ☐

Does your child wear spectacles? Yes ☐ No ☐

At what age did they commence wearing them (approximately)? Years

Education

What year is your child in at school? .....

Is the school private or public? ..... Public ☐ Private ☐

Has your child repeated or skipped a grade? ..... Repeated ☐ Skipped ☐ Neither ☐

Based on assessments (school reports, NAPLAN etc) what is your child's performance in the following areas?

Reading ..... Lower than average ☐ Average ☐ Higher than average ☐

Writing ..... Lower than average ☐ Average ☐ Higher than average ☐

Spelling ..... Lower than average ☐ Average ☐ Higher than average ☐

Mathematics ..... Lower than average ☐ Average ☐ Higher than average ☐

Behaviour ..... Lower than average ☐ Average ☐ Higher than average ☐

Visual Environment

How much daylight outdoor play time does your child engage in, on average, per day? ..... <30 minutes ☐ ..... 30 minutes to one hour ☐ ..... ≥ 1 hour ☐

How much evening outdoor play time (after dark/under lights) does your child engage in, on average, per day? ..... <30 minutes ☐ ..... 30 minutes to one hour ☐ ..... ≥ 1 hour ☐

How much study time does your child engage in, on average, per day?

<30 minutes ☐ 30 minutes to one hour ☐ > 1 hour☐

How much study screen time does your child engage in, on average, per day?

<30 minutes ☐ 30 minutes to one hour ☐ > 1 hour☐

How much recreational screen time does your child engage in, on average, per day?

<30 minutes ☐ 30 minutes to one hour ☐ > 1 hour☐

Where does your child perform their study/homework?

dedicated study area ☐ kitchen/living room ☐ unsure☐

Does your child play organized sports? Yes ☐ No ☐

Please specify

Approximately how many hours per week does your child engage in these sports?

How would you describe your home?

Apartment/flat ☐ Townhouse/semi-detached ☐ Small Residential block (<500m^2) ☐

Large residential block (>500m^{2}to 1 acre) ☐ Semi Rural/Rural (acreage) ☐

How much time off school did your child have due to COVID-19 and the lockdowns?

Weeks/Months

Parental/Family History

Maternal (Birth Mother) Age ..... Years (if known)

Country of Birth ..... Ethnicity (how do you self identify) .....

Education ..... High School or equivalent ☐ ..... TAFE ☐ ..... University

Employment ..... N/A ☐ ..... Casual ☐ ..... Part Time ☐ ..... Full Time ☐

Maternal visual performance ..... Spectacles ☐ ..... Myopia ☐ .....
Hyperopia ☐

Presbyopia ☐ ..... Glaucoma ☐ ..... Other: .....
.....

Paternal (Birth Fathers) ..... Years (If known)

Country of Birth ..... Ethnicity (how do you self identify) .....

Education ..... High School or equivalent ☐ ..... TAFE ☐ ..... University ☐

Employment ..... N/A ☐ ..... Casual ☐ ..... Part Time ☐ ..... Full Time ☐

Paternal visual performance ..... Spectacles ☐ ..... Myopia ☐ .....
Hyperopia ☐

Presbyopia ☐ ..... Glaucoma ☐ ..... Other: .....
.....

Is there a smoker in the household? Mother ☐ ..... Other ☐ ..... None ☐

Date: ...../...../.....

Received By: .....

Participant Ref: .....