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Prevalence of Ametropia, Amblyopia and visual impairment in schoolchildren in Ireland

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PREVALENCE OF AMETROPIA, AMBLYOPIA, AND VISUAL IMPAIRMENT IN SCHOOLCHILDREN IN IRELAND

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ABSTRACT

Background: Uncorrected refractive error is an avoidable cause of visual impairment (Naidoo *et al.,* 2016). Currently, there is a lack of adequate data on eye and vision disorders in schoolchildren in Ireland. Accurate prevalence estimates of refractive error and vision disorders are necessary to determine their impact on public health and to assess the need for interventions (McCarty and Taylor, 2000).

Purpose: This study reports the prevalence of ametropia, presenting visual impairment, amblyopia and provides population norms for ocular biometric measures in schoolchildren in Ireland. Links between refractive error and demographic and lifestyle factors were investigated. The impact of poor presenting vision, on participants' educational performance, was also examined.

Methods: The Ireland Eye Study examined 1,626 children (881 boys, 745 girls) in two age groups, 6-7 years (728) and 12-13 years (898), in the Republic of Ireland (henceforth Ireland) between June 2016 and January 2018. Participating schools were selected by stratified random sampling, representing a mix of school type (primary/post-primary), location (urban/rural) and socioeconomic status (disadvantaged/advantaged). Parents completed a questionnaire which provided information on participants' lifestyle and participants' school performance. Examination included monocular logMAR visual acuity (both presenting with spectacles if worn and through a pinhole), cycloplegic auto-refraction (Cyclopentolate Hydrochloride 1%), non-contact ocular biometry (IOLMaster), and ocular alignment (cover test).

Results: The prevalence of myopia ($\leq$-0.50 D), hyperopia ($\geq$+2.00 D), and astigmatism ($\geq$1.00 DC) in 6-7-year-olds was 3.3%, 25.0%, 19.2%, respectively, and amongst 12-13-year-old children, 19.9%, 8.9% and 15.9%, respectively. Astigmatism axes were mostly with-the-rule (80.3%). The prevalence of presenting visual impairment in the "better

eye" (≥0.3logMAR, with spectacles, if worn) was 3.7% amongst younger and 3.4% amongst older participants and associated with Traveller and non-White ethnicity. Amblyopia prevalence (pin-hole visual acuity ≥0.3logMAR plus an amblyogenic factor), was high (6-7 years 5.5%, 12-13 years 3.7%) compared to other studies. Amblyopia prevalence was primarily due to uncorrected refractive error. Compliance with spectacle wear, socioeconomic disadvantage and sedentary lifestyle were also contributing factors. Factors associated with myopia included age group, ethnicity, screen-time, time spent outdoors during daylight, obesity and sedentary lifestyle. Astigmatism was significantly associated with visual impairment and amblyopia. Time spent outdoors during daylight in summer was associated with a significantly less myopic SER and shorter axial length in White participants. Poor educational performance was associated with presenting visual impairment and amblyopia.

Conclusion: The Ireland Eye Study was the first ever population-based study to report on refractive error prevalence and visual impairment in Ireland. Myopia prevalence was similar to comparable studies of White European children. In particular, this study identified a relatively high prevalence of severe and preventable eye conditions such as amblyopia, mainly due to uncorrected refractive error, suggesting that pre-school children, in particular, should be the focus of future public eye health policy.

DECLARATION

I certify that this thesis which I now submit for examination for the award of PhD is entirely my own work and has not been taken from the work of others, save and to the extent that such work has been cited and acknowledged within the text of my work.

This thesis was prepared according to the regulations for graduate study by research of the Technological University Dublin (TU Dublin) and has not been submitted in whole or in part for another award in any other third level institution.

The work reported on in this thesis conforms to the principles and requirements of the TU Dublin's guidelines for ethics in research.

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Candidate: Síofra Harrington

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ABBREVIATIONS

AES	Aston Eye Study
AL/CR	Axial length/corneal curvature ratio
ALSPAC	Avon Longitudinal Study of Parents and Children
BPEDS	Baltimore Pediatric Eye Disease Study
BCVA	Best corrected visual acuity
BCVI	Best corrected visual impairment
BMI	Body mass index
CIs	Confidence intervals
CR	Corneal radius
DC	Dioptre cylinder
DEIS	Delivering Equality of Opportunity In Schools
DS	Dioptre sphere
HSE	Health Service Executive
IES	Ireland Eye Study
MEPEDS	The Multi-ethnic Pediatric Eye Disease Study
NICER	Northern Ireland Childhood Errors of Refraction Study
OR	Odds Ratio
PEDIG	Pediatric Eye Investigator Group
PVA	Presenting visual acuity
PVI	Presenting visual impairment
RESC	Refractive Error Studies in Children
SER	Spherical equivalent refraction
SD	Standard deviation
SMS	Sydney Myopia Study
TNO	Toegepast Natuurwetenschappelijk Onderzoek test
TU Dublin	Technological University Dublin
UK	United Kingdom
US	United States of America

VA   Visual acuity

VI   Visual impairment

VIP   Vision in pre-schoolers

WHO   World Health Organisation

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1.1 Importance of epidemiological eye care studies

The World Health Organisation (WHO) and the International Agency for the Prevention of Blindness has identified refractive error, the second leading cause of blindness after cataracts and the principal cause of global visual impairment (VI), as a Vision 2020 priority (Resnikoff *et al.,* 2008; Bourne *et al.*, 2013; Naidoo *et al.*, 2016). Furthermore, research suggests that refractive errors, along with amblyopia and strabismus, are common in children (Negrel *et al.*, 2000), with the WHO estimating that 15 million children worldwide suffer due to uncorrected refractive error (Gilbert and Foster, 2001). Schoolchildren, in particular, are vulnerable as uncorrected refractive error can impact on educational potential, with consequent implications on employment and social prospects (Smith *et al.*, 2009; Rahi and Gilbert, 2012). Prior to Vision 2020, blindness was defined using a measure of best corrected visual acuity (BCVA), overlooking those who struggled visually due to uncorrected or undercorrected refractive error (Schwab and Steinkuller, 1983; Schneider *et al.*, 2010). Currently, presenting VI (PVI) is accepted as providing a better index of visual disability, as it includes those with uncorrected refractive error (Resnikoff *et al.,* 2008). Consequently, identifying PVI prevalence in the Republic of Ireland (henceforth Ireland) is critical.

The WHO review by Resnikoff *et al.* (2008), estimated global PVI prevalence and highlighted the magnitude of this problem as a public health concern. However, this review did not address the paucity of data and the factors associated with PVI, particularly concerning children (Schneider *et al.*, 2010). For this reason, beginning in

1998, the Refractive Error Studies in Children (RESC) were designed to assess the prevalence of refractive error and VI in children of different ethnic origins and cultural settings (Negrel *et al.*, 2000). Subsequently, the Northern Ireland Childhood Errors of Refraction (NICER) study (closest comparator to the current study) (O'Donoghue *et al.*, 2010), the Aston Eye Study (AES) (Logan *et al.*, 2011), and the Sydney Myopia Study (SMS) (Ojaimi *et al.*, 2005), adopted the RESC definitions and protocols for refractive error and VI (Negrel *et al.*, 2000), in order to facilitate comparison of study findings. Although the RESC addressed the relationship between refractive error and VI, including amblyopia in many diverse locations, no previous studies have taken place in Ireland, and only very few studies with children have taken place in other European countries.

Consequently, the Ireland Eye Study (IES) fills this gap by reporting age-specific and gender-specific data of the prevalence of ametropia, amblyopia, and associated VI, in school children in Ireland. Ideally, the prevalence of ametropia, amblyopia and VI ought to be established before proceeding to therapeutic or prophylactic epidemiological research areas, as it is only through prevalence studies that the extent of these conditions can be outlined (Fledelius, 1988). In order to formulate targeted and effective policies to reduce VI, it is essential to first fully understand both the extent of the problem as well as its determinants.

1.2   Introduction

1.2.1 Study aims and objectives

The study aims: The primary aim of the IES was to understand the prevalence of ametropia, amblyopia, PVI and their relationship with ocular biometric measures in schoolchildren in Ireland. The secondary aim was to investigate the relationships between vision and demographic and lifestyle variables and assess the impact of vision

on children's educational performance. Results from this study ought to inform public policy on the resources required for paediatric eye care services, including the cost of providing spectacles and amblyopia treatment.

The study objectives: Produce a comprehensive database on the distribution of refractive error, vision, and ocular biometric measures. Report prevalence of ametropia, amblyopia and VI for schoolchildren in Ireland. Investigate the effect of age, gender, ethnicity, socioeconomic status and urban/ rural living on vision and refractive state in schoolchildren in Ireland. Explore the relationships between vision, diet and lifestyle, including the increasing use of digital technology, which was less relevant to previous studies in other countries. Assess the impact of VI on children's school academic performance.

Finally, the long-term aim is to continue the IES as a longitudinal study to examine the effect of time and environment on the dynamic relationships between the growing ocular biometric parameters and the consequent refractive error status. Understanding the magnitude of uncorrected refractive error, VI and amblyopia, and the age cohorts most in need of intervention will provide the basis from which future eye-care interventions can be evaluated.

1.3   Ireland Eye Study background

1.3.1 Refractive errors

The relationship between the eyes' ocular components, which continually grow from birth to adulthood, are regulated by a homeostatic control process called emmetropisation (Saunders, 1995; Troilo, 1992; Troilo & Wallman 1991).   Disruption to emmetropisation results in refractive error (Flitcroft, 2014). Recent epidemiological studies suggest that the prevalence of myopia is increasing (Mak *et al.*, 2006; Pan, Ramamurthy and Saw, 2012), which may be due to a failure of homeostasis (Flitcroft,

2013). Refractive errors result in an unfocused image falling on the retina which, uncorrected, reduces visual acuity (VA). Vision 2020 targeted refractive error due to its frequent occurrence and its simple and relatively inexpensive correction with spectacles. However, there is a considerable variation in the prevalence of refractive errors in differing populations (Pokharel *et al.*, 2000; Dandona *et al.*, 2002; Naidoo *et al.*, 2003; He *et al.*, 2004; O'Donoghue *et al.*, 2010). Accordingly, it is challenging to target resources in a uniform manner across geographical locations which can result in lost education and employment opportunities, lower productivity and impaired quality of life for those who fail to access the necessary eye care services (Jaggernath and Naidoo, 2012; Sewunet *et al.*, 2014).

Furthermore, discussions regarding myopia have dominated research in recent years due to the wide global variation and a dramatic increase in myopia prevalence from the late 20th century onwards (Holden *et al.*, 2016). Myopia is internationally acknowledged as one of the critical public health issues of the 21st century (Resnikoff *et al.,* 2019). This is particularly evident in East Asia, where myopia is a growing health issue with a prevalence of 80-90% among teenagers on completing school (Seet *et al.*, 2001). Rapid increases in myopia prevalence across diverse geographic locations reflects the environmental role in child myopia susceptibility (Lin *et al.*, 2004; McCullough, O'Donoghue and Saunders, 2016), and is particularly evident amongst children in areas where lifestyle and living conditions have been impacted by significant economic growth (Rudnicka *et al.*, 2016). While myopia prevalence is influenced by ethnicity (Donovan *et al.*, 2012), the environment has also been demonstrated to play a significant role in the onset and progression of the condition (Ip *et al.*, 2008a; Rose *et al.*, 2008). For example, myopia prevalence amongst Chinese children living in Singapore is significantly higher than amongst Chinese children in Australia and lower in White children living in Australia than White children in the United Kingdom (UK)

(Rose *et al.*, 2008; French *et al.,* 2012). Hence, ethnicity alone could not explain the differences in myopia prevalence between populations and environmental factors may also play a role (French *et al.,* 2012). This highlights the difficulties associated with planning budgetary requirements for paediatric eye services in Ireland based on extrapolated data from other jurisdictions. Thus, understanding the relationship between environmental, socioeconomic parameters, and refractive error status in schoolchildren in Ireland is essential when planning paediatric eye-care provision.

1.3.2 The cost burden of uncorrected refractive error

Since refractive error is easily corrected, its importance as a public health issue is often underestimated. However, health costs can be considerable (Morgan and Rose, 2005). In Australia, vision disorders cost 9.95 billion Australian dollars in 2004 of which 263.1 million was due to refractive error such as the provision of spectacles, contact lenses and refractive surgery (Taylor, Pezzullo and Keeffe, 2006). The global burden and economic cost to society in lost productivity due to uncorrected refractive error are conservatively estimated at 202,000 million US dollars annually; in addition, the estimated costs associated with addressing uncorrected refractive error are 28,000 million US dollars over five years (Fricke *et al.*, 2012). With regard to Ireland, in 2010 224,832 people were reported as visually impaired (BCVA poorer than 6/12 in the better eye) with 12,995 classified as legally blind (BCVA poorer than 6/60 in the better eye) with consequent annual direct costs of €116.75 million and annual indirect costs (lost productivity, costs of carers and inefficient allocation of resources) of €269.34 million (Deloitte Access Economics, 2011).

Moreover, the global myopia prevalence is estimated at two billion in 2010 and predicted to rise to five billion (half the projected world's population) by 2050 (Holden *et al.*, 2016), which will result in increased costs associated with the care of uncorrected

myopes. As well as the provision of refractive correction, health costs include the management cost of any associated ocular morbidity (Rose *et al.*, 2003). The public healthcare costs will also be exacerbated by the estimated increase in the prevalence of pathologic myopia (high myopia ≤-6.00DS), which is estimated at one in ten of the world's population by 2050 with associated costs of ophthalmologic care and vision impairment services (Holden *et al.*, 2016). For example, there is a strong association between myopia and a higher risk of glaucoma (Qiu *et al.*, 2013), myopic maculopathy (Wong *et al.*, 2014), retinal detachment (Saw *et al.*, 2005), earlier onset of posterior subcapsular cataract (Younan *et al.*, 2002), and an increased risk of retinal disorders (Shih *et al.*, 2004; Ojaimi, *et al.*, 2005). Hence, the public health costs associated with myopia also include the management of associated conditions. In addition, there are also the costs of social care and rehabilitation, which may be required with VI (Dandona and Dandona, 2006). The indirect costs associated with VI include premature mortality rates (McCarthy, Nanjan and Taylor, 2001), costs of carers, visual aids, housing and workplace modifications, lost earnings, lower productivity and less personal tax paid which is also relevant for families of those with VI leading to earlier retirement and also lower income (Taylor, Pezzullo and Keeffe, 2006). Also, there may be psychological costs associated with VI; for example, depression and anxiety are commonplace in visually impaired adults (Van Der Aa *et al.,* 2015). Furthermore, best-corrected VI in Swedish adolescent males was associated with higher rates of psychosis in Hayes *et al.*'s (2019) study which included data on over one million male adolescents with up to 38 years of follow-up. Hayes *et al.* (2019) postulated impairments in reading, stereo acuity and face recognition may result in abnormal social interactions and perception. Consequently, the society cost of VI is multifaceted.

Prior research generally confirms that myopia is the third leading cause of blindness worldwide (Cook *et al.*, 2008), with associated public health and social care costs.

Therefore, quantification of the risk factors associated with myopia progression and resultant biometric changes through childhood is an integral part of epidemiology studies (Rudnicka *et al.*, 2010). Identifying those at risk of developing myopia or at risk of rapid myopia progression, enables a more significant understanding of the myopia condition, ensuring preventative treatments are targeted correctly (Bappsc, 2016). The IES provides valuable data regarding the prevalence of refractive error prior to and during myopic progression in Ireland. Further longitudinal studies will conclude more fully on study findings, particularly about myopia progression and associated factors.

In addition to increasing myopia prevalence, the NICER study reported significantly higher prevalence of hyperopia and astigmatism when compared to Australia (French *et al.,* 2012). Moreover, moderate to high hyperopia was also found to be a risk factor for age-related maculopathy in the Blue Mountains population-based study (Wang, Mitchell and Smith, 1998) and also in clinical studies (Lavanya *et al.,* 2010; Li *et al.,* 2014). Thus highlighting the importance of formulating targeted and effective policies to reduce VI due to refractive error in Ireland. Accordingly, baseline data are required to ascertain if interventional strategies (school vision screening, amblyopia treatment, myopia control) have been successful (McCarty and Taylor, 2000). Once the prevalence of refractive error, amblyopia and VI are established, researchers are better placed to plan for and monitor the progress of more specific issues of epidemiological research such as therapeutic or prophylactic measures (Fledelius, 1988).

With regard to addressing uncorrected refractive error in schoolchildren, spectacles are the most frequently used and simplest and cheapest option. Contact lenses are not suitable for all patients or environments, and refractive surgery is inappropriate for children as the eye is not fully developed. A component of the IES questionnaire (see Appendix 3) addressed whether children were wearing prescribed spectacles.

Dispensing well-fitting glasses with the correct prescription; reinforcing compliance with a prescription; ensuring proper care of the spectacles and repair and replacement if required, is imperative to prevent unnecessary vision loss due to refractive error amongst children who need glasses to see clearly or maintain ocular alignment. This is important as the "See well to learn well" project in China reported inaccurate spectacle prescriptions as common and recommended annual refractions to address this issue (Zhang *et al.*, 2009). Spectacle compliance is another area of interest and concern; reported at 57% in South India, 30% in Pune and 20% in rural India (Pavithra, Hamsa and Madhukumar, 2014), and as low as 13.5% in Mexico despite being provided free of charge (Holguin *et al.*, 2006). In contrast, spectacle compliance was between 76% in 6-7-year-olds and 77% in 12-13-year-olds in the NICER study (O'Donoghue *et al.,* 2010).

1.3.3 Amblyopia

Amblyopia is a condition involving reduced VA compared to the age norm value. Amblyopia is typically uni-ocular (rarely binocular) (Wallace *et al.*, 2007), and affects 1-5% of the population contingent on the definition used and the population observed (Holmes and Clarke, 2006). Amblyopia is the leading cause of monocular VI in children (Ciuffreda, Levi and Selenow, 1991), and is usually associated with a history of strabismus (misalignment of the eyes), anisometropia (significant difference in refractive error between the two eyes) or form deprivation (cataract, corneal scar, lid ptosis) (Ciuffreda, Levi and Selenow, 1991). Visual impairment due to amblyopia persists through life if untreated (Kulp *et al.*, 2014). What is more, individuals with amblyopia have a doubled risk of bilateral VI in later life (van Leeuwen *et al.*, 2007). Moreover, amblyopic adults are more at risk of bilateral blindness due to trauma in their fellow eye, compared to the general population (Tommila and Tarkkanen, 1981; Rahi *et al.*, 2002). Therefore, it is essential to treat amblyopia in early childhood to decrease the

likelihood of visual disability in later life resulting from a loss of vision in the non-amblyopic eye (Wallace *et al.*, 2018).

Since most of the consequential cost associated with amblyopia in children will be incurred later in their lives, there is, unfortunately, a tendency to underestimate the importance of treating amblyopia (Kulp *et al.,* 2014). Furthermore, some clinicians feel amblyopia should not be treated contending reported improvements in vision, post-treatment, are possibly due to visual maturation and learning effects and not amblyopia treatment (Lempert, 2006).

The importance of early detection: Amblyopia does not self-rectify (Holmes, 2011). For this reason, failure to treat amblyopia during the sensitive period of visual development (Hubel, Wiesel and LeVay, 1976), due to inadequate screening and delayed treatment, results in life long VI (Webber and Wood, 2005). Consequently, addressing vision disorders in children is crucial to prevent them impacting on children's education, social and physical development (Rahi, Cumberland and Peckham, 2006; Wilson and Welch, 2013; Birch *et al.*, 2018). Specifically, treating amblyopia in childhood is essential to prevent potential visual disability in later life (Wallace *et al.*, 2018). In other words, detecting vision problems early, when children are more responsive to treatment, is crucial (Koo, Gilbert and VanderVeen, 2017).

Vision 2020's target for the prevention of blindness in children states that all children should have an eye examination and spectacles should be provided to all who have a significant refractive error (Gilbert and Foster, 2001). Ideally, this examination should be integrated into the school health programme in order to optimise the 'capture' of children.

1.3.4 Academic attainment and visual impairment

Haupt and Humer (2008) purport that up to 80% of content children learn in school is absorbed visually as 80% of perception, learning and cognition are mediated by vision. Similarly, Ernst and Bu (2004) proposed the amount of information each of our senses processes in the brain at the same time is as follows: sight 83%, hearing 11%, smell 3.5%, touch 1.5% and taste 1.0%. Furthermore, Ernst (2008) reported children less than eight years old do not optimally integrate information from two modalities. Consequently, uncorrected refractive error, untreated amblyopia and the consequent VI may influence children's educational attainment (Sylva, 1997; Ehri, 2005; Scheiman and Rouse, 2006; Khalaj *et al.*, 2011), resulting in reduced educational opportunities, and impacting employment options (Rahi and Gilbert, 2012). For these reasons, the relationship between vision, and participants' educational performance was also examined in the IES.

1.3.5 Paediatric eye care services in Ireland

In Ireland, children have their eyes checked during developmental checks: at birth (paediatrician), six-week postnatal check (paediatrician or general practitioner) and at 18-24 months (public health nurse and community health doctors) (Health Service Executive, 2005). Also, children attending primary school are entitled to free eye examinations, if referred by their general practitioner or public health nurse, and any subsequent treatment free of charge in public hospitals' outpatient departments or with community-based ophthalmologists (Primary Care Reimbursement Services, 2017). Screening for reduced vision, conducted by a public health school nurse, is offered to children attending non-fee-paying state-funded schools within two years of starting primary school (5-6 years of age) (Hearing and vision tests for children, 2017). Children with VA worse than 0.2logMAR (6/9.5) in one or both eyes or with strabismus are referred into the public health system via the local health clinic in accordance with

Best Health for Children Revisited guidelines (Health Service Executive, 2005). However, vision screening coverage is reported at 80% in Ireland, which is considerably lower than the UK where it was reported at more than 95% (Sloot *et al.,* 2015). Paediatric eye care provision in Ireland is based on a hospital ophthalmology centric structure with little community-based services and very little involvement of optometrists.

In contrast, in the UK, all children ≤16 years, or up until 19 years if still in fulltime education, are entitled to a free eye examination and spectacles with a high street optometrist. On the contrary, children in Ireland are not entitled to either a free eye examination or free glasses with an optometrist. Moreover, per capita ratios of optometrists are almost 35% lower in Ireland (1.5 per 10,000) than in the UK (2.3 per 10,000) (Optometry in the European Union, 2019). The number of qualifying optometrists per 10,000 of the population is over 70% lower in Ireland (0.05 per 10,000) than in the UK (0.17 per 10,000). Furthermore, per capita ratios of ophthalmologists are lower (Ireland 0.38 per 10,000 and UK 0.46 per 10,000), and orthoptists (UK 0.23 per 10,000, Ireland 0.14 per 10,000) are lower in Ireland than the UK (*Irish Association of Orthoptists - About us*, 2017; Resnikoff *et al.*, 2019).

In Ireland, the HSE website advises parents with concerns regarding their child's vision to visit their general practitioner or public health nurse who will refer their child to a consultant ophthalmologist if necessary (www.hse.ie/eng/health/az/h/hearing-and-vision-tests-for-children/). Hence, paediatric ophthalmology eye-care services in Ireland are overloaded (Murphy, 2017). Indeed, the HSE Primary Care Eye Services Review Group (2014-2017) reported inadequate existing capacity, with 26.77 whole-time-equivalent HSE community ophthalmic physicians and 10.89 whole-time-equivalent HSE orthoptists (Power *et al.*, 2017) for the entire country. Also, insufficient levels of

training and a lack of standardised referral protocol amongst those involved in HSE school-vision screening were highlighted by this report (Power *et al.*, 2017). For example, the Primary Care Eye Services Review Group Report highlighted a concerning variation (6.5% to 28.5%) in referral rates post vision screening at school entry in Ireland and demonstrated inconsistent or inefficient practice or inadequate training in vision screening in some areas in Ireland (Murphy *et al.,* 2017). Specifically highlighted were the inadequately resourced clinics; for instance, many community ophthalmic physicians work in isolation without supporting optometrists or orthoptists. Hence, the skill utilisation is inefficient with the broader medical resource poorly utilised; also noted were the limited roles for optometrists within the publicly provided services (Power *et al*., 2017). Of further concern was the limited paediatric eye-care information and community technology system due to the absence of integrated electronic health records (Power *et al.,* 2017). Under the current contractual arrangements with the HSE, children in Ireland are not entitled to a free eye examination with an optometrist. Furthermore, children attending post-primary school have no entitlement to free eye-care, and for children of medical card holders in this age-cohort, services are variable depending on location (Power *et al.,* 2017). A private eye examination with an optometrist can cost up to €50 in Ireland, and the cost of spectacles is an additional burden. To date, optometrists have not been employed by the HSE and public eye-care services are provided by doctors, nurses and orthoptists.

However, the Children's University Hospital, Temple Street, recently employed two full-time optometrists, for their paediatric eye department. (Hospital Optometrist Job Advert Temple Street Children's Hospital. July 2017. http://www.cuh.ie/job/hr251-senior-optometrist/ (accessed 5 Aug 2017)). In addition, in December 2014, the HSE Primary Eye Care Services Review Group recommended more community-based primary eye-care provision in Ireland (Murphy, 2017). The Irish government committed

to a mere €1 million budget allocation to implement the recommendations of this group. One of the main priorities of this action plan was to address the current paediatric eye-care services issue. However, deadlines have not been published, and resources are inadequate. The consequence is delayed access to eye-care services for children in Ireland. Delayed access to paediatric ophthalmology services in Ireland is a longstanding problem. Figures for the 25th April 2019 showed that 42,669 people (7,626 children) were on waiting lists for outpatient ophthalmology appointments in Ireland, of which 12,107 (2,397 children) were waiting for over 18 months. On the 1st January 2019 Temple Street Children's University Hospital, Our Lady's Children's Hospital in Crumlin and the National Children's Hospital in Tallaght were amalgamated together as Children's Health Ireland; as of the 25th April 2019 there were 4,182 children waiting for outpatients hospital appointments in one of the three Children's Health Ireland hospitals, 1,702 of which have been waiting over 18 months (National Treatment Purchase Fund: Outpatient Speciality by Hospital for ophthalmology appointments., 2019). There were a further 716 children waiting to be seen in the Royal Victoria Eye and Ear Hospital, 149 of which are waiting for more than 18 months. Protracted delays in accessing follow-up appointments, post failed vision screening, mean many children in Ireland are not seen in time to effect the treatments necessary to treat amblyopia (Holmes *et al.,* 2011; Fronius *et al.,* 2014) resulting in life-long preventable VI (Chua and Mitchell, 2004), thereby impacting the quality of life (Carlton and Kaltenthaler, 2011). Furthermore, life expectancy is now 78 years for men and 83 years for women in Ireland (Central Statistics Office, 2016), hence, as people are living longer lives, the duration of time with impaired eyesight is also longer. The consequential increased cost to the public health system further goes to emphasise the importance of addressing eye care conditions in early life.

In this context, the HSE National Service Plan (2015) involved the setting up of community integrated eye-care teams which are "responsive to the needs of communities". The plan involved setting up nine community health organisations, each with ten primary care networks, which would each support a population of 50,000. Publication of the Primary Eye-Care Services Review Group Report confirmed that teams in each Primary eye-care clinic would consist of an orthoptist and an ophthalmologist (Murphy, 2017), and optometrists would be employed on a per session basis. In any event, the initiation date for this plan is as yet unknown. Perhaps the most immediate impact optometry in Ireland can deliver through primary care pathway reform is for primary paediatric eye-care, without a need for additional training or significant overhaul of existing systems. Alternatively, by providing child optical benefit for children through optometrists, ophthalmologists and orthoptists working together in local primary eye-care clinics, this could be the stimulus to eliminate the current paediatric ophthalmic waiting list.

1.4   Conclusion

To conclude, this study took place at a critical time of change to the Irish primary eye-care system, particularly concerning paediatric eye-care. The prevalence data from this study provides valuable information on the magnitude of uncorrected refractive error, population groups and age cohorts most in need of intervention, and, also provides the basis from which interventions such as the provision of spectacles can be evaluated. The results ought to inform the public health budgetary requirements for paediatric eye-care in Ireland as well as briefing potential future public health and social care costs associated with ocular morbidity due to ocular conditions related to refractive error.

The IES involved 1,626 participants in 38 schools in Ireland (primary and secondary, urban and rural, socioeconomically disadvantaged and advantaged), randomly selected

from a list provided by the Irish Department of Education and Skills. These data provide robust information surrounding the extent and magnitude of childhood refractive error and associated risk factors in Ireland. Considerable advances in technology have been made since the data in the NICER study was published ten years ago, such as the increased use of technology, which has changed the classroom learning environment. There is a need to examine whether this changing learning environment has changed children's vision. The current study findings provide the prevalence estimates necessary to inform public health care policy on the resources required to address refractive error, amblyopia, and VI in Ireland. Chapter two examines and provides a synopsis of significant refractive error, and VI, in schoolchildren prevalence studies.

2 EPIDEMIOLOGICAL REFRACTIVE ERROR AND VISUAL IMPAIRMENT STUDY REVIEW

This chapter examines and outlines previous epidemiological studies of refractive error and VI involving children.

2.1 Introduction

The WHO estimated that 12.8 million children worldwide are visually impaired due to uncorrected refractive error (Resnikoff *et al.,* 2008). Population-based studies in Europe (Villarreal *et al.*, 2000; Kleinstein *et al.*, 2003; O'Donoghue *et al.*, 2010), South Asia (Pokharel *et al.*, 2000; Dandona *et al.*, 2002; Murthy *et al.*, 2002), East Asia (Zhao *et al.*, 2000; Goh *et al.*, 2005; Fan *et al.*, 2011), South-East Asia (Goh *et al.*, 2005; Casson *et al.*, 2007; Hashim *et al.*, 2008; Yingyong, 2010), Latin America (Maul *et al.*, 2000) and Africa (Naidoo *et al.*, 2003) support this. Prior to the RESC, comparisons between population-based studies were difficult due to different definitions used to describe VI and blindness. Specifically, the WHO defines blindness as VA < 20/400 (6/120) (Dandona and Dandona, 2006). Conversely, the definition of legal blindness in America, Australia and many other countries is VA poorer than or equal to 1.0logMAR (6/60) (Dandona and Dandona, 2006). The WHO defines VI (low vision) as VA worse than or equal to 0.5logMAR (~6/18), compared to a VA < 0.3logMAR (6/12) recognised in many countries (Dandona and Dandona, 2006). In addition, definitions for myopia, high myopia, hyperopia, astigmatism and anisometropia have not been standardised, which further impedes comparisons between studies.

In 1998, the RESC studies involved children of diverse ethnicity and locations and were carried out in China (Zhao *et al.* 2000), Nepal (Pokharel *et al*. 2000), Chile (Maul *et al.* 2000), India (Murthy *et al.* 2002), South Africa (Naidoo *et al.,* 2003) and Malaysia

(Goh *et al.*, 2005). Due to the commonality of methods, for the first time, a comparison of findings between these studies was possible (Negrel *et al.,* 2000). The UK based NICER study adopted the RESC definitions for refractive error and VI and equivalent methodology, therefore to facilitate comparison with these studies, the IES adopted standardised methodology and protocols similar to NICER as it was the closest comparator with a genetically similar population.

2.2 Epidemiological study methodology

Table 2.1 summarises the definitions of refractive error used in a selection of previous studies involving children.

Table 2.1 Definitions of refractive error in previous studies involving children

Study	Myopia (SER) D	Hyperopia (SER) D	Astigmatism (CYL) DC
Northern Ireland Childhood Errors of Refraction study	≤-0.50	≥+2.00	≥1.00
Aston Eye Study	≤-0.50	≥+2.00	
Refractive error studies in Children	≤-0.50	≥+2.00	≥0.75
Sydney Myopia Study	≤-0.50	≥+0.50 ≥+2.00	≥1.00
The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study	≤-0.75	≥+1.25	≥1.00
The Avon Longitudinal Study of Parents and Children study	≤-0.75 High ≤-6.00	≥+1.00	≥1.00
Multi-Ethnic Pediatric Eye Disease Study	≤-1.00	≥+2.00	≥1.50 ≥3.00
Sydney Myopia Study	≤-0.50	≥+2.00	≥1.00
Head Start Program	<-2.00	>+3.25	>1.50

Dioptre (D); cylinder (CYL); spherical equivalent refraction (SER); dioptre cylinder (DC).

The following sections outline the methodology in a number of paediatric refractive error epidemiology studies:

2.2.1 The Northern Ireland Childhood Errors of Refraction Study

The NICER study (2010) was a population-based cross-sectional study which examined 661 12-13-year-old children and 392 6-7-year-old children in Northern Ireland (UK) (O'Donoghue *et al.,* 2010). The examination involved: monocular logarithm of the minimum angle of resolution (logMAR) distance presenting VA (unaided and with spectacles if worn); cycloplegic autorefraction (Cyclopentolate Hydrochloride 1%) binocular open-field autorefraction, ocular biometry (Zeiss IOLMaster), and parental-participant questionnaire. Participants were classified as myopic if either eye was myopic and hyperopic if either eye was hyperopic and had not been classified as myopic. Myopia was defined as spherical equivalent refraction (SER) ≤-0.50 D; hyperopia SER≥+2.00 D; and astigmatism as ≥1.00 dioptre cylinder (DC) (O'Donoghue *et al.*, 2011). When examining the relationship between vision and refractive error, data from the right eye were used (O'Donoghue *et al.* 2010).

2.2.2 The Aston Eye Study

The AES (2010) was a population-based cross-sectional study (sister study to the NICER study) in Birmingham (UK), which examined 655 participants from South Asian (6-7 years 213, 12-13 years 114), Black (6-7 years 44, 12-13 years 40) and White (6-7 years 70, 12-13 years 115) ethnic backgrounds (Logan *et al.,* 2011). The examination involved: monocular logMAR distance presenting VA (unaided and with spectacles if worn) and cycloplegic autorefraction (Cyclopentolate Hydrochloride 1%) using binocular open-field autorefraction, ocular biometry (Zeiss IOLMaster). In line

with the NICER study, participants were classified as myopic if either eye was myopic and hyperopic if either eye was hyperopic and had not been classified as myopic. Myopia was defined as SER≤-0.50 D and hyperopia SER≥+2.00 D.

2.2.3 Generation R study

The Generation R study took place in Rotterdam the Netherlands and involved 6,690 6-year-olds, 31% of which were non-European (Surinamese, Moroccan) and the remainder European (Tideman *et al.,* 2017). The examination involved: monocular VA assessment with Lea logMAR chart at three metres; participants with VA poorer than 1.0logMAR in either eye had cycloplegic (two drops of Cyclopentolate Hydrochloride 1%) autorefraction (Topcon autorefractor KR8900 (Topcon, Tokyo, Japan)). Myopia was defined as SER≤-0.50 D. The prevalence of hyperopia and astigmatism were not reported during phase one but may be reported at phase two when participants are 9-years-old and universal cycloplegic autorefraction formed part of the study protocol for all participants (personal communication Dr W. Tideman on May 28th 2019).

2.2.4 The Refractive Errors Study in Children

The RESC (1998) was a population-based cross-sectional study which initially took place in China, Nepal and Chile. Participants (5-15-years-old) were obtained through random cluster sampling (Negrel *et al.*, 2000). The examination protocol included: presenting, best corrected and unaided VA measurements; standardised acuity measurements using a retro-illuminated logMAR chart with five tumbling "E" optotype or letters on each line; ocular motility and alignment; cycloplegic (Cyclopentolate Hydrochloride 1%) retinoscopy and auto-refraction using a hand-held Nikon Retinomax K-Plus (Nikon Corporation, Tokyo, Japan); external eye/anterior segment examination; participative refraction (uncorrected acuity ≤0.625logMAR); media/fundus examination and cause of impairment designation. Myopia was defined as SER≤-0.50 D. Hyperopia:

SER≥+2.00 D. Participants were deemed to be myopic if one or both eyes were myopic and hyperopic if one or both eyes were hyperopic, as long as neither eye was myopic and participants were considered emmetropic if neither eye was hyperopic nor myopic. Astigmatism was assessed at two levels: ≥0.75 DC and ≤2.00 DC, and ≥2.00 DC. Refractive error was reported as the cause of VI if VA improved to 20/32 (6/7.5, 0.20logMAR) or better with correction (Negrel *et al.*, 2000).

2.2.5 The Sydney Myopia Study

The SMS (2005) was a population-based study involving two age cohorts (6-years-old and 12-years-old) which formed part of the Sydney Childhood Eye Study in Sydney Australia. Participants were 1,740 6-7-year-olds and 2,353 12-13-year-olds and predominately white (60%) and also East Asian (15%), South Asian (5.5%), Middle Eastern (7.1%), mixed (7.6%) and other (4.8%). Examinations included a detailed assessment of monocular logMAR VA (presenting with spectacles if worn, best corrected and unaided), cover testing for strabismus, identification of amblyopia, slit-lamp examination, non-contact ocular biometry and cycloplegia (Cyclopentolate Hydrochloride 1%), followed by auto-refraction, optical coherence tomography, retinal thickness measurement and dilated fundus photography (Ojaimi *et al.*, 2005).

2.2.6 The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study

The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study (Kleinstein *et al.*, 2003), was a multi-centre (US states: Alabama, California, and Texas) population-based longitudinal study of refractive error in children aged 5-17 years drawn from four different ethnic groups: African American; Asian; Hispanic and White. Myopia was defined as SER≤-0.75 D; Hyperopia as SER≥+1.25 D and astigmatism as ≥1.00 DC difference between two principal meridians. For comparisons with other

studies, readings were also taken for myopia $\leq$-0.50 D; hyperopia $\geq$+1.00 D and astigmatism $\geq$1.25 DC difference between two principal meridians. The examination protocol included: auto-keratometry; video-phakometry and cycloplegic (Cyclopentolate Hydrochloride 1% plus Tropicamide 1%) autorefraction - Canon R-1(Canon United States of America, Lake Success New York). Measurements were taken for the right eye only, and the left eye was occluded during autorefraction.

2.2.7 The Strabismus Amblyopia and Refractive Error Study

The Strabismus Amblyopia and Refractive Error Study in Singaporean children (Dirani *et al.*, 2010) was a population-based study in Singapore; door to door recruitment and random sampling was employed. The study involved 3,009 participants aged 6-72 months. Study protocol included: parental questionnaire; logMAR VA (children aged 30-72 months, non-illuminated ETDRS chart with Sloan letters; cycloplegic autorefraction (Auto RK-F1 Canon for children aged 24-72 months and the Retinomax K-plus 2 Nikon for children aged 12-24 months, streak retinoscopy was used for the rest); ocular biometry; ocular motility; stereo-acuity (Randot preschool stereo-acuity test); fixation preference; cover test and fundus photography. Myopia was defined as SER$\leq$-0.50 D; hyperopia as SER$\geq$+3.00 D; astigmatism $\geq$1.50 DC; anisometropia $\geq$2.00 D. High myopia was defined as SER$\leq$-6.00 D. For comparison with other studies, myopia was further defined as SER$\leq$-0.75 D, SER$\leq$-1.00 D and SER$\leq$-5.00 D.

2.2.8 The Multi-Ethnic Pediatric Eye Disease Study

The Multi-Ethnic Pediatric Eye Disease Study (MEPEDS) (2009) was a population-based cross-sectional study of children aged 6-72 months. The objective was to assess the prevalence of strabismus, amblyopia and refractive error in four ethnic groups: African American; Asian, Hispanic and non-Hispanic White in Los Angeles County, California. In 2010, MEPEDS reported on the results from the African-American (2,994

participants) and Hispanic (3,030 participants) cohort (Tarczy-Hornoch *et al.,* 2009). The study protocol included: an interview which comprised of an assessment of health status, ocular risk factors, and demographic factors; cycloplegic (Cyclopentolate Hydrochloride 1%) autorefraction using the Retinomax autorefractor; fixation preference testing; VA (Electronic VA system using the HTOV test); Randot stereo-acuity testing; height; weight; biometry (IOLMaster on participants aged 30 months or over); focimetry; keratometry; cover test; posterior and anterior segment examination and colour vision testing using Colour Vision Testing Made Easy (Varma *et al.*, 2006). Myopia was defined as SER≤-1.00 D; hyperopia SER≥+2.00 D; emmetropia SER>-1.00 D and SER<+1.00 D. Astigmatism was defined as ≥1.50 DC in the worst eye (Wen *et al.,* 2013). Wen *et al.* (2013) reported on non-Hispanic White (1,501) and Asian (1,507). Tarczy-Hornoch *et al.* (2009) reported on the African-American and Hispanic cohorts.

2.2.9 The Vision in Pre-schoolers Study

The Vision in Pre-schoolers (VIP) (2014) was a multi-centre cross-sectional study involving 4,040 pre-schoolers aged 3-5-years-old in one of the five US VIP Study clinical centres (Berkeley, California; Boston, Massachusetts; Columbus, Ohio; Philadelphia, Pennsylvania; Tahlequah, Oklahoma). The VIP study investigated the prevalence of refractive error and vision disorders in African-American; American Indian; Asian; Hispanic and non-Hispanic White children. All participants who failed the Head Start screening programme and a sample (circa 20%) of those who passed the screening were enrolled in this study which may result in an overestimation in the prevalence of refractive error and VI reported when compared to randomly selected population-based studies. The eye examination included: monocular VA using electronic VA system using HOTV optotype; presenting VA when spectacles were worn; cover test; cycloplegic (Cyclopentolate Hydrochloride 1% and Tropicamide 1 %)

retinoscopy; anterior segment and fundus assessment. Myopia was defined as SER: <-2.00 D; hyperopia SER: >+3.25 D; astigmatism>1.50 DC between principal meridians; anisometropia: SER>1.00 D inter-ocular difference in hyperopia; SER>3.00 D inter-ocular difference in myopia; >1.50 DC inter-ocular difference in astigmatism; antimetropia difference SER>1.00 D and one eye SER>1.00 D hyperopia and antimetropia difference >3.00 D and one eye >2.00 D myopia (Ying *et al.*, 2014).

2.2.10   The Head Start study

The Head Start study involved 507 pre-school children aged 3-5 years in San-Diego, California in the US. Seventy-four per cent of the participants were Latino from low-income families. The examination included: uncorrected monocular logMAR VA using B-VAT PC version 2.3 software (Medtronic Solan, Jacksonville, Florida) and cycloplegic retinoscopy (Cyclopentolate Hydrochloride 1.3%, plus Tropicamide 0.167% and Phenylephrine 1.6%). Refractive error definitions: myopia 3-4-year-olds SER≤-2.00 D; myopia 4-year-olds SER≤-1.00 D; hyperopia 3-4-year-olds SER≥+4.00 D; hyperopia 4-year-olds SER≥+3.00 D; astigmatism 3-4-year-olds ≥1.75 DC and astigmatism 4-year-olds ≥1.5 DC; anisometropia all ≥1.25 D inter-ocular difference in SER (Brody *et al.*, 2007).

2.3   Presenting visual impairment in previous epidemiological studies

The association between PVI and refractive error was well established in the RESC, NICER and SMS studies (He *et al.,* 2004; Robaei *et al.,* 2006a; O'Donoghue *et al.,* 2010). The level of PVI in the 'better eye' reported varied from 1.5% in Australia (Robaei *et al.*, 2005a) to 10.3% detected in China (He *et al.,* 2004). The NICER study found a PVI prevalence of 1.5% (O'Donoghue *et al*., 2010).

The RESC studies standardised VA measurements using presenting, uncorrected and BCVA and defined PVI as VA ≤ 20/40 (6/12) (Negrel *et al.*, 2000). The NICER study reported PVI of 3.6% in 12-13-year-olds and 1.5% in 6-7-year-old participants (Donoghue *et al.,* 2010). Interestingly, the RESC studies found PVI prevalence to vary from the lowest value of 1.2% in South Africa (Naidoo *et al.,* 2003) to a highest of 19.4% in Vietnam (Paudel *et al.*, 2014). Of further interest in the RESC studies was that of those with PVI, the proportion whose vision improved with the pinhole to ≥ 20/32 (6/9.5) varied from a minimum of 0.9% in South Africa (Naidoo *et al.,* 2003) to more than 9.0% or more in China (Zhao *et al.* 2000; He *et al.* 2004). Table 2.2 presents findings for PVI, BCVI and correctable VI in the RESC.

Table 2.2 Prevalence of presenting, best-corrected and correctable visual impairment in Refractive Error Studies in Children involving participants aged 5-15 years

Region	Presenting visual impairment	Best corrected visual impairment	Correctable visual impairment
China (Zhao *et al.*, 2000)	10.9%	0.8%	10.1%
Nepal (Pokharel *et al.*, 2000)	2.8%	1.4%	1.4%
Chile (Maul *et al.*, 2000)	7.3%	3.3%	4%
New Delhi (Murthy *et al.,* 2002)	4.9%	0.81%	4.1%
South Africa (Naidoo *et al.*, 2003)	1.2%	0.32%	0.88%
Iran (Hashemi *et al.*, 2015)	3.6%	0.7%	2.9%
Malaysia (Goh *et al.,* 2005)	10.1%	1.4%	8.7%
India (Dandona *et al.*, 1999)	2.6%	0.78%	1.8%
China (He *et al.*, 2004)	10.3%	0.62%	9.7%
Lao (Casson *et al.*, 2012)	1.9%	0.4%	1.5%
Vietnam (Paudel *et al.*, 2014)	19.4%	7.2%	12.2%

Presenting visual impairment (measured with spectacles if worn); best corrected visual impairment (following subjective refraction/pin hole acuity); correctable visual impairment (proportion uncorrected, presenting visual impairment –best corrected visual impairment).

Other studies used different definitions for PVI, which poses a challenge when comparing study findings. For instance, Robaei *et al.* (2006) reported a prevalence of 1.5% PVI in the 1,723 six-year-old Australian children they examined (Robaei *et al.* 2006) using a higher threshold for PVI of vision poorer than 20/40. In any event, the prevalence of PVI (<20/40, 6/12) amongst the 2,353 children aged 12 years was 5%

(Robaei *et al.,* 2006b) and in 82% of this group with PVI, the vision could be improved by ≥ 2 lines with refraction alone (Robaei *et al.,* 2006b).

Higher levels of PVI were reported elsewhere using the RESC definition for VI ≤20/40 (6/12) for both eyes. For instance, He *et al.* (2004) found the prevalence of PVI to be 16.6% amongst 2,454 Chinese 13-17-year-olds of which 98% improved to ≥20/32 in the better eye with refractive correction, and consequently, the reported correctable VI was 16%.

2.4 Factors associated with presenting visual impairment

In Australia, PVI was more common in girls than boys and more common in those of East Asian or South Asian ethnicity and significantly associated with parent education (Robaei *et al.,* 2005a). In New Delhi, Murthy *et al.*'s (2002) RESC study found the educational attainment of fathers was a determining factor as to whether children had spectacles with socioeconomic disadvantage associated with PVI (Murthy *et al.,* 2002). Likewise, in Cairo, a higher frequency of PVI was found in those from lower socioeconomic status (El Bayoumy, Saad and Choudhury, 2007). Thus, highlighting the financial barriers to accessing affordable eye-care that may exist in Cairo and New Delhi. He *et al.*'s (2005) study of Chinese children aged 5-15 years found that: parental awareness of vision problems was associated with older children's PVI and spectacle purchase was associated with only severe levels of PVI. Likewise, Zhang *et al.* (2009) reported undercorrection and less frequent eye checks to be associated with PVI in Chinese school children. Hence, the impact of under-correction of refractive errors is a concern, particularly about myopia, as two studies have demonstrated a trend whereby under-correction can lead to increasing rather than inhibiting myopia progression (Chung, Mohidin and O'Leary, 2002; Adler and Millodot, 2006).

In summary, PVI has been associated with socioeconomic disadvantage in many studies (see the Schneider *et al.* (2010) review). In addition, parental education, less frequent review and inaccurately corrected refractive error further exacerbate the issue of PVI in schoolchildren internationally (Zhang *et al.,* 2009; He *et al.,* 2005).

2.5 Presenting visual impairment and academic attainment.

To what extent PVI influences children's education is not precisely known as few studies have examined the relationship between visual problems and educational achievement. Studies which have addressed the relationship between vision and education include the Born in Bradford study, which involved 2,025 4-5-year-olds, and reported decreased VA at school entry was associated with reduced literacy (Bruce *et al.*, 2016). Also, Fulk and Goss's (2001) study of 272 children aged 4-15-years-old found a significant correlation between uncorrected refractive error and academic performance as reported by the teachers, those with uncorrected hyperopia performing less well. Ayed *et al.*'s (2002) study involving 708 Tunisian schoolchildren, in a socially disadvantaged area, found that uncorrected refractive error was significantly associated with academic failure. However, how this academic failure was assessed in the context of healthcare screening campaigns was unclear. The relationship between hyperopia and academic performance found in previous studies is noteworthy; Kulp *et al.* (2016), Williams (2005) and Rosner and Rosner (1997) reported poorer educational attainment in hyperopic children. While in Iran, astigmatism was significantly associated with reduced educational achievement (Akrami *et al.*, 2012). In contrast, Saw *et al.* (2007) found myopes performed above average academically with the odds ratio (OR) for myopia 2.5 times for those within the upper quartile academically.

Research conducted in Iran, involving children aged 9-15 years, found amblyopia was associated with reduced quality of life and educational attainment (Khalaj *et al.*, 2011).

Moreover, recent studies identified a link between vision and amblyopia and academic attainment (Birch *et al.,* 2018; Wood *et al.,* 2018), which may impact career options and possible earning ability. Therefore the IES examined the relationship between vision and academic performance in schoolchildren in Ireland.

2.6   Possible reasons for presenting visual impairment

Social barriers: Financial barriers have been found to be an issue with many studies reporting a higher prevalence of PVI in lower socioeconomic areas (Dandona and Dandona, 2001). Furthermore, financial barriers have been cited as the primary reason for non-attendance to eye care services or the failure to purchase spectacles (Schneider *et al.*, 2010).

Service barriers: accessibility, particularly in developing countries (Resnikoff, 2008). Accessibility of eye-care services is also an issue in Ireland where waiting lists for eye examinations were acknowledged as longer than two years and even longer in some areas as many waiting lists closed at the two-year mark (Murphy *et al.,* 2017). Refer to section 1.3.5 for more detail on waiting lists for eye-care appointments in Ireland.

Individual barriers: concerns that spectacles will make vision worse (He *et al.,* 2004); parents attitudes towards VI (He *et al.,* 2004) and concerns over appearance (Khandekar, Mohammed and Al Raisi, 2002). A recent Irish study reported that parents viewed childhood myopia as a cosmetic disadvantage, a potential expense and an optical inconvenience and they were less concerned about the health risks associated with myopia (McCrann *et al.*, 2018). In Saudi Arabia, children reported they did not

wear their spectacles due to parental disapproval, spectacle discomfort, visual appearance and peer pressure (Aldebasi, 2013). A recent study in India involving 8,442 13-17-year-olds, found spectacle compliance was four times better amongst their positive intervention group (a series of interventions to improve spectacle wear compliance) when compared to the control group (Narayanan and Ramani, 2018).

Societal factors which may influence access to eye care include family responsibilities, parents' inability to leave work to attend eye care appointments with their child, and a lack of awareness of the importance of vision checks within the community (Schneider *et al.*, 2010).

Consequently, addressing VI is a priority, as the cost of treating and correcting VI due to uncorrected refractive error is a fraction of the global loss of productivity associated with that vision impairment (Fricke *et al.*, 2012). In addition to the lifelong psychological costs of VI (Chia *et al.,* 2004; Hayes *et al.,* 2019).

2.7   Prevalence of refractive error in children

The prevalence of refractive error varies widely with both age (O'Donoghue *et al.,* 2010), ethnicity (Logan *et al.,* 2011) and location (French *et al.,* 2012). The RESC examination protocol, standardised definitions and methodology, facilitates comparison between the RESC studies (Negrel *et al.,* 2000) conducted in China (Zhao *et al.*, 2000), Chile (Maul *et al.*, 2000), and Nepal (Pokharel *et al.*, 2000). Before the RESC protocols, the variety of definitions for myopia, hyperopia, astigmatism and anisometropia impeded inter-study comparisons. Furthermore, different methodologies (autorefraction, focimetry, retinoscopy, subjective refraction, use of cycloplegic) and diverse sampling methods (population-based studies or selected groups such as those reviewed from clinic settings), can influence findings (Shah *et al.*, 2009). Some limitations remain; for at least the last three decades the terms used to define ethnic groups has changed,

previously used terms Caucasian, Mongoloid and Negroid referred to race categorisation based on skull measurements and now social scientists have replaced these terms with White, Asian and Black respectively (Ford and Harawa, 2010). Furthermore, there is a lack of consistency with regard to how ethnicity/race is reported with subdivisions, for example, amongst Whites (European White or Non-Hispanic White). For the purposes of this literary review the ethnic terms and definitions quoted in this thesis are those used by the authors of the quoted studies.

The IES adopted definitions of refractive error to facilitate comparison with the NICER study (O'Donoghue *et al.,* 2010), the AES (Logan *et al.,* 2011), the SMS (Ojaimi *et al.,* 2005), and the RESC (Negrel *et al.,* 2000). Table 2.3 presents summary findings for the prevalence of refractive error and VI prevalence in other comparable international studies where cycloplegic autorefraction post instillation of Cyclopentolate Hydrochloride 1% was reported. Chapter 3 discusses myopia prevalence and its aetiology, as reported in previous studies in other countries.

Table 2.3 Prevalence of refractive error and visual impairment in international studies where cycloplegic autorefraction post instillation of Cyclopentolate Hydrochloride 1% was reported

Study	Location	Age	N	Myopia*	Hyperopia†	Astigmatism‡	PVI §
		years		%	%	*%*	%
NICER (2006-08)	NI	6-7	392	2.8	26.0	24.0	1.5
		12-13	661	17.7	14.7	20.0	3.6
AES (2011)	UK White	6-7	70	5.7	22.9	+	+
		12-13	115	18.6	10.4	+	+
	Asian	6-7	213	10.8	10.3	+	+
		12-13	114	36.8	2.6	+	+
	Black	6-7	44	11.4	9.1	+	+
		12-13	40	27.5	0.0	+	+
Poland (2007)	Poland	6-7	825	4.1	27.5	+	+
		12-13	729	12.5	8.2	+	+
SMS (2005-06)	Australia	6	1,740	1.6	13.2	7.6	1.5¶
		12	2,353	12.8	5.0	9.4	3.7
RESC (2004)	China	5	271	5.7	17.0	+	+
		15	376	78.4	0.5	+	+
		5-15	4,364	38.1	+	26.3 (≥0.75)	10.3
RESC (2003)	South Africa	7	469	2.5	2.8	+	+
		13	420	3.4	2.9	+	+
		5-15	4,890	4.0		14.6 (**≥0.75**)	1.2
Dobson (2006)	US††	5-16	963	+	+	42 (≥1.5)	+

*Number of participants (N); Northern Ireland (NI); United Kingdom (UK); United States of America (US); Presenting visual impairment (PVI); * (≤-0.5); † (≥2.00); ‡(≥1DC); §('better eye' ≥0.3logMAR); + indicates information not available; ¶ visual impairment >0.3logMAR; †† Tohono O'odhan reservation*

3 MYOPIA PREVALENCE IN CHILDREN

3.1 Introduction

Discussions regarding myopia development and progression have dominated research in recent years due to the dramatic increase in myopia prevalence in the late 20th century (Holden *et al.,* 2016). Not only myopia in East Asia (Seet *et al.*, 2001; Lin *et al.*, 2004), but also in White populations such as the UK where myopia prevalence doubled over the last 50 years (McCullough *et al.,* 2016). With half the world's population projected to be myopic by 2050 (five billion) (Holden *et al.*, 2016), and the prevalence of high myopia ($\leq$-6.00 D) also increasing (Rose, French and Morgan, 2016), research addressing risk factors associated with myopia progression is crucial (Logan *et al.,* 2018). Many reviews and studies suggest myopia has a multifactorial aetiology (Flitcroft, 2012; Rose, French and Morgan, 2016). Asian ethnicity has been associated with high myopia prevalence (Saw, 2006; Ip *et al.*, 2007), as data collected from the Singapore Armed Forces revealed a significant increase in the prevalence and severity of myopia over the last two decades (Seet *et al.,* 2001). Notably, in military conscripts, the prevalence of myopia was 26% in the late 1970s increasing to 43% in the 1980s, 66% in the mid-1990s, 83% by the late 1990s and as high as 96.5% of the South Korean male military conscripts aged 19 years in 2010 (Chew, Chia and Lee, 1988; Seet *et al.*, 2001; Wu *et al.*, 2001; Jung *et al.*, 2012).

By way of contrast, myopia prevalence in Chinese children living in Sydney (French *et al.*, 2013a) was considerably less than myopia prevalence of Chinese children living in Singapore (Dirani *et al.*, 2010). Consequently, the rapid rise in myopia prevalence has led some researchers to suggest that environmental factors may play an important role (Morgan and Rose, 2005). For example, educational pressures and time spent outdoors have been proposed by Rose *et al.* (2008) and supported by Guggenheim *et al.* (2012),

who both found that less time spent both outdoors and in outdoor physical activities impacted the progression of myopia, with time spent outdoors having a more significant effect. Indeed, time outdoors greater than 2.5 hours per day during daylight has been reported to delay the onset of myopia (Sankaridurg and Holden, 2014), but results regarding the effect of daylight exposure on myopia progression are equivocal (Dharani *et al.*, 2012; Jones-Jordan *et al.*, 2012; Li *et al.*, 2015). Jones-Jordan *et al.* (2012) suggest that time outdoors during daylight does not slow myopia progression in already myopic children. Nevertheless, whether increasing myopia prevalence is to do with less daylight exposure or due to activities pursued indoors is still a matter for speculation (Ngo *et al.*, 2013).

Likewise, urban living conditions, primarily those living compressed and congested living conditions in higher population densities and smaller homes are statistically more likely to be myopic by age six years (Choi *et al.*, 2017; Tideman *et al.,* 2019).

Traditionally myopia has been associated with near work (Saw *et al.,* 2002; Morgan and Rose, 2005), inasmuch as myopia onset and progression mainly occur during the school years. On this subject, all schoolchildren in Ireland now have daily access to screen-based technologies in schools. The "Digital strategy for Schools" in Ireland, which is jointly funded by the Department of Communication, Energy, and Natural Resources and the Department of Education and Skills, supports and recognises the increasingly important role the internet, cloud computing and technology play in school life and education (Cullen, 2009; Digital Strategy for Schools, 2015). Hence, the impact of these new and developing technologies have on the growing eye is as yet an open question.

The IES examined the relationship between myopia prevalence and age, gender, ethnicity, urban/rural living, family history of myopia, obesity, diet, afterschool physical

activities, daylight exposure, and time spent engaged in reading/writing/screen-based technologies.

3.2   Biological basis and definition of myopia

Refractive status is determined by the balance of optical power of the cornea and the lens, with the axial length (AL) of the eye (the component parts of which are the anterior chamber depth (ACD), lens thickness and vitreous chamber depth). Emmetropisation involves the proportional enlargement of a child's eye, whereby the power of the dioptric system reduces in proportion to increasing axial elongation (Brown, Koretz and Bron, 1999). Over the age of six years children's eyes become less hyperopic due to eyes growing axially and thinning of the crystalline lens (Flitcroft, 2013). Failure of the emmetropisation process results in a refractive error. For example, excessive axial eye growth relative to the combined optical power of the lens and cornea results in myopia (Ojaimi *et al.*, 2005; Morgan, Ohno-Matsui and Saw, 2012). Longitudinal studies have reported a consistent increase in AL with progressing myopia (Lee *et al.,* 2019; Tideman *et al.,* 2018). Moreover, Sergienko and Shargorogska (2012) demonstrated a biomechanical weakness of the scleral shell in myopic eyes, which can result in elongation of the posterior vitreous chamber; in contrast, hyperopic and emmetropic eyes possess a relatively stiff sclera. In addition, failure of the crystalline lens to adapt to AL elongation resulted in myopia development in children (Mutti *et al.,* 2012), as reported by the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study. Mutti *et al.* (2012) reported participants became myopic when the lens stopped adapting in response to eye growth, which started one year in advance of the onset of myopia. Moreover, longitudinal changes in the crystalline lens thickness, with a pattern of lens thinning associated with myopia onset and progression were reported by Wong *et al.*'s (2010) Singapore Cohort Study of the Risk Factors for

Myopia longitudinal research, and Li *et al.*'s (2016) Anyang Eye Study. Wong *et al.* (2010) found emmetropic 10-year-olds had thinner crystalline lens than hyperopic children with myopic children having the thinnest lens. In contrast, the Correction of Myopia Evaluation Trial longitudinal study (Gwiazda *et al.,* 2016), reported no significant difference in the pattern of change in lens thickness with age, with the course of myopia progression, however, Gwiazda *et al.* (2016) involved only myopic participants, hence study findings could not be compared with emmetropic and hyperopic children. Li *et al.* (2016) found myopia associated with thinner lens, longer AL and deeper ACD but not CR. Likewise, Wong *et al.,* (2010) found myopia progression associated lens thinning, AL elongation, and vitreous chamber depth elongation, with no significant difference in growth patterns for CR between emmetropes, hyperopes and myopes.

The International Myopia Institute proposed standardised definitions for myopia (SER≤-0.50 D) and high myopia (SER≤-6.00 D) which apply when accommodation is relaxed in a single eye (Flitcroft *et al.,* 2019). The IES explored the relationship between refractive error and ocular biometric measures in schoolchildren in Ireland.

3.3   Animal models in myopia research

Since the mid-1970 there has been a focus on researching the mechanisms underlying refractive error and myopia in particular. Several animal models were developed to disentangle the relative roles of heredity and environment on refractive error development (Norton, 1999). Animal models have broadened our understanding of active emmetropisation, in other words how visual feedback influences ocular growth (Schaeffel and Feldkaemper, 2015). Several species have been examined such as chicks (Wallman *et al.,* 1978), tree shrews (Shermann *et al.,* 1977) and monkeys (Wiesel and Raviola, 1977). Research involving chicks demonstrated that the growing chick eye can

compensate for lens induced defocus (independent of image size), by altering AL growth (Schaeffel, Glasser and Howland, 1988; Schmid, Strang and Wildsoet, 1999); deprivation myopia can be restricted to certain retinal areas (Wallmann et al., 1987), and that chicks choroids thicken or thin in order to move the retina closer to the focal plane, thereby speeding recovery of deprivation myopia (Wallmann *et al.,* 1995).

Likewise, research which involved tree shrews established deprivation myopia could be induced in restricted retinal areas (Norton, Essinger and McBrien, 1994). Moreover, bright light exposure was found to offset the effects of both lens induced and deprivation myopia (Norton 1991; Ward and Norton, 2012) in tree shrews. In addition, alterations in protein expression in tree shrew sclera, which resulted in increased scleral viscoelasticity leading to faster axial elongation as a consequence of lens induced myopia, was reported (Frost and Norton, 2012). Unlike chicks and tree shrews, marmosets have a fovea and hence better visual acuity (Troilo 1993). In agreement with the above studies involving tree shrews and chicks, changes in choroidal thickness in response to retinal defocus were also observed in marmosets (Troilo, Nickla and Wildsoet, 2000). What is more, recent studies involving marmosets addressed the role of peripheral refractive error and accommodation in emmetropisation and found lens induced peripheral hyperopic defocus was associated with axial myopia and induced peripheral myopic defocus was associated with axial hyperopia (Benavente-Pérez, Nour and Troilo, 2014).

The rhesus monkey most closely resembles humans; rhesus monkeys have a fovea, excellent acuity and large amplitudes of accommodation. Luvone *et al.* (1991) reported that local administration of a dopamine receptor antagonist retarded axial elongation in rhesus monkeys with experimentally induced form deprivation myopia. Subsequent studies involving rhesus monkeys with form deprivation myopia, demonstrated the

fovea was not needed for emmetropisation as foveal ablation had no impact on emmetropisation (Smith *et al.,* 2007). Smith, Hung and Huang (2009) showed that emmetropisation in the rhesus monkey was largely controlled by the peripheral retina; their research involved fitting diffusers, which facilitated foveal vision and restricted peripheral vision, which resulted in form deprivation myopia. Smith *et al.* (2009) postulated that emmetropisation is by and large guided by the peripheral retina with accommodation guided by the fovea. The effect of bright light on myopia development in rhesus monkeys established lens induced myopia was not affected by bright light (Smith *et al.,* 2013). However, in agreement with studies involving chicks and tree shrews, experimentally induced deprivation myopia was inhibited by bright light exposure in rhesus monkeys (Smith *et al.,* 2012).

Research on mice (Barathi, Weon and Beuerman, 2009) and guinea pigs (Le *et al.,* 2005) demonstrated that topical administration of muscarinic antagonists can prevent axial elongation and experimentally induced form deprivation myopia.

In summary, research involving animal models has broadened our knowledge of the emmetropisation process and the part the visual environment plays on the development of refractive error, however, whether this research translates into humans is an area of intense research an as yet an open question.

3.3.1 High myopia and its association with pathological changes

High myopia is associated with axial elongation of the posterior chamber (Strang, Winn and Bradley, 1998) which, when excessive, can result in biomechanical stretching and thinning of the sclera and choroid giving rise to ocular complications such as posterior staphyloma, myopic maculopathy and optic neuropathy (Verkicharla, Ohno-Matsui and Saw, 2015). Axial elongation is also associated with changes and enlargement of the optic disc, peripapillary atrophy and ''myopia-associated glaucoma-like optic

neuropathy'' (Flitcroft *et al.*, 2019). Furthermore, myopic macular degeneration, which is a sight-threatening condition, is associated with high myopia and comprised of macular atrophy, lacquer cracks, macular Bruch's membrane defects, choroidal neovascularisation and Fuchs spot (Fang *et al.*, 2018). Also, myopia is associated with myopic traction maculopathy (Cheung *et al.*, 2017) and an increased risk of glaucoma (Chen *et al.*, 2012). Pathological myopia is reported to result in severe VI in 7.0% of Europeans and between 12.0% and 27.0% in Asian populations (Verkicharla, Ohno-Matsui and Saw, 2015). The recently published International Myopia Institute White paper authored by Flitcroft *et al.* (2019) suggested a set of terms and definitions to be adopted within the myopia research community which cover optics, aetiology, diagnostic thresholds, progression and the structural complications of myopia. These definitions have been adopted in the IES.

3.4   Epidemiological studies of myopia in children

There are many studies on the prevalence of myopia (refer to Table 3.1). However, standardised definitions for myopia are essential when comparing study findings. For example, myopia prevalence values, found by the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study, increased from 9.2% to 10.5% by altering the definition of myopia from ≤-0.75 D to ≤-0.50 D for comparison with other studies (Kleinstein *et al.*, 2003). Similarly, when NICER data employed a similar definition to the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study (≤-0.75 D), the myopia prevalence fell to 12% from 17.7% in the children aged 12-13 years (O'Donoghue *et al.*, 2011). Table 3.1 provides an overview of some of the literature pertaining to myopia prevalence in schoolchildren studies.

Table 3.1 Myopia prevalence in schoolchildren studies

Study/Authors	Location	Ethnicity	N	Age years	Myopia* (%)
NICER (2010)	NI	White	392	6-7	2.8
			661	12-13	17.7
AES (2011)	The UK	White, South Asian, Black	70, 213, 44	6-7	5.7, 10.8, 11.4
				12-13	18.6, 36.8, 27.5
		White, South Asian, Black	115, 114, 40		
Generation R study (2017)	Rotterdam	European, non-European (31%)	5,711	6	2.4
Sydney Myopia Study Robaei *et al.* (2005, 2006)	Australia	Predominately White	1738	6	1.6
			2353	12	12.8
RESC 2000 Maul *et al.* (2000)	Chile		5303	5-15	5.8
				5	3.5
				15	12.5
RESC 2000 Zhao *et al.* (2000)	China rural	Asian	5884	5-15	21.6
				5	1.2
				15	38.8
RESC 2004 He *et al.* (2004)	China Urban	Asian	4364	5-15	38.1
				5	5.7
				15	78.4
RESC 2002 Murthy *et al.* (2002)	India urban	Indian	6447	5-15	7.4
				5	4.8
				15	10.8
RESC 2002 Dandona *et al.* (2002)	India rural	Indian	4074	7-15	5.6
				7	2.8
RESC Goh *et al.* (2005)	Malaysia	Malay	4634	7-15	20.7
				7	10.0
				15	32.5

Study/Authors	Location	Ethnicity	N	Age years	Myopia* (%)
RESC model 2013 Paudel *et al.* (2014)	Vietnam	Asian	2238	12-15	20.4
RESC model 2012 Casson *et al.* (2012)	Lao	Predominately Tai	2899	6-11	0.8%
RESC model 2012 Rezvan *et al.* (2012)	Iran	Persian	1551	6-17	4.3
Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error 2003† Kleinstein *et al.* (2003)	USA	AA Asian Hispanic	534 491 463	5-17	6.6 18.5 13.2
RESC model Naidoo *et al.* (2003)	South Africa	AA	4890	5-15 5 15	4.0 3.2 9.6
RESC model Ovenseri-Ogbomo & Omuemu (2010)	Ghana	AA	961	5-19 5-7 17-19	6.9 0.9 12.5

∗ Myopia definition spherical equivalent ≤-0.50D; Number of participants (N); Northern Ireland Childhood Errors of Refraction (NICER); Aston Eye Study (AES); Refractive Errors Studies in Children (RESC); † myopia spherical equivalent≤-0.75D; United Kingdom (UK), Northern Ireland (NI), African American (AA).

Regarding the RESC, the study carried out in Chile was described as urban with a socioeconomic status described as "upper-middle" (Maul *et al.*, 2000), and the authors described the Chinese and Nepalese samples as rural. Notably, the increasing rise in the prevalence of myopia in RESC Chinese studies was alarming (Zhao *et al.*, 2000). The

prevalence of myopia amongst the five-year-olds was negligible, within both the male and female cohorts. However, of the 15-year-old cohort, myopia prevalence increased dramatically to 36.7% in males and 55.0% in females (Zhao *et al.*, 2000). Urban schooling was significantly associated with increased levels of myopia in the RESC Chinese studies; the risk of myopia was doubled in urban areas compared to the combined results from rural and semi-urban (Zhao *et al.*, 2000; He *et al.*, 2004).

By comparison, Maul *et al.* (2000) reported no significant difference between the results found in the male and female cohorts in Chile, but found a gradual shift towards less hyperopic/more myopic refractive errors in the older children (myopia $\leq$-0.50 D was found in 3.5% of five-year-olds and 12.5% of 15-year-olds). The RESC study carried out in Nepal by Pokharel *et al.* (2000) found results differing greatly from those in China and Chile. Myopia prevalence of 1.2% (between 1% and 2%) was reported for 5-15-year-old Chilean participants (Pokharel *et al.*, 2000). In South Africa, Naidoo *et al.* (2003) also found a relatively low myopia prevalence, ranging from 3.4% in five-year-olds to 6.3% in 14-year-olds and 9.6% of 15-year-olds.

The RESC examination protocol and methodology were also adopted in Vietnam where participants ranged in age from 12-15 years (Paudel *et al.*, 2014); VI, due to myopia, was higher in females (22.4%) than males (18%).

3.5   Ethnicity

Ethnic differences in myopia prevalence have been reported in many studies (Kleinstein *et al.,* 2003; Rudnicka *et al.,* 2010; Logan e*t al.,* 2010). However, inter-study comparisons are challenging due to the variety of ways in which ethnicity is defined (socio-cultural differences or racial differences) (Ford *et al.,* 2010; Blanton, 2015). Also, many studies involve biracial participants (Ojaimi *et al.,* 2005; Tideman *et al.,*

2015), hence, the relationship between myopia and ethnicity is less clear cut, refer to section 2.7 where the ethnicity and study methodology is addressed.

Studies which involved predominately White paediatric populations include the NICER study (O'Donoghue *et al.*, 2010), and the SMS study (Ojaimi *et al.*, 2005). The NICER study reported low levels of myopia in 6-7-year-olds (2.8%) increasing in 12-13-year-olds (17.7%) (O'Donoghue *et al.*, 2011). By contrast, the SMS reported significantly lower levels of myopia (1.4% in 6-year-olds and 12.8% in 12-13-year-olds) in their White participants (Robaei *et al*., 2005b; 2006d); environmental factors such as daylight exposure were suggested as possible reasons for the differential in myopia prevalence between these two samples of White schoolchildren (French *et al.,* 2012). Similarly, the Generation R study in Rotterdam found a higher myopia prevalence in non-European 6-year-olds compared to European Dutch 6-year-old participants odds ratio (OR) 2.6 (95% CI: 1.8 to 3.7) (Tideman *et al.,* 2017). The Orinda Longitudinal Study of Myopia in the USA which involved mainly White participants aged 13-years-old reported a prevalence of myopia (SER≤-0.75 D) of 20% in participant's right eyes (Kleinstein *et al.*, 2003).

Of the RESC, the highest levels of myopia reported were in the urban Chinese population (5 years 5.7%, 15 years 78.4%) (He *et al.,* 2004) and the lowest were in Nepal (0.3%) and South Africa (3.0%) (Naidoo *et al.,* 2003; Pokharel *et al.,* 2000), where there was little change in myopia prevalence with increasing age (refer Table 3.1 which provides an overview of some of the literature pertaining to myopia prevalence in schoolchildren studies).

 The highest myopia prevalence in schoolchildren aged 6-7 years was in East Asians living in Singapore (12.3%), even higher than in East Asian 6-7-year-olds living in China (9.1%) (Zhang *et al.*, 2000). Also, Rudnicka *et al.*'s (2016) review of childhood

myopia, revealed a higher incidence of myopia in South Asians living in South Asia when compared to migrant South Asian communities. Moreover, South Asian children living in Australia, Singapore or England, were almost five times more likely to be myopic as South Asian children living in Nepal or India (Rudnicka *et al.*, 2016).

Gao *et al.* (2012) examined Cambodian children of a similar age to those observed in the RESC model study in Vietnam (Paudel *et al.*, 2014); both involved participants aged 12-14 years in urban and rural settings. The RESC examination protocol and definitions for myopia were adopted and myopia ($\leq$-0.50 D) was associated with: female gender (6.5% in females and 5% of males); urban schooling (2.2% rural and 12.3% in urban) and age (5.5% at 12 years and 6% at 14 years) (Gao *et al.*, 2012) in Cambodia. The corresponding figures in Vietnamese participants were 22.4% in females and 18.0% in males; 26.6% in urban participants and 16.3% in rural participants; 19.2% in 12 year-olds and 22.8% in 14-year-olds (Paudel *et al.,* 2014). Hence, despite equivalent study protocols, methodology and genetic profiles in both study cohorts, the prevalence of myopia found in Vietnam was significantly higher. Geographically these locations are close; Vietnamese ethnicity is 85% Kink ethnic group, which is close to the Chinese and Oriental populations, and Cambodian population is 92% Khmer which is thought to be of Southern Indian descent. Gao *et al.* (2012) speculated that this difference could be due to increased close work in Vietnam when compared to Cambodia. Thus, a comparison of children of Chinese ethnicity of the same age in different locations demonstrates a wide variety of prevalence results emphasising the role environment may play in myopia prevalence and progression. An additional example of the variation in myopia prevalence was demonstrated in the Singapore Cohort Study On the Risk factors for Myopia where 70% of participants were myopic (13.7 years was the mean age of study participants) (Dirani *et al.*, 2010). In contrast, myopia prevalence was lower, at 21.1% in participants, with a mean age of 10.4 years (Pi *et al.*, 2012) in rural

China. Furthermore, in Laos, which is part of the East Asian genetic cluster, myopia prevalence was 0.8% in 6-11 year-olds (6 years 0%, 11 years 1.6%) (Casson *et al.*, 2012). Australian children aged 6-7 years, of Chinese ethnicity, have a considerably lower prevalence of myopia (3.3%) when compared to Chinese children, aged 6-7 years, living in Singapore (29.1%); time outdoors appeared to be the dominant contributing factor (Rose *et al.*, 2008). Subsequent research demonstrated that Asian children might be habitually spending less time outdoors than White children (Read *et al.*, 2018).

Inasmuch as myopia and high myopia prevalence seen in African Americans was similar to European Americans, environmental factors, as opposed to ethnicity, may play a more significant role in the prevalence of refractive error (Vitale *et al.*, 2008). However, ethnic differences in myopia prevalence also exist in population studies drawn from the same living environment (Ip *et al.*, 2007; Rudnicka *et al.*, 2010; Wong and Saw, 2016). In contrast, Logan *et al.*'s (2005) study involving White and South Asian students in the UK engaged in the same educational system found no significant difference in ametropia. Hence the relationship between myopia and ethnicity is variable and appears to be multifaceted and influenced by the environment.

Regarding schoolchildren in Ireland, according to the Ireland Census 2016, 9.9% of children aged 5-15 years were non-White. What is more, this report stated that the average age of the White Irish community was significantly higher than the Black Irish, Black African, and Chinese communities which are significantly steadily increasing in number since 2006 when the Ireland Census first included a question addressing ethnicity (Pavee Point, 2016). For this reason, the IES examined the link between myopia and White, Traveller and non-White ethnicities in schoolchildren in Ireland.

3.6   Age and myopia

Globally, there are significant differences in myopia prevalence reported, which become more exaggerated with age (Rudnicka *et al.*, 2016). For example, research suggests myopia most commonly develops during the early to middle childhood years (Morgan, Ohno-Matsui and Saw, 2012; Zadnik *et al.*, 2015), progresses during childhood before stabilising in late adolescent years (Sankaridurg and Holden, 2014). An exception to this was the RESC study in South Africa (82% black, 9% South Asian, 6% White) where a relatively low and stable myopia prevalence was found with age (7 years 2.5%, 13 years 3.4%) (Naidoo *et al.*, 2003). Some ethnic groups showed a rapid increase in myopia prevalence for the younger age groups which tended to level off: East Asian, White, and South Asian (Zhang *et al.*, 2000; O'Donoghue *et al.*, 2010; Rudnicka *et al.*, 2016). Other studies revealed a progression in myopia which was approaching linear: South East Asian, American Indian, Alaska, Hawaii and South Korea (Crawford and Hamman, 1949; Alward *et al.*, 1985; Harvey, Dobson and Miller, 2006; Hashim *et al.*, 2008; Jung *et al.*, 2012).

While the RESC examined children aged 5-15 years, MEPEDS and Baltimore Pediatric Eye Disease Study (BPEDS) investigated the prevalence of refractive error and vision disorders in younger children aged 6-72 months (Tarczy-Hornoch *et al.,* 2009; Borchert *et al.*, 2011; Wen *et al.*, 2013). These studies found that the mean refractive error for all age groups and ethnicities was hyperopic, thus highlighting that myopia is not a problem associated with pre-school in particular (Tarczy-Hornoch *et al.,* 2009; Wen *et al.*, 2013). However, compared to non-Hispanic White participants in the combined MEPED and BPEDs populations, African-American (OR 6.0) and Hispanic (OR 3.2) participants were more likely to be myopic (Borchert *et al.,* 2011). Overall, the prevalence of myopia found in the MEPEDS and BPEDS studies was lower than that found in the Strabismus Amblyopia and Refractive Error Study in Singaporean children

who used equivalent study protocols and methodology (Dirani *et al.*, 2010). Interestingly, myopia (≤-0.50 D) in 5-year-old Asian participants in the MEPEDS was 6.6%, which was similar to that found in urban Chinese 5-year-olds (5.7%) in the RESC (Zhao *et al.*, 2000; Wen *et al.*, 2013). This similarity was repeated in the MEPEDS Hispanic 5-year-olds in (myopia 3-4%), which was similar to that reported for 5-year-old Chilean participants (3.4%) in the RESC (Maul *et al.*, 2000; Tarczy-Hornoch *et al.,* 2009). In contrast, MEPEDS found a significantly higher prevalence of myopia 7.8% in black five-year-olds compared to 3.0% found in South Africa 5-year-olds RESC (Naidoo *et al.*, 2003; Tarczy-Hornoch *et al.,* 2009).

In previous studies, early onset myopia appears to be associated with non-White ethnicity with higher prevalence in Asian (Logan *et al.*, 2011) and African American children (Rudnicka *et al.*, 2010).

Prior research generally confirms that early onset of myopia is a significant factor for high myopia in adulthood (Gwiazda *et al.*, 2007). Myopia progressing by more than one dioptre per year has been shown to take longer to reach stability, resulting in pathological myopia (Wong and Saw, 2016). For this reason, the IES examined the prevalence of myopia, in schoolchildren in two age-groups ages 6-7 years and 12-13 years. Recruiting these age groups enabled an analysis of myopia in schoolchildren in Ireland both prior to and during the onset and progression of myopia as evidenced in the NICER (McCullough *et al.,* 2016). Furthermore, as the NICER study, the AES, SMS and RESC reported myopia prevalence in these age-groups direct comparisons with IES data were possible.

3.7   Outdoor activities and their influence on myopia

Daylight exposure has significantly shaped queries on myopia over the last two decades. Prior research substantiates the theory that increasing time spent outdoors influences

myopia development and progression; see Xiong *et al.*'s (2017a) review of the relationships between daylight exposure and myopia development and progression. Deng and Pang's (2019) meta-analyses, which involved five clinical trials, reported a pooled reduced relative risk of myopic shift and slower axial elongation in the intervention groups (more hours outdoors activities) when compared to the controls. In addition, the SMS and Singapore Cohort study On the Risk factors for Myopia reported a lower prevalence of myopia in children who embarked in more outdoor activities (Saw *et al.*, 2002; Rose *et al.*, 2008).

Daylight appears to slow axial elongation in non-myopic teenage eyes; however, not in pre-existing myopes (Li *et al.*, 2015). Xiong *et al.*'s (2017a) review further examined the relationship between time outdoors and myopia and concluded that while time spent outdoors appeared to delay the onset of myopia, evidence of any relationship between daylight exposure and a slowing of AL elongation and myopia progression was lacking.

Whether this is entirely due to the flat dioptric topography of the visual field outdoors, which appears to be a strong signal to slow eye-growth, or due to increased light levels outdoors, almost 100 times brighter than indoors (Ashby, Ohlendorf and Schaeffel, 2009), is not fully understood (Ngo *et al.*, 2013). As an illustration, the three-dimensional structure of the environment outdoors is sufficiently distant; this renders it flatter to the visual system when considering the world in dioptric terms (the reciprocal of the distance of objects from the eye in metres). In comparison, the environment indoors results in scenes which have highly heterogeneous dioptric topography. Therefore the eyes experience a considerable degree of hyperopic defocus (Flitcroft, 2012).

Sherwin *et al.*'s (2012) review and meta-analysis proffered a 2% reduction in the incidence of myopia for every additional hour spent outdoors per week. Increased depth

of focus plus low accommodative demand associated with time spent outdoors have been proposed as possible biological mechanisms associated with this reduction of myopia (Rose *et al.*, 2008b; French *et al.,* 2012). Likewise, Prepas (2008) contended the increase in myopia prevalence and severity seen over the last 125 years might be due to ultraviolet-free light (200-400nm), as Wollensak and Iomdina (2008) demonstrated that ultraviolet A hardens collagen and in rabbits blocks scleral remodelling. Moreover, low 25(OH) D serum levels vitamin D has been associated with increased AL and myopia progression in 2,666 Dutch children (aged 6-years-old) independent of exposure to daylight (Tideman *et al.*, 2016).

Guo *et al.* (2013) found myopia to be associated with less time outdoors and hypothesised that the association between less time spent outdoors and the progression of myopia might be independent of ethnicity. Studies dealing with other ethnic groups in Jordan and Turkey also reported finding an association between outdoor activity and myopia (Khader *et al.*, 2006; Onal *et al.*, 2007).

A longitudinal study in Taiwan involving 572 children aged 7-11 years further explored the relationship between time outdoors and myopia (Wu *et al.*, 2013). The study included 333 children who spent an additional 6.5 hours outdoors per week compared to a control group (238 children). Results following 12 months of this programme showed a considerable reduction in the onset of new myopia in the interventional programme group (8.41% vs. 17.65%) and significantly lower myopic shift in the interventional programme group compared to the control group (-0.25 D/year vs. -0.38 D/year) (Wu *et al.,* 2013).

In the Avon Longitudinal Study of Parents and Children (ALSPAC), (non-cycloplegic autorefraction of children aged 7-15-years-old) found that time spent outdoors, independent of sporting activities, had a preventative effect on myopia progression as

children who spent less time outdoors were 40% more likely to develop myopia (Guggenheim *et al.*, 2012). However, as cycloplegic agents ought to be used in any epidemiological studies involving children under the age of 18 years (Holden *et al.*, 2016), Guggenheim *et al.'s* (2012) results should be viewed with caution.

Furthermore, in animal studies which examined the effect of ambient light levels on lens-induced and form-deprivation myopia (Ashby, Ohlendorf and Schaeffel, 2009; Ashby and Schaeffel, 2010; Smith, Hung and Huang, 2012), ambient light levels as high as 18000 to 28000 lux were found to retard form-deprivation myopia in monkeys (Smith, Hung and Huang, 2012), but only slow down the progression of lens-induced myopia and so did not appear to alter the endpoint refraction (Ashby and Schaeffel, 2010).

Higher light levels and intensity have been shown to alter myopia progression, which is, most likely, related to dopamine levels; dopamine is a neurotransmitter involved in controlling eye growth through vision (Feldkaemper and Schaeffel, 2013). It has been postulated that as dopamine is released in a light-dependent fashion and plays a distinct diurnal rhythm, which may link it to diurnal growth changes in progressing myopia (Feldkaemper and Schaeffel, 2013). Hence, if retinal dopamine release drops, myopia develops (Hosoya, Baccus and Meister, 2005).

Birth during summer months was found to be associated with myopia in an Israeli study, possibly due to exposure to natural light during the perinatal period (Mandel *et al.*, 2008). A study of Korean males found myopia to be associated with spring birth (Lee, Lee and Kim, 2018). In contrast, a retrospective study in the UK based on subjects attending optometric practices found myopia to be associated with summer and autumn births when compared to winter (McMahon *et al.*, 2009).

Cultural patterns can play a part in the number of hours children spend outdoors which may further affect the prevalence of myopia, varying in different ethnic communities; this is an area that requires further analysis (Khader *et al.*, 2006; Read *et al.*, 2018).

In summary, the protective effects of outdoor activities against myopia progression in children could be due to: the greater light levels; or the structure of the visual environment - large amounts of peripheral defocus, associated with vision indoors, is minimised considerably by pupil miosis when outdoors in very bright light (Ngo *et al.*, 2013). However, future random control trials should include a more objective definition of time spent outdoors to include biomarkers of outdoor exposure such as Vitamin D or conjunctival auto-fluorescence (Sherwin *et al.*, 2012; Kearney *et al.*, 2016) or wearable devices (Ulaganthan *et al.,* 2018; Read *et al.,* 2018).

The IES examined relationships between the amount of time spent outdoors during daylight hours with refractive error prevalence both in summer and wintertime, as faster myopia progression has been reported in winter months when compared to summer (Donovan *et al.*, 2012; Gwiazda *et al.*, 2014).

3.8   Peripheral refractive error

In children, and non-human primates, peripheral refractions are variable and peripheral acuity is relatively poor (Tabernero *et al.*, 2011). As foveal vision is dominant in humans it was presumed that visual signals from the fovea guides emmetropisation (Feldkaemper and Schaeffel, 2013), however, the fovea covers only a tiny portion of the visual field and recent evidence suggests the peripheral retina plays a more significant role in refractive error development than previously understood (Radhakrishnan *et al.*, 2013; Benavente-Pérez, Nour and Troilo, 2014). By way of explanation, there are retinal cells that detect the sign of retinal defocus, and it is likely that the eye detects defocus in more than one way (Smith, Hung and Huang, 2009; Benavente-Pérez, Nour

and Troilo, 2014). Furthermore, the peripheral retina is important in regulating eye-growth, in that visual signals in the periphery seem to have a stronger influence in eye-growth (Smith *et al.*, 2005), and dominate eye-growth regulation (Smith, Hung and Huang, 2009). Thus, it appears that the eye uses defocus to determine whether it is myopic or hyperopic, via spatial tuning of the retinal neurons which determine the signal for eye growth; in other words, the eye accordingly alters its growth to achieve the optimal refractive error (Smith, Hung and Arumugam, 2014).

However, while dopamine levels represent a measure of the blur, they do not measure the sign of defocus, i.e. the blur sensor. Accordingly, there is strong evidence to suggest dopamine D2/4 receptors are involved in the spatial tuning of the retinal receptors, which in turn determines the signals for growth. Previous research determined that dopamine receptors can be influenced by environmental factors, which can modify gene expression via epigenetic mechanisms (Kaminski *et al.*, 2018). Accordingly, myopic defocus may be the stronger signal for eye-growth (Schaeffel and Feldkaemper, 2015). Notwithstanding the fact that the myopic eye appears to be more myopic centrally and less myopic peripherally (Atchison, Pritchard and Schmid, 2006); subjects demonstrating relative peripheral hyperopia are more likely to develop central myopia than those demonstrating relative peripheral myopia (Smith, Hung and Huang, 2009; Chen *et al.*, 2010).

Consequently, peripheral hyperopia (image defocus on the peripheral retina with image focus behind the retina) may provide a stimulus for axial elongation (Smith *et al.*, 2005). Also, retinal electrical responses sensitive to hyperopic and myopic defocus are more vigorous in the paracentral retina than in the central retina (Ho *et al.*, 2012). However, much of the research addressing peripheral refractive error involved animals (see section 3.3). More recent research involving humans such as Chen *et al.*'s (2010)

study which examined the relative peripheral refractive errors in Chinese adults and children concluded that for adults and children with moderate myopia (≤-3.00 D ≥-6.00 D) the relative peripheral refractive errors profile had a hyperopic shift. However, as this was a cross-sectional study it was not possible to ascertain whether the peripheral hyperopia provided a stimulus for axial elongation or merely resulted from increased axial growth (Chen *et al.*, 2010). For example, Strang, Cagnolati and Gray's (2012) four-year longitudinal study reported relative peripheral refraction as correlated rather than causative of myopic development.

In summary, it is thought that eye growth is regulated by a closed feedback loop mechanism which employs retinal defocus as an error signal which induces structural changes in the sclera and choroid (Wallman and Winawer, 2004; Flitcroft, 2013). Peripheral refractive errors provide a signal that triggers myopia progression. Our daily environment is not dioptrically uniform; stronger blurring (peripheral defocus) occurs when fixing on near objects (Flitcroft, 2012; García *et al.*, 2018). Thus, subjects engaging in large amounts of near work in congested living conditions are more prone to myopia.

3.9 The choroid and myopia progression

Recent studies proposed the choroid plays a part in myopia progression; the choroid appears to change its thickness in response to optical defocus such that the retina moves closer to the defocused optical plane (Read, Collins, and Sander 2010; Read *et al.,* 2018). While changes in the thickness of the choroid are not enough to significantly alter AL, it appears changes in choroidal thickness act as a biomarker for a stimulus for myopic progression (Read *et al.,* 2019). Furthermore, increased time outdoors during daylight was associated with choroidal thickening (Read, 2016).

3.10 Urban versus rural populations

Studies addressing children of the same ethnicity in both urban and rural populations have found an increase in myopia prevalence in urban populations (Zhang *et al.*, 2010; Paudel *et al.*, 2014; Hashemi *et al.*, 2015). This difference in the odds of myopia prevalence is more significant in South-Asians and may be due to the greater differential in living conditions compared to high-income countries (Rudnicka *et al.*, 2016). Choi *et al.*'s (2017) study of 1,075 children average age 9.95 years in Hong Kong, found an increased AL and myopic refractive error to be associated with increased population density and smaller home size. The authors concluded that crowded living conditions, or constricted living space, may be a risk factor for myopia development and progression (Choi *et al.*, 2017).

Populations who migrate from rural to urban settings appear to adopt the prevalence of the host population; Pacific Islanders who migrated to Taiwan are one example of this (Lin *et al.*, 1988; Yekta *et al.*, 2010). The prevalence of myopia in South Asian children living in the UK is significantly higher than South Asian children living in rural environments in India (Dandona *et al.*, 2002). A study of Indian children aged 7-15 years, from both urban and rural environments, in Hyderabad, reported a higher prevalence of myopia ($\leq$-0.50 D), in the urban (51.4%) than the rural group (16.7%) with myopia prevalence associated with (Uzma *et al.*, 2009).

Likewise, Indians in India have a lower prevalence of myopia than Indians living in Singapore where the prevalence is more similar to Singapore Chinese (Au, Tay and Lim, 1993; Wu *et al.*, 2001). Potential explanations for the increase in myopia prevalence in urban environments include congested living environment and therefore less relaxation of accommodation (Ip *et al.*, 2008a; Zhang *et al.*, 2010; Rudnicka *et al.*, 2016). In addition, a greater emphasis on education in urban environments resulting in

increased near-work (Wu *et al.*, 2001; Mutti *et al.*, 2002; Saw *et al.*, 2002; Quek *et al.*, 2004) may be a confounding factor. Furthermore, as time spent outdoors is different for children in urban and rural environments and rural children tend to spend more time outdoors, it may be increased light levels which affect myopia prevalence and not urban living (Ip *et al.*, 2008a; Zhang *et al.*, 2010).

The IES examined any possible links between myopia and urban versus rural living conditions.

3.11 Diet and myopia prevalence

Nutrition affects retinal development and eye growth, which may play a role in the onset of juvenile-onset myopia (Heller *et al.*, 2015). The Strabismus Amblyopia and Refractive Error Study in Singaporean children found myopia prevalence was significantly higher in non-breast-fed than in breastfed babies (Sham *et al.*, 2010), with breastfeeding significantly associated with more hyperopic refraction in Chinese children (Sham *et al.*, 2010). Breast milk consists of long-chain polyunsaturated fatty acids and anti-oxidants which are cited to affect retina development, eye growth and neural development in early life and therefore, may offer a protective effect against juvenile-onset myopia (Rudnicka *et al.*, 2008; Sham *et al.*, 2010). Breast milk is the primary source of polyunsaturated fatty acids (such as docosahexaenoic acid) until weaning occurs and docosahexaenoic acid is known to be essential for photoreceptor visual cortical development (Williams *et al.,* 2001). Breastfeeding, even for a short period (≤ one month), was found to be protective against myopia (Rahi, Cumberland and Peckham, 2011).

Similarly, myopic children, aged 5-13 years, attending Guy's Hospital, in London, given a diet including additional animal protein demonstrated a reduced rate of mean deterioration of myopia when compared to the control group (Gardiner, 1958).

Moreover, myopia has been associated with a high glycaemic diet (Cordain *et al.*, 2002); suggesting the western diet, with high levels of refined carbohydrates, may be a risk factor for myopia. The reason for this is because of the interaction of chronic hyperinsulinemia with the hormonal regulation of vitreous chamber growth (Cordain *et al.*, 2002). Diets higher in saturated fat and cholesterol intake were associated with longer AL in Singapore Chinese children (Lim *et al.,* 2010). Furthermore, children presenting with myopia before the age of six years have a higher body mass index (BMI) and a more sedentary lifestyle (Tideman *et al.,* 2017). The IES examined the relationship between diet, BMI and myopia prevalence.

3.12 Parental history and myopia

After adjusting for environmental factors, there appears to be a strong link between parental myopia and the risk of developing myopia in their children (Mutti *et al.*, 2002; Jones-Jordan *et al.*, 2010; Lim *et al.,* 2014). Saw *et al.* (2002) found an OR, in Singaporean children, of 1.63 if one of the parents was myopic and 1.7 if both were myopic, indeed this effect increased where parents had myopia ≤-6.00 D where myopia progression was -0.90 D compared to -0.42 D in children with no myopic parents (Saw *et al.*, 2002). Thus children with a family history of myopia have faster myopia progression resulting in significantly higher levels of myopia in adulthood (Kurtz *et al.*, 2007).

The SMS looked at the relationship between refractive errors as a function of the number of myopic parents in both White and East Asian children (Ip *et al.*, 2007). Amongst White participants, the mean refractive error was: +0.99 D where neither parent was myopic; +0.70 D, where one parent was myopic and +0.32 D when both parents were myopic. In comparison, amongst the East Asian children, the mean refractive error at 12 years of age was: -0.06 D where neither parent was myopic; -

0.91D where one parent was myopic and -2.29 D when both parents were myopic (Ip *et al.*, 2007).

Likewise, the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study found that of their Asian participants in first grade, the average refractive error was +0.61 D when neither parent was myopic and +0.04 D when both parents were myopic (Jones-Jordan *et al.*, 2010). The Strabismus Amblyopia and Refractive Error Study in Singaporean children found that family history of myopia was strongly associated with preschool (participants <6 years old) myopia and a more myopic SER (Low *et al.*, 2010). The IES examined the relationship between participant myopia and parental myopia.

3.12.1   Genetic analysis in human myopia

There are a number of inherited syndromes where myopia is one of a complex of symptoms, these include Marfan (Dietz *et al.*, 1991), Stickler type 1 (Knowlton *et al.*, 1989), Stickler type 2 (Brunner *et al.*, 1994); Weil-Marchesani (Faivre *et al.*, 2003); Knobloch (Sertié *et al.*, 2000), and X-linked congenital stationary night blindness (Bech-Hansen *et al.*, 1998). A feature common to these syndromes is the participation of genes involved in the scleral extracellular matrix (Wojciechowski, 2011). Most of these syndromes are characterised by congenital or early onset myopia (Morgan, Ohno-Matsui and Saw, 2012). See Table 3.2.

Table 3.2 Syndromes associated with high myopia

Syndrome	Locus	Gene	Reference
Marfan	15q15–q21.1	Fibrillin	Dietz *et al.* (1991)
Weill–Marchesani	15q15–q21.1	Fibrillin	Faivre *et al.* (2003)
Stickler type1	12q13.1–q13.3	Collagen 2A1	Knowlton *et al.* (1989)
Stickler type2	6p21.3–p22.3	Collagen 11A2	Brunner *et al.* (1994)
Ehlers–Danlos type 4	2q24.3–q31	Collagen 3A1	Tiller *et al*. (1994)
Knobloch	21q22.3	Collagen18a1	Sertié *et al.* (2000)
Congenital stationary night blindness 1	Xp11.4	Retinal nyctalopin	Pusch *et al.* (2000)
Congenital stationary night blindness 2	Xp11.23	Retinal Ca++ channela1F	Bech-Hansen *et al.* (1998)

3.12.2 Non-syndromic inherited high myopia

Genome-wide association studies scans of non-syndromic inherited high myopia (refer Table 3.3) have also reported chromosomal localisation (MYP1-MYP17) (Morgan and Rose, 2005). Mutations in CTNND2 (cadherin-associated protein) in MYP16 have been identified (Li *et al.*, 2011). Li *et al*. (2011) examined susceptibility genes, for high myopia, in Singaporean Chinese, and used two Genome-wide association datasets of Singaporean Chinese, and a follow-up replication study involving Japanese participants. This study found a significant association of the CNND2 gene on chromosome 5p15 to high myopia (Li *et al.,* 2011).

Wojciechowski (2011) demonstrated that many of the reported mutations are in genes which are involved in biological pathways known to mediate connective tissue growth and extracellular matrix composition.

Table 3.3 Non-syndromic inherited high myopia (Morgan and Rose, 2005)

Chromosomal localisation	Reference
Between D18S59 and D18S11 on 18p11.31	Young *et al.* (1998)
Between D18S63 and D18S52 on 18p11.31	Young *et al.* (2001)
Between D12S1684 and D12S1605 on 12q21–23	Young *et al.* (1998)
Between D17S787 and D17S1811 on 17q21–22	Paluru *et al.* (2003)
Between D7S798 and the telomere on 7q36	Naiglin (2002)

Epidemiological studies of genetically or culturally isolated populations are interesting when examining the multifactorial aetiology of refractive error. Two genetic loci for myopia susceptibility – MYP6 which is associated with myopia susceptibility (Stambolian *et al.*, 2004), and MYP14, which is related to ocular refraction (Wojciechowski *et al.*, 2006) have been found in an international consortium of high-grade myopia (Li *et al.*, 2009).

In American Orthodox Jewish families MYP6 and MYP14 were identified (Stambolian *et al.*, 2004), and replicated in linkage studies in the Old Order Amish (Stambolian *et al.*, 2005; Wojciechowski, 2011), and Midwestern American pedigrees (Klein *et al.*, 2007).

The Genes in Myopia twin study ascertained that the same genetic factors that influence academic attainment might be involved in refractive error (Dirani, Shekar and Baird, 2008; Low *et al.*, 2010). The genes in myopia twin study also established evidence of shared genes in refraction and AL in myopia (Dirani, Shekar and Baird, 2008).

3.13 Myopia and near work

The influence of an intense educational system and focus on academic success in South Asia has significantly shaped queries on myopia progression in recent years (Gifford *et al.,* 2019). Higher levels of education have been associated with a higher prevalence of myopia (Dandona *et al.*, 1999). Regarding near work and myopia prevalence, Saw *et al.* (2015) found an OR of 3.05 of developing significant myopia (≤-3.00 D) for Singaporean children aged 7-9 years who read more than two books per week. Conversely, Low *et al.* (2010) found near work not to be associated with early myopia.

Nevertheless, the Sydney Adolescent Vascular Eye Study five-six-year follow-up of the SMS identified near work as a risk factor for myopia for the younger participants (children who were six years old at baseline) (French *et al.,* 2013b); suggesting that significant time engaged in near work may have a greater impact on myopia progression in younger children (≤6 years), when compared to older children (≥12 years). Also, Fulk and Goss (2001) discovered that the rate of change of myopia was slower over the summer months which may be due to the reduced amount of near work during the summer holidays or the increased time spent outdoors during daylight. Another example of an association between near work and myopia was reported in Israel, where the prevalence of myopia found in ultra-orthodox children was higher than that in non-orthodox children (Zylbermann, Landau and Berson, 1993). The authors hypothesised that higher myopia prevalence was associated with the near intensive work undertaken by the ultra-orthodox children; six hours per day for three-year-olds increasing to 16 hours per day for children aged 13 years and over. Although this may be true, it should be noted that there is reported evidence of myopia susceptibility, in orthodox Ashkenazi Jews in America, where evidence of linkage to chromosome 22q12, which has been associated with myopia susceptibility (Li *et al.*, 2014), was found (Stambolian *et al.*, 2006).

The IES examined the relationship between time spent reading, engaged with near visual tasks, including screen-based technologies and myopia prevalence.

3.13.1 Myopia, binocular vision and accommodation

The academic community has extensively researched the relationship between myopia and binocular vision; higher levels of esotropia (Gwiazda, Grice and Thorn, 1999; Gwiazda, Thorn and Held, 2005) and accommodative lag at near are reported in progressing myopes (Abbott, Schmid and Strang, 1998; Gwiazda, Thorn and Held, 2005; Day *et al.*, 2006; Schmid and Strang, 2015). Additionally, near work induced transient myopia has been demonstrated in progressing myopes (Vera-Díaz, Strang and Winn, 2002). In addition, reduced accommodative facility and increased accommodative convergence to accommodation ratios have been associated with myopia progression in children when compared to emmetropic children (Mutti *et al.,* 2000; Gwiazda, Thorn and Held 2005; Mutti *et al.,* 2017). Furthermore, myopia control research which involved prescribing reading adds demonstrated that executive bifocals with base in prism (Cheng *et al.,* 2014) and progressive addition lenses were more effective for those participants who demonstrated the highest levels of accommodative lag (Gwiazda *et al.,* 2004). However, the precise role accommodative errors play in myopia progression is at yet not fully understood (Gifford *et al.,* 2019).

3.13.2 Myopia prevalence and intelligence and educational attainment

Many studies established an association between myopia and intelligence (Onal *et al.*, 2007; Williams, Miller, *et al.*, 2008). Mutti *et al.*, (2002) and Saw *et al.* (2007) reported a link between higher scores on Intelligence Quotient tests and myopia.

The Orinda Longitudinal Study revealed that myopic children performed better on the Iowa Test of Basic Skills Reading and Total Language scores (Mutti *et al.*, 2002). The

Singapore cohort study on the risk factors for myopia found school grades were positively associated with myopia in Singaporean children, and that the associations with language scores were higher than with mathematics (Saw *et al.*, 2007). The ALSPAC study discovered that at seven years of age, myopia was associated with better scores on school-based Standardised Assessments Tests (Williams *et al.*, 2008). Cohn *et al.* (1988) suggested a pleiotropic genetic relationship between myopia and intelligence, based on the highly significant gifted/non-gifted sibling difference in myopia found in their study (Cohn, Cohn and Jensen, 1988), in other words, a strong link was found between myopia and gifted siblings. The inheritance of myopia as a pleiotropic gene positively selected for its facilitation of human intelligence has been proposed; the myopic component is a latent phenotype which is only activated when novel external factors, such as excessive reading and near work activities in preschool, are encountered (Mak *et al.*, 2006).

The Genes in Myopia twin study established that the higher educational attainment was significantly associated with more myopic refraction and strongly influenced by genes (Dirani, Shekar and Baird, 2008; Baird, Schäche and Dirani, 2010). However, the number of years spent in formal education may affect the prevalence of myopia levels (Morgan and Rose, 2005; Rose *et al.*, 2008). For example, in East Asian countries children embark on formal education at a relatively young age (Rose *et al.*, 2008; Lu *et al.*, 2009); in Singapore, this can be as young as two to three years (Saw *et al.*, 2001; Ip *et al.,* 2008a). In contrast, the prevalence of myopia was considerably lower in African countries where the literacy rates are also markedly lower; in general, children embark on formal education between six and eight years of age (Anera *et al.*, 2006; Jimenez *et al.*, 2012).

The IES examined the relationship between myopia prevalence, and school performance, as reported by the participants' parents/guardian.

3.14 Early life biological and social factors

Early life influences on growth may underlie the excessive eye growth that accompanies myopia progression (Rahi, Cumberland and Peckham, 2011). Rahi, Cumberland and Peckham (2011) undertook a life-course epidemiologic investigation in myopia (≤-0.75 D, severe myopia ≤-6.00 D) in a nationally representative cohort of British adults. The 1958 British birth cohort comprised of everybody born in one week in 1958 in Britain. This detailed longitudinal study collected biological social and lifestyle data and thus was uniquely placed to identify key biological and social determinants of health and disease and explore associations with refractive error status. Ophthalmic data were collected at ages 7, 11, 16 and 44 years. The ophthalmic investigation was carried out on 2,487 participants who were a randomly selected subset of the 9,377 participants examined at 44 years of age. The eye examination included: distance and near VA, stereo-vision, autorefraction without cycloplegia, and a biomedical survey which included vision-related quality of life (Power and Elliott, 2006; Rahi, Cumberland and Peckham, 2011). Myopia was significantly associated with higher maternal age (myopia prevalence 49% with maternal age >44 years), increasing maternal height, more senior paternal occupational social class, lower birth weight for gestational age and gender, lower birth weight (independent of gestational age) and maternal smoking during the first trimester.

The finding that maternal smoking during pregnancy may be associated with increased risk of myopia is in direct contrast with Stone (2006) who found that maternal smoking during pregnancy to be associated with a more hyperopic prescription (Stone *et al.*, 2006). Saw *et al.* (2004) also considered that there might be a connection between

parental smoking and a more hyperopic prescription. However, so few mothers smoked at any stage during their children's lives in this study that this precluded a specific link between passive smoking and smoking during pregnancy and refraction (Saw, 2004). Breast milk may offer a protective effect against juvenile-onset myopia due to the long-chain polyunsaturated fatty acids (Rudnicka *et al.*, 2008), (see section 3.9).

The IES examined relationships between myopia prevalence and early life factors such as premature birth, birth weight, twin or single birth, breast/bottle feeding, maternal and paternal smoking, socioeconomic status and parental education level.

3.15   Gender and myopia prevalence

The effect of gender on myopia is inconclusive; Chinese girls were more likely to be myopic than Chinese boys in an urban setting (Wu *et al.*, 2015a). In comparison, the reverse was unveiled in Iran; 29.5% of their male study sample were myopic, whereas only 15.8% of the females were myopic (Hashemi *et al.*, 2014).   A gender effect on myopia seems unlikely; however, differential access to education or participation in outdoor activities and light exposure may influence the development of myopia (Holden *et al.*, 2016). The IES examined the relationship between myopia prevalence and gender.

3.16   Prevalence of myopia summary

Discussions regarding myopia have dominated research in recent years, and while family history (Jones-Jordan *et al.*, 2010; Low *et al.*, 2010); and ethnicity (Saw 2006; French *et al.,* 2012) are undoubtedly important factors, environmental factors have propelled to the forefront in investigations. The academic community has extensively explored the role daylight/bright light exposure plays in delaying the onset and progression of myopia of late (Read, 2016; Read *et al.,* 2018; Ulaganathan *et al.,* 2019). In addition, changes in lifestyle including increased near work activities including the

excessive use of electronic devices, and high-pressure educational systems such as those in East Asia coupled with a reduction in time spent outdoors, are considered to be the driving factors in the increase in the prevalence of myopia and high myopia (Morgan, Ohno-Matsui and Saw, 2012; Tideman *et al.*, 2019).

Thus, it is hard to disentangle the influence of genetics and environmental factors associated with myopia. While the environment appears to have a significant effect on refractive development (Galvis *et al.*, 2016), genetics determines susceptibility to environmental modification (Wojciechowski, 2011), and refractive errors are changing too fast to reflect just changes in genetics (Nickla, 2013). Due to the increase in myopia prevalence, many studies have investigated the myopia prevalence worldwide.

The IES examined the relationship between myopia prevalence and inter alia demographic and lifestyle factors, including parental history and time spent on screens.

Chapter 4 discusses hyperopia and astigmatism and their aetiology, as reported in previous studies in other countries.

4 PREVALENCE OF HYPEROPIA AND ASTIGMATISM IN CHILDREN

4.1 A review of hyperopia

Previous studies proffer that low levels of hyperopia are normal in early infancy (Mohindra and Held, 1981; Saunders, 1995; Wen *et al.*, 2011). Comparisons between studies are difficult due to: different criteria used to define hyperopia; different methods used to measure refractive state of infants and the repeatability of the techniques used to establish refractive error has not been established (Saunders, 1995). Hyperopia prevalence in school children in the standardised RESC varied widely from 0.6% to 26% SER $\geq$+2.00 D (Pokharel *et al.,* 2000; He *et al.,* 2004; Goh *et al.,* 2005). Twin studies support a higher concurrence of hyperopia in monozygotic in comparison with dizygotic twins, which suggests a genetic component (Hammond *et al.*, 2001).

When compared to myopia, there is a paucity of research into the epidemiology of hyperopia in schoolchildren possibly due to the global increase in myopia prevalence (Holden *et al.*, 2016), and the increased risk of pathology associated with myopia (Wong *et al.*, 2014). Nevertheless, previous research identified an association between hyperopia and age-related macular degeneration (Li *et al.,* 2014) and glaucoma (Wong *et al.,* 2003). Hence, identification and analysis of risk factors related to hyperopia should be explored to understand better the emmetropisation process and why some children fail to become emmetropic, and others fail to remain emmetropic (Flitcroft, 2014).

4.1.1 Hyperopia and ocular pathology

Lavanya *et al.*'s (2010) study in Singapore reported early onset age-related macular degeneration was 1.5 times more likely in hyperopes than myopes in Asian Malays;

which aligns with the Blue Mountains population-based study where hyperopes were twice as likely to have age-related macular degeneration (Wang, Mitchell and Smith, 1998). Furthermore, the Age-Related Eye Disease Study Research Group reported hyperopes to be 2.3 times more likely to have exudative age-related macular degeneration when compared to myopes (Age-Related Eye Disease Study Research Group, 2000). An explanation for the association between hyperopia and age-related macular degeneration is not accurately known. Theories include a reduction in choroidal blood flow in hyperopic eyes due to the shorter AL resulting in choroidal neovascularisation (Ulvik, Seland and Wentzel-Larsen, 2005). For example, shorter hyperopic eyes have higher scleral rigidity which may interfere with choroidal blood flow; decreased ocular blood flow interferes with the exchange of nutrients and metabolic products across the retinal pigment epithelium resulting in the formation of drusen; or increased concentration of vascular endothelial growth factor with decreasing AL leading to increased angiogenesis (Li *et al.,* 2010).

Also, primary angle closure glaucoma, which is a devastating disease associated with half of the global glaucoma-related blindness (Wright *et al.,* 2016), tends to develop in smaller eyes (hyperopic eyes) (Schuster *et al.,* 2016). In hyperopes, the ACD and diameter are shallower, and the lens is thicker and positioned more anteriorly leading to crowding of the ocular structures in the anterior chamber which can result in the iris blocking the trabecular meshwork and increased intraocular pressure causing damage (Wright *et al.,* 2016).

4.1.2 Age

Wood and Hodi (1992) and Thompson (1987) examined the refractive status of infants from birth to 6-months-old using cycloplegic retinoscopy and recorded refractive error in terms of the SER. Wood and Hodi's (1992) results suggest an increase in hyperopia

during the first six months of life and a decrease after that. Thompson's (1987) findings are similar to Edwards (1991) and Zonis *et al.*'s (1974) study, which all show a decline in hyperopia with age.

The NICER study and SMS found hyperopia prevalence to decline with age (NICER: 6-7 years 26.0%, 12-13 years 14.7%. SMS: 6 years 13.2% and 12 years 5.0%) (Ip *et al.*, 2008b; O'Donoghue *et al.*, 2010). Likewise, the RESCS reported reduced hyperopia prevalence with age in all studies bar the South African study (7 years 2.8%, 13 years 2.9%) (Naidoo *et al.*, 2003). The IES examined the prevalence of hyperopia in schoolchildren aged 6-7yrs and 12-13yrs.

4.1.3 Studies addressing the prevalence of hyperopia in children

Table 4.1 provides an overview of hyperopia prevalence in children studies where cycloplegia was part of the study protocol.

The NICER study reported hyperopia prevalence of 26.0% amongst 6-7-year-old and 14.7% amongst 12-13-year-old Caucasian participants (O'Donoghue *et al.*, 2010). The AES found hyperopia prevalence was significantly higher amongst White participants (6-7 years 22.9%, 12-13 years 10.4%) than Black participants (6-7 years 9.1%, 12-13 years 0%) and South Asians (6-7 years 10.3%, 12-13 years 2.6%) (Logan *et al.*, 2011). The higher hyperopia prevalence in White Northern Ireland children compared to White Australian children (refer Table 4.1) may be due to genetic susceptibility, for example Northern Ireland is a relatively isolated community with little outside genetic influence (O'Donoghue *et al.,* 2010). Similarly, Dobson *et al.* (2008) reported higher degrees of refractive error in their study of school aged members of a relatively isolated Native American tribe.

The MEPEDS examined children aged 6-72 months of African American, Hispanic, Non-Hispanic White and Asian ethnicities (Eye, Study and Group, 2009; Wen *et al.*, 2013). The prevalence of hyperopia (SER $\geq$+2.00 D) was lowest in the Asian children (13.5%) when compared to the African American (20.8%), Hispanic (26.9%) and non-Hispanic White children (25.7%). The MEPEDS also found that the prevalence of hyperopia decreased from six months to its lowest point between 24 months (Asian children) and 30 months (non-Hispanic White children); the Hispanic children followed this trend, but the prevalence of hyperopia appeared to increase again from 24-72 months (Tarczy-Hornoch *et al.*, 2009; Wen *et al.*, 2013). The MEPEDS found hyperopia to be associated with ethnicity, exposure to maternal smoking during pregnancy and not having health insurance; myopia and hyperopia were both found to be associated with astigmatism. Moreover, the MEPEDS found that although the prevalence of hyperopia dropped in children at 12 months, reaching a low point at 24 months, it appeared to increase again in children aged 72 months (Tarczy-Hornoch *et al.,* 2009; Borchert *et al.*, 2011) thus querying the emmetropisation process for high hyperopes.

Ying *et al.* (2014), VIP Study, found the prevalence of hyperopia, > +3.25 D in 4,040 pre-schoolers aged 3-5-years-old, to be: 5.5% in Asians, 6.8% in African-Americans, 6.9% in Hispanics, 8.9% in American Indians and 11.9% in non-Hispanic Whites. Kulp *et al.*'s *(*2014) study involved secondary data analysis of the VIP study (methods previously described in section 2.2.9) and investigated any possible associations between different levels of hyperopia and vision disorders such as amblyopia, strabismus, reduced stereo acuity, astigmatism and anisometropia. Hyperopia >+3.25 D was found in 11.7% of the population; 4% had hyperopia >+3.25 D and $\leq$+5.00 D, and 7.7% had hyperopia $\geq$+5.00 D (Kulp *et al.*, 2014). The authors found that (a) the higher the magnitude of hyperopia the higher, the odds of developing strabismus and

amblyopia; and (b) even low levels of hyperopia (≥+3.25 D and <+5.00 D) were associated with an increased odds of amblyopia and strabismus and in addition reduced stereo-acuity in non-strabismic non-amblyopic hyperopic children. The consequence of this was poorer literacy amongst 3-4-year-old participants with >+3.25 D when compared to those their peers with SER ≤+3.25 D (Kulp *et al.*, 2016).

The RESC study in Chile found that, over an age range of 5-15 years, hyperopia ≥+2.00 D decreased from 22.7% to 7.1% in males and 26.3% to 8.9% in females and concluded that females had a statistically significant higher risk of developing hyperopia (Maul *et al.*, 2000). Zhao *et al.* (2000) RESC study of rural Chinese children found over the same age range the prevalence of hyperopia to decrease from 8.8% in males and 19.6% in females to less than 2% in both. Chinese children living in an urban environment were found to have a hyperopia prevalence of 17.0% in five-year-olds and less than 1.0% in 15-year-olds (He *et al.*, 2004). Amongst Nepalese children aged 5-15-years-olds, hyperopia prevalence (≥+2.00 D) was less than 2.1%; this study found the risk of hyperopia to be associated with females but not with age (Pokharel *et al.*, 2000).

Murthy *et al.*'s (2002) RESC study of urban Indian children aged 5-15-year-old found the prevalence of hyperopia to be 15.6% at five years decreasing to 3.9% at 15-years-old; hyperopia was again associated with female gender. Goh *et al.* (2005) found hyperopia prevalence to drop from 5.0% at age seven years to 1.0% at 15-years-old.

Casson *et al.*'s (2012) RESC model study found an exceptionally low prevalence of hyperopia in Lao (6 years 3.1%, 11 years 1.1%). However, unlike the RESC studies, the study in Lao involved school-based sampling. The authors concluded that as many children in Lao did not have access to education and those that were in schools had little access to books the effects of intense education seen in other East Asian studies were not an issue for children in Lao and selection bias was a limitation of the study.

The SMS reported hyperopia prevalence of 13.2% in participants aged 6-years-old, 5% in 12-year-olds (Ip *et al.*, 2008b), and found hyperopia to be significantly associated with amblyopia and strabismus.

4.1.4 Association with strabismus and amblyopia

The persistence of hyperopia beyond 12 months is associated with an increased risk of VI (Aurell and Norrsell, 1990; Ingram *et al.*, 1991; Kulp *et al.,* 2014). As emmetropisation is mainly complete by six years, any residual hyperopia may be considered a failure of emmetropisation and therefore, a public health concern due to its association with amblyopia and strabismus (Flitcroft, 2014). Why some infant hyperopes emmetropise and others remain hyperopic remains unknown (Troilo, 1992; Saunders, 1995). Previous studies investigated higher hyperopia ≥+2.75 D, and its association with amblyopia and strabismus (Fulton *et al.*, 1980; Aurell and Norrsell, 1990; Ingram *et al.*, 1991). Colburn *et al.*'s (2010) longitudinal study concluded that moderate to high hyperopia (>+3.50 D) should be corrected by age 40 months to reduce the risk of amblyopia. In the VIP study, bilateral hyperopia ≥+4.00 D was associated with an increased adds for bilateral amblyopia (9.4 for OR, p<0.001) (Pascual *et al.*, 2014). Meridional hyperopia ≥+3.50 D in any meridian at age 12 months resulted in amblyopia for 48% of the study population when aged 3.5 years (Ingram *et al.*, 1991). Fulton *et al.* (1980) found only 8.6% of their study population, (which comprised of children with hyperopia ≥+2.75 D between birth and three years), did not have either strabismus or amblyopia. Aurell and Norrsell's (1990) study found the failure of hyperopia to reduce with age to be associated with strabismus and amblyopia. The Pediatric Eye Disease Investigator Group (PEDIG) study examined whether immediately prescribing spectacles for children aged 12-24 months with moderate hyperopia (+3.00 D to +6.00 D SE), and without manifest strabismus, versus delaying the prescription (Kulp *et al.*, 2019). The authors concluded that in the absence of

strabismus or amblyopia, there was no significant benefit in prescribing spectacles immediately and recommended six-monthly reviews and close monitoring (Kulp *et al.*, 2019). The IES examined the relationship between hyperopia prevalence and amblyopia and strabismus. Refer to sections 5.7 and 5.8 for more detail on the relationship between hyperopia and strabismus and amblyopia.

4.1.5 Social class

Socioeconomic disadvantage is a reported cause of poor health in society (Marmot and Commission on Social Determinants of Health, 2007). The association between socioeconomic advantage and the conditions this fosters have been referred to in the literature due to the association with myopia prevalence (Peckham, Gardiner and Goldstein, 1977; Rahi, Cumberland and Peckham, 2011; Galvis *et al.*, 2018). However, there is limited literature on the contrasting link between social class and the higher prevalence of hyperopia (Williams *et al.,* 2008b). Social class and lifestyle patterns such as smoking may play a part, in refractive error development (Saw, 2004; Stone *et al.*, 2006; Borchert *et al.*, 2011). Hyperopia may indicate delayed development, and social disadvantage may be a marker for developmental delay (Najman *et al.*, 1992; Atkinson *et al.*, 2005; Williams *et al.,* 2008b). Furthermore, hyperopia ≥+4.00 D in 3-4-year-old Latino children was found to be associated with socioeconomic disadvantage (Brody *et al.*, 2007). The IES examined the relationship between hyperopia prevalence and socioeconomic status.

4.1.6 Hyperopia and educational attainment

Hyperopia has been associated with poorer educational performance (Rosner and Rosner, 1997; Stewart-Brown, Haslum and Butler, 2008; Williams, Miller, *et al.*, 2008), and developmental deficits (Atkinson *et al.*, 2002). Ip *et al.* (2008) found hyperopia (SER≥+2.00 D) to be strongly associated with self-reported eye-strain, and parent-

reported reading difficulties in their study involving 6-year-old and 12-year-old Australian participants. Kulp *et al.*'s (2016) study found uncorrected hyperopia (≥+4.00 D) to be associated with reduced stereoacuity, poorer near vision and significantly worse performance on early literacy test in 4-5-year-olds.

4.1.7 Summary

The prevalence of hyperopia in childhood appears to decline with age (Czepita *et al.*, 2007; Yekta *et al.*, 2010). The ALSPAC study found a link between smoking in pregnancy and the prevalence of moderate hyperopia and disadvantaged children were more likely to be hyperopic than advantaged children (Majeed *et al.*, 2008; Williams *et al.*, 2008b).

There is a paucity of research relating to childhood hyperopia, this may be due to the perception that it is not a significant health concern as typically, neonatal hyperopia regresses; unlike high myopia, hyperopia is rarely associated with blinding eye disease and cycloplegic is also required in order to adequately detect hyperopia (Colburn *et al.*, 2010), hence screening children for hyperopia is not straightforward. Mezer *et al.* (2015) reviewed medical records from 145 hyperopic children from birth to over 29 years and reported children with hyperopia ≤+3.00 D will most likely experience a reduction in hyperopia over time and may outgrow the need for corrective lenses; however, children with hyperopia ≥+5.00 D are unlikely to experience any reduction in refractive error (Mezer *et al.*, 2015). The PEDIG recommended close monitoring of children with moderate hyperopia in the absence of amblyopia and strabismus (Kulp *et al.*, 2019). Uncorrected hyperopia can cause reduced vision due to monocular or binocular amblyopia (Kulp *et al.*, 2014), thus addressing uncorrected hyperopia is a public health issue due to the increased odds of bilateral VI in later life (Rahi *et al.,*

2002; Chua and Mitchell, 2004) and consequential increased cost to the public health system associated with VI in later life.

The IES examined the relationship between hyperopia prevalence and ethnicity, gender, age, socioeconomic status, urban-rural living conditions and school performance.

Table 4.1 displays a summary of hyperopia prevalence in children studies.

Table 4.1 Hyperopia prevalence in schoolchildren studies

Study Authors	Location	Ethnicity	N	Age years	Hyperopia (SER≥+2.00) (%)
NICER (2010)	Northern Ireland	White	392 661	6-7 12-13	26 14.7
AES (2011)	UK	White, South Asian, Black White, South Asian, Black	70, 213, 44 115, 114, 40	6-7 12-13	22.9, 10.3, 9.1 10.4, 2.6, 0.0
SMS (2005, 2006)	Australia	Predominately White	1,738 2,353	6-7 12-13	13.2 5.0
RESC (200)	Chile	South American	5,303	5-15	1.4
RESC (2000)	Nepal	Nepalese	5,067	5-15	2.1
RESC (200)	China Rural	Chinese	5,884	5-15 5-7 14-15	2.7 8.5 1.1
RESC (2004)	China Urban	Chinese	4,364	5-15 5 15	4.6 17.0 1.0
RESC	India Rural	Indian	4,074	7-15 7 15	0.7 0.7 1.2
RESC (2002)	India Urban	Indian	6,447	5-15 5 15	7.7 15.6 3.9
RESC (2005)	Malaysia	Malay	4,634	7-15 7 15	1.6 5.0 1.0
RESC (2012)	Lao	Lao (predominately Tai)	2,899	6-11 6 11	2.8 3.1 1.1
RESC model (2009)	India	Indian Urban Indian Rural	5,021 7,401	6-15 6-15	1.06% 0.39%
RESC model (2010)	Ghana	African	961	5-19	4.6%
RESC model (2003)	South Africa	African	4,890	5-15 5 15	2.6% 2.7% 0.7%

Number of participants (N); Spherical equivalent (SE); Northern Ireland Childhood Errors of Refraction (NICER); Aston Eye Study (AES); Refractive Errors Studies in Children (RESC); United Kingdom (UK).

4.2 A review of astigmatism

Astigmatism is a relatively standard refractive error where parallel light rays entering the eye are not brought to focus in a single point, but in two focal lines perpendicular to each other (Read, Vincent and Collins, 2014). Astigmatism is due to an irregular refractive surface in either the lens or the cornea (Read, Collins and Carney, 2007). Astigmatism is thought to be associated with both genetic (Clementi *et al.*, 1998), and environmental factors (Read, Collins and Carney, 2007). Furthermore, an association between some genetic syndromes such as Downs Syndrome and astigmatism have been reported (Woodhouse *et al.*, 1997; Cregg *et al.*, 2003). The Ojai study, involving a cohort of Californian children reported 4.2% of children aged 6.5 years and 6.0% of children aged 12.5-years-old had astigmatism ≥0.75 DC (Hirsch, 1963). Studies that have examined the prevalence of astigmatism in infant populations have reported a higher prevalence than this (Mohindra *et al.*, 1978; Ingram *et al.*, 1979; Gwiazda *et al.*, 1984; Dobson *et al.*, 2003). The Howland and Sayles (1984) study discovered a prevalence of astigmatism of 65.0% in the first year of life, which decreased with age approaching adult levels between 18 months and 3.5-years-old.

The NICER study and SMS defined astigmatism as ≥1.00 DC (Huynh *et al.*, 2006; O'Donoghue *et al.*, 2011), whereas the RESC studies defined astigmatism as ≥0.75 DC (Negrel *et al.*, 2000) and reported findings for cyclopleged retinoscopy and cyclopleged autorefraction, hence inter-study comparisons of astigmatism are challenging.

Most infant astigmatism is corneal (Howland and Sayles, 1984). Many studies have shown that infant astigmatism decreases in the first two years of life (Mohindra *et al.*, 1978; Atkinson, Braddick and French, 1980; Gwiazda *et al.*, 1984; Howland and Sayles, 1984; Mutti *et a.l,* 2004). As the refractive power of the cornea decreases from +50.00D

to +43.00D during the first year of life, as the cornea becomes flatter due to the increasing eye size (Mutti *et al.,* 2005) this may be responsible for the decrease in astigmatism (Hirsch, 1963; Howland and Sayles, 1984).

4.2.1 Age and astigmatism prevalence

Abrahamsson *et al.*'s (1988) longitudinal study of 299 infants, who demonstrated ≥1.00 DC astigmatism at 12 months, reported that by four years of age one-third of the group had no astigmatism at all and the remainder had much-reduced astigmatism, with the most significant change taking place between 12-24 months. Lyle *et al.*'s (1971) study found that "with the rule" (WTR): vertical meridian has higher refractive power than horizontal meridian) astigmatism was the most prevalent in school-aged children and adults. Many studies of preschool children found "against the rule" (ATR) to be more prevalent (Atkinson, Braddick and French, 1980; Gwiazda *et al.*, 1984). Other studies determined WTR to be the norm (Thompson, 1987; Edwards, 1991; Saunders, 1995). Gwiazda *et al.*'s (1984) study established that children with a high amount of ATR astigmatism at 24 months tended to lose it by six years. In a later study, Gwiazda *et al.* (2000) monitored children with astigmatism over 6-23-years-old, and key findings included: a correlation between the degree of initial astigmatism and subsequent astigmatism and myopia in school years; and ATR astigmatism was almost twice as frequent as WTR (Gwiazda *et al.*, 2000).

4.2.2 Ethnicity and astigmatism prevalence

The NICER study examined 661 White children aged 12-13-years-old and 392 children aged 6-7 years; the prevalence of refractive astigmatism ≥1.00 DC was 24% in the younger age group and 20% in the older age group. Astigmatism was, in the main, oblique (76% in the 6-7 age group and 59% in the older age group). Astigmatism was associated with increasing hyperopia and myopia (O'Donoghue *et al.*, 2011). The

NICER study defined: WTR astigmatism as a negative cylinder axis between 1° to 15° and 165° to 180°; ATR astigmatism as a negative cylinder axis 75° to 105° and oblique astigmatism as a negative cylinder axis 16° to 74° and 106° to 165°. The presence of astigmatism ≥1.00 DC found in the NICER study was considerably higher than that found in the SMS (4.8% in children aged 6 years and 6.7% in children aged 12 years); both studies dealt with a mainly White population (Huynh *et al.*, 2006; Huynh *et al.*, 2007; O'Donoghue *et al.*, 2011). The SMS study reported an astigmatism prevalence of 4.8% amongst six-year-old participants (Huynh *et al.*, 2006) and 6.7% amongst 12-year-old participants (Huynh *et al.*, 2007). The IES adopted the same definition for astigmatism as the NICER and SMS to facilitate comparison of results.

The MEPEDS involved 1,501 non-Hispanic White children and 1,507 Asian children aged 6-72 months and found the prevalence of astigmatism (≥1.50 DC) to be 6.33% in non-Hispanic White children, 12.7% in African American children, 16.8% in Hispanic children, and 8.29% in Asian children (Fozailoff *et al.*, 2011; Wen, Tarczy-Hornoch, McKean-Cowdin, Cotter, *et al.*, 2013). The prevalence of astigmatism ≥1.50 DC in non-Hispanic-White children (6.33%) was significantly lower than found in African American children (12.7%), Hispanic children (16.8%) or Asian children (8.29%) (Tarczy-Hornoch *et al.,* 2009; Wen *et al.*, 2013).

The BPEDS also found a lower prevalence of astigmatism ≥1.50 DC in its Caucasian participants when compared to the African-American participants although it did find a higher prevalence of astigmatism in its White participants (11.4%) compared to 6.32% found in MEPEDS (Giordano *et al.*, 2009; Wen *et al.*, 2013). The MEPEDS found in all four racial/ethnic groups (Hispanic, non-Hispanic-White, Asian, and African American) that the mean absolute cylindrical power decreased with age and a stable prevalence level of astigmatism was reached between 24 and 36 months. Hispanic

children showed a higher prevalence of astigmatism ≥3.00 DC than African American (2.9% vs 1%) (McKean-Cowdin *et al.*, 2011). McKean-Cowdin *et al.*'s (2011) study examined the combined MEPEDS and BPEDS results taken from 9,970 pre-school children aged 6-72 months from three ethnic groups (African-American, Hispanic and non-Hispanic White). The authors concluded that astigmatism was associated with: infancy (<12 months); race/ethnicity (Hispanics more likely than African American and non-Hispanic-White); correctable refractive errors such as hyperopia (≥+2.00 D, 1.6 times more likely to have astigmatism ≥1.50 DC); myopia (≤-1.00 D, 4.6 times more likely to have astigmatism ≥1.50 DC) and maternal smoking during pregnancy (McKean-Cowdin *et al.*, 2011). With-the-rule astigmatism was nine times more prevalent than ATR astigmatism (McKean-Cowdin *et al.,* 2011).

The Strabismus Amblyopia and Refractive Error Study in Singaporean children of 3,009 Singaporean children aged 6-72 months found the prevalence of astigmatism ≥1.50 DC was 8.6% and 95% of astigmatism found was WTR (Dirani *et al.*, 2010). The Strabismus Amblyopia and Refractive Error Study in Singaporean children found that the prevalence of astigmatism increased with age; 3.6% in children aged 12-23.9 months and 11.3% in children aged 60-72 months; boys were more likely to have astigmatism than girls (9.2% vs 7.3%). In Singaporean children (7-9 years) a prevalence of astigmatism (≥ 1.00 DC) of 19.2% was found and an association between astigmatism and a high accommodative convergence/convergence ratio (Tong *et al.*, 2002).

Dobson *et al.* (1999) examined the prevalence of astigmatism in 250 children aged 3-5 years in the Tohono O'odham nation (Native American people of the Sonoran Desert) and found that 44% of the population had astigmatism ≥1.00 DC; 22% ≥2.00 DC and 11% ≥3.00 DC. Of those with astigmatism ≥1.00 DC, 92% had WTR astigmatism. This

study agreed with previous studies that there is a very high level of astigmatism in this Native American community and astigmatism (Dobson, Miller and Harvey, 1999; Harvey, Dobson and Miller, 2006).

4.2.3 Astigmatism prevalence in Refractive Error Studies in Children

The RESC studies assessed the prevalence of astigmatism at two levels: ≥0.75 DC to ≤2.00 DC and ≥2.00 DC (Negrel *et al.*, 2000); and results reported with cyclopleged autorefraction are presented here. Maul *et al.*'s (2000) study of 5,303 children aged 5-15 years in Chile found a 27% prevalence of astigmatism (≥0.75 DC). Astigmatism prevalence ≥0.75 DC and ≤2.00 DC was revealed in 12%. Astigmatism ≥2.00 DC was found in just under 15% (Maul *et al.*, 2000). Zhao *et al.*'s (2000) study of 5,884 Chinese children, in a rural setting, aged 5-15 years and discovered a 10% prevalence of astigmatism (≥0.75 DC). He *et al.*'s (2004) study of 4,814 urban Chinese children, aged 5-15 years, revealed a 42.7% prevalence of astigmatism ≥0.75 DC (≥0.75 DC to <2.00 DC in 34.3% and ≥2.00 DC in 8.5%).

Murthy *et al.*'s (2002) study of 6,447 children aged 5-15 years in an urban population in New Delhi uncovered a 14.6% prevalence of astigmatism (≥0.75 DC) in either eye.

Naidoo *et al.*'s (2003) study of 4,890 South African children aged 5-15 years determined the prevalence of astigmatism of 14.6% (≥0.75 DC). The RESC study of 5,067 Nepalese children aged 5-15 years found a 3.5% prevalence of astigmatism ≥0.75 DC (Pokharel *et al*., 2000). Goh *et al.* (2005) examined data relating to 5,528 Malaysian children aged 7-15-years-old; a decision was made to exclude children aged 5-6-years-old from this RESC study due to perceived difficulties measuring VA in children without schooling experience and found a prevalence of astigmatism (≥0.75 DC) in 21.3% of participants. Table 4.2 displays a summary of astigmatism found in prevalence

studies. The IES reported astigmatism as reported by cycloplegic autorefraction to facilitate comparison with the NICER study and the SMS. The IES examined the relationship between astigmatism and ethnicity, gender, urban/rural living and sociodemographic variables in children aged 6-7yrs and 12-13yrs.

Table 4.2 Prevalence of astigmatism in schoolchildren studies

Study Authors	Location	Ethnicity	N	Age years	Astigmatism definition	Astigmatism (%)
NICER (2010)	Northern Ireland	Caucasian	392 661	6-7 12-13	≥1.00 DC	24% 20%
SMS (2005, 2006)	Australia	Predominately White	1,738 2,353	6 12	≥1.00 DC	7.6% 9.4%
RESC (2000)	Chile	South American	5,303	5-15	≥0.75 DC	12.1%
RESC (2000)	Nepal	Nepalese	5,067	5-15	≥0.75 DC	3.5%
RESC (2000)	China Rural	Chinese	5,884	5-15	≥0.75 DC	9.5%
RESC (2004)	China urban	Chinese	4,364	5-15	≥0.75 DC	42.7%
RESC (2002)	India rural	Indian	4,074	5-15	≥0.75 DC	9.7%
RESC (2002)	India urban	Indian	6,447	5-15	≥0.75 DC	5.4%
RESC (2003)	South Africa	African	4,890	5-15	≥0.75 DC	14.6%
RESC (2005)	Malaysia	Malay	4,634	7-15	≥0.75 DC	21.3%

Number of participants (N); Spherical equivalent (SE); Northern Ireland Childhood Errors of Refraction (NICER); Refractive Errors Studies in Children (RESC).

Chapter 5 discusses amblyopia prevalence and its aetiology, as reported in previous studies in other countries.

5 AMBLYOPIA PREVALENCE IN SCHOOLCHILDREN REVIEW

5.1 Introduction

Amblyopia, described by Von Noorden (1985) as a condition where "the doctor and the patient see nothing", is a common cause of un-correctable monocular, and rarely binocular, vision loss in both children and adults and is therefore a public health concern (Simons, 2005; Holmes and Clarke, 2006; Wang *et al.*, 2011). Amblyopia is a reduction in BCVA, in one or both eyes, that cannot be explained by observable ocular pathology (Barrett, Bradley and McGraw, 2004). Amblyopia is a visual disorder resulting from an atypical visual experience during the critical period of visual development, thought to develop during childhood up to 7-8 years (Levi, 2006), and can be treated up to the age of 8 years (Holmes and Clarke, 2006; Simons, 2005).

Amblyopia prevalence studies involving children in developed countries reported 0.8%-3.9% prevalence (Robaei *et al.*, 2006a; Williams *et al.,* 2008a; Xiao *et al.*, 2015; Aldebasi *et al.,* 2015). An 8.9% prevalence was reported in a clinical population (Noche *et al.*, 2012). Failure to treat amblyopia during the critical period of visual development, and possibly reverse with therapeutic intervention (Hubel, Wiesel and LeVay, 1976), due to inadequate screening and delayed treatment, results in life long VI (Holmes, 2011). Rahi *et al.* (2002) found an increased risk of bilateral blindness due to a traumatic eye injury in younger people with an amblyopic eye and age-related macular degeneration in older people with an amblyopic eye emphasising the importance of addressing amblyopia as a significant public health concern.

In the US, health economists working with the United States Census Bureau's Sickness Impact Profile, conducted a third party life insurance evaluation which addressed

Quality Adjusted Life Years assessment of the impact of amblyopes losing vision in their non-amblyopia eye (Membreno *et al.*, 2002). Membreno *et al.* (2002) assumed a 2% amblyopia prevalence, with 1% of amblyopes losing vision in their non-amblyopic eye during their working life, which was estimated would reduce male average monthly income by over 40% and female average monthly income by over 30%, resulting in $7 billion annual lost earnings (using 1994 average wage data) due to amblyopia. Additionally, the estimated economic benefit of amblyopia treatment was $22 return to the Gross Domestic Product for every $1 invested, allowing for the cost of national screening and treating of amblyopia (1994 cost data), this return is especially enhanced due to the early intervention of amblyopia treatment and the subsequent lifelong impact on income. Consequently, amblyopia may affect the quality of life, educational attainment (Chua and Mitchell, 2004), sports involvement (Packwood *et al.*, 1999), self-esteem (Webber *et al.*, 2008) and career choice (Carlton and Kaltenthaler, 2011). Many occupations preclude those without good binocular vision such as pilot, navigator, aircrew, fire brigade, air traffic controller and large goods vehicle driver (Adams and Karas, 1999).

Amblyopia not only results in a reduction in high contrast VA, but in addition, reduced contrast sensitivity in the amblyopic and also in the fellow eye, spatial distortions, positional uncertainty in visual alignment tasks (Barrett *et al.*, 2003), defects in global motion detection (Hess and Aaen-Stockdale, 2008), defective multisensory processing as evidenced by a reduced McGuirk effect (Wallace and Stein, 2007; Stein, Stanford and Rowland, 2014; Burgmeier *et al.*, 2015; Lacey and Sathian, 2015; Cappagli *et al.*, 2017) and diminished perception of scenes and objects during everyday activities (Mirabella, Hay and Wong, 2011), has been reported.

Amblyopia has many causes such as the presence of strabismus (misalignment of the eyes in which the visual axis of one eye deviates up, down, in or out) preventing bi-foveal fixation. Constant unilateral strabismus or unequal alternating strabismus (usually eso- deviations) can result in amblyopia (Wallace *et al.*, 2018). Anisometropia where a significant difference in refractive error between fellow eyes exists may cause amblyopia (Barrett, Bradley and Candy, 2013). Also, form deprivation (exclusion of all visual information except light due to physical obstructions such as corneal or lenticular opacification, eyelid ptosis) and significant refractive error (high levels of astigmatism or hyperopia) may result in amblyopia (Simons, 2005; Barrett, Bradley and Candy, 2013). Amblyopia never occurs in isolation; it is the result of disuse (retinal blur due to defocus in refractive amblyopia or anisometropia and form deprivation due to structures such as cataract that obscure images), or misuse (strabismus, a failure to maintain alignment of the eyes) of the visual system, or a combination of these features (Holmes, 2011; Solebo, Cumberland and Rahi, 2014). Form deprivation is rare, and in general, there appears to be a three-way split with almost one-third of amblyopia caused by anisometropia, one third caused by strabismus and one third caused by both (Barrett *et al.,* 2013). From birth, developmental neuroplasticity influences structural and functional changes in the eyes and visual system. This process continues during the sensitive period. Any disruption during this period can give rise to amblyopia (Solebo, Cumberland and Rahi, 2014). Unilateral amblyopia may be asymptomatic in younger children, due to the clear image in the non-amblyopic eye, and coupled with the lack of any obvious visible physical signs possibly results in a later diagnosis (Weakley, 2001). Thus, the detection of orthotropic amblyopia tends to be later than strabismic amblyopia (Chua and Johnson, 2004).

Risk factors for the development of amblyopia and strabismus include the retention of high hyperopic, myopic and astigmatic refractive errors in childhood (Saunders, 1995).

Non-reducing hyperopia and astigmatism as early as the second year of life may require correction (Saunders, Woodhouse and Westall, 1995) and anisometropia persisting into the third year of life is highly amblyogenic (Donahue, 2006; Leon *et al.*, 2008; Donahue *et al.*, 2013).

There are numerous studies on the prevalence of amblyopia. However, inter-study comparisons are difficult due to the variety of definitions used to describe amblyopia (Ohlsson, 2005). This review aims to provide an update on the most recent studies on the prevalence of amblyopia in children and to examine whether the incidence varies between ages and ethnicities.

Von Noorden (1981) suggested the following definition for amblyopia:

"*Amblyopia is a unilateral or bilateral decrease in VA caused by form vision deprivation and/or abnormal binocular interaction for which no organic cause can be detected by physical examination of the eye and which in appropriate cases is reversible by therapeutic measures.*"

Prevalence studies use tighter definitions of amblyopia (see Table 5.1). Most studies also required the presence of amblyogenic factors (Ohlsson *et al.*, 2001, 2003; Varma *et al.*, 2006; Xiao *et al.*, 2015). Amblyogenic factors include the following: anisometropia >1.00 D; strabismus; hyperopia >3.50 D; astigmatism >1.50 D; any media opacities and ptosis (Donahue *et al.*, 2003).

As amblyopia is one of the most common forms of VI, prevalence studies are essential for clinicians and health policy decision makers (Campos, 1995; Simons, 2005; Holmes and Clarke, 2006).

5.2 Amblyopia prevalence in international studies

Before looking at the figures for amblyopia, and comparing results with the current study, there were certain factors which were considered: criteria used to define amblyopia; clinical or population-based sample selection; subject age and ethnicity; cross-sectional or longitudinal and study methodology (Weale, 2003). A variety of definitions for amblyopia can be found in the literature, for example, clinically significant cut-off points of 6/12 or 6/9 with or without the presence or absence of amblyogenic factors have been used. The subsequent international studies involving children have used different definitions for amblyopia:

5.2.1 The Multi-Ethnic Pediatric Eye Disease Study and Baltimore Pediatric Eye Disease study

The MEPEDS and BPEDS defined amblyopia as follows: Unilateral: BCVA ≥0.2logMAR (6/9.5); in the worse eye; inter-ocular difference ≥2-lines and with≥ one of the following amblyogenic factors: (1) strabismus (constant or intermittent); (2) previous strabismus surgery; (3) anisometropia (≥1.00 D SER aniso-hyperopia, ≥3.00 D SER aniso-myopia or ≥1.50 D aniso-astigmatism) or (4) past or present obstruction of visual axis. Bilateral: bilateral BCVA worse than 0.4logMAR (6/15) (30-47 months) or worse than 0.3logMAR (6/12) (age 40-72 months); with bilateral ametropia (≥4.00 D SER hyperopia, ≤-6.00 D myopia; or ≥2.50DC) or with the past or present obstruction of the visual axis (Varma *et al.*, 2006). The BPEDS cross-sectional, population-based study used the same examination protocols as MEPEDS (see above) (Friedman *et al.*, 2009).

5.2.2 The Sydney childhood eye study

The Sydney Childhood Eye Study adopted the following definitions for amblyopia: unilateral: BCVA < 20/40 in weaker eye, inter-ocular difference in BCVA ≥2-lines

plus≥1 of the following amblyogenic factors: (1) anisometropic amblyopia:≥1.00 D SER between fellow eyes without strabismus; (2) strabismic amblyopia: any heterotropia or history of strabismus surgery without anisometropia or high refractive error; and (3) mixed strabismic-anisometropic amblyopia: (1) and (2) were present in combination; (4) stimulus deprivation amblyopia: past or present obstruction of visual axis. Bilateral: bilateral BCVA < 20/40 (6/12 Snellen, 0.3logMAR), with bilateral ametropia (≥4.00 D SER hyperopia, ≥ 6.00 D SER myopia, or ≥2.50 DC astigmatism), or with the past or present bilateral obstruction of the visual axis. History of amblyopia treatment (Robaei *et al.*, 2006a, 2008). Amblyopia prevalence was reported for 6-year-olds (1.8%) and 12-year-olds (1.9%), which included those previously treated for amblyopia.

5.2.3 The Refractive Error Studies in Children

The RESC examined 46,260 children aged 5-15 years, 39,321 of which were included for the RESC assessment of amblyopia prevalence (methodology detailed in 2.2.3.). This large-scale population-based study was conducted at eight sites representing a mix of ethnic origins and environments (Xiao *et al.,* 2015). The RESC definition for amblyopia was as follows: BCVA (measured through a pin-hole) ≥0.3logMAR (≤6/12) in at least one eye associated with one or more of the following potential causes: (1) esotropia, exotropia, or vertical tropia at 4m fixation, or esotropia or vertical tropia at 0.5 m (strabismic amblyopia); (2) anisometropia of ≥2.00 D SER (anisometropic amblyopia); or (3) hyperopia of ≥ +6.00 D SER. Unilateral amblyopia: If only one eye met the criteria. Bilateral amblyopia: If both eyes met the criteria separately (Xiao *et al.*, 2015). The RESC study did not include in its definition of amblyopia an inter-ocular difference ≥ two lines or astigmatism ≥1.50 DC.

5.2.4 The Avon Longitudinal Study of Parents and Children

The Avon Longitudinal Study of Parents and Children (ALSPAC): Williams *et al.* (2008) examined 7,825 children aged 7-years-old. Participants defined as amblyopic (3.6%) included those with a history of patching treatment and/or participants with an inter-ocular difference in BCVA of greater than or equal to two logMAR lines with BCVA worse than 0.3logMAR in the weaker eye in the absence of pathology. Note, cycloplegic refraction was not measured; hence the 4.8% hyperopia prevalence reported was most likely an underestimate.

5.2.5 The Vision in Pre-schoolers Study

Ying *et al.,* (2014) conducted a post-hoc secondary analysis of the VIP study data (for more detail, see section 2.2.9). All participants were part of the Head Start screening programme and were from low-income families of a variety of racial/ethnic groups. Amblyopia was defined as three lines or more inter-ocular difference in acuity with an amblyogenic factor (strabismus, anisometropia, an inter-ocular difference in SER ≥0.50 D when one or both eyes had hyperopia >+3.50 D) (Ying *et al.*, 2014). Bilateral amblyopia was defined as BCVA worse than 20/50 (6/15) for 3-year-olds and 20/40 (6/12) for 4-5-year-olds (Pascual *et al.*, 2014). One limitation to the VIP study may be that "presenting vision" and not "BCVA" was measured during the initial screening (Ying *et al.*, 2014).

5.2.6 Amblyopia prevalence in Sweden and Mexico

Ohlsson *et al.,* 2001 (Sweden) and 2003 (Mexico), defined amblyopia as BCVA < 20/40 worse eye, inter-ocular difference ≥ two-line, or history of treatment for amblyopia treatment. Ohlsson *et al.* (2001, 2003) examined 1,046 Swedish children aged 12-13 years in 2001 (amblyopia prevalence: 1.1%) and 1,035 Mexican children aged 12-13 years in 2003 (amblyopia prevalence: 2.5%). The examination included:

presenting VA using a LogMAR chart; cover test; examination of the red reflex and posterior pole; and refractive retinoscopy (note: Tropicamide 0.5% was used in preference to Cyclopentolate Hydrochloride 1%).

5.2.7 Amblyopia prevalence in Poland

Polling, Loudon and Klaver (2012) examined 591 children ranging in age from 2 months to 12 years; participants aged 3-12-years-old (453) were checked for amblyopia. Amblyopia was defined as BCVA≥0.3logMAR in the affected eye plus an inter-ocular acuity difference ≥ two lines, plus the presence of an amblyogenic factor (anisometropia ≥1.00 D, strabismus or co-existing anisometropia and strabismus). Amblyopia prevalence (3.1%) was primarily due to refractive error (69%). The examination included cycloplegic autorefraction, monocular presenting VA using a LogMAR chart at 3m (Lea symbols for participants aged 2-3 years, HTOV charts for children aged 4-6 years, ETDRS charts for participants aged ≥7-years-old); Stereo-acuity was measured using Lang II, cover test and motility testing.

5.2.8 Amblyopia in the Kingdom of Saudi Arabia

Aldebasi *et al.* (2015) examined 5,176 children aged 6-13 years in the Kingdom of Saudi Arabia. Amblyopia was defined as a difference in BCVA ≥ two lines between eyes or an absolute reduction in acuity poorer than 0.2logMAR (6/9.5 Snellen) in either eye; the amblyopia prevalence reported was 3.9%. The eye examination included: assessment of eye health (anterior and posterior segment examination plus funduscopic examination); presenting distance monocular VA using a logMAR chart; fixation pattern; cycloplegic retinoscopy/refraction and Brückner test and pupil examination.

5.2.9 Amblyopia prevalence in Japan

Matsuo and Matsuo (2005) conducted a retrospective study of 86,531 Japanese school children aged 6-12 years. Vision screening was carried out by school teachers and eye

disease screening by school ophthalmologists. A detailed questionnaire was sent to the teachers, responsible for health, in each elementary school in the Okayama prefecture. Amblyopia prevalence was 0.14%. However, strabismus prevalence was 1.28%. The questionnaires were completed by the teachers and provided information as to the number of children with a diagnosis of amblyopia and strabismus, and if known, a more detailed classification of amblyopia and strabismus was requested.

5.2.10   Amblyopia prevalence in Denmark

The Copenhagen Child Cohort 2000 study involved 1,335 11-12-year-old children (Hansen *et al.,* 2019). Amblyopia (1.5%) was defined as ≥ difference of 10 logMAR letters between fellow eyes with a BCVA<0.1logMAR in the affected eye. Bilateral amblyopia was defined as bilateral BCVA worse than or equal to 80 logMAR letters (0.1logMAR) combined with an AL shorter than 21.00mm. Cycloplegic refraction was not performed. When a definition of BCVA poorer than or equal to 0.3logMAR (70 logMAR letters) was applied, the reported amblyopia prevalence dropped to 1.0%.

5.2.11   Amblyopia prevalence in southwest China

The Mojiang Myopia Progression Study involved 1,656 7-8-year-old participants and 1,394 13-14-year-old Chinese Hani participants in southwest China. This study adopted the MEPEDS definition (see section 5.2.1) for amblyopia. Refractive error was reported as the major cause of amblyopia and strabismus (Zhu *et al.,* 2019). Amblyopia prevalence was 0.97% in 7-8-year-olds and 0.65% in 13-14-year-olds. Strabismus prevalence was 1.50% in 7-8-year-olds and 2.44% in 13-14-year-olds. Refer to Table 5.1, which summarises previous amblyopia prevalence studies.

Table 5.1 Amblyopia prevalence in schoolchildren studies

Source	Location	Number	Age (years)	Prevalence
Oliver and Nawratzki (1971)	Israel	5,329	1.5-6	1.2%
Ohlsson *et al.* (2001) *	Sweden	1,046	12-13	1.1%
Ohlsson *et al.* (2003) *	Mexico	1,035	12-13	2.5%
(RESC)†	China, India, Chile, Africa, Nepal, Malaysia	39,321	5-15	0.74%
Xiao *et al.* (2015)			5-7	0.78%
			11-13	0.76%
Robaei *et al.* (2006) § Robaei *et al.* (2008)	Sydney Australia	1,739	6	1.8%
		2,353	12	1.9%
Williams *et al.* (2008) ‡	United Kingdom	7,825	7	3.6%
Polling *et al.* (2012)	Poland	420	5-12	3.1%
Aldebasi *et al.* (2015)**	Saudi Arabia	5,176	5-15	3.9%
Hansen *et al.* (2019) ††	Denmark	1,335	11-12	1.5%
Zhu *et al.* (2019) **	Southwest China	1,656	7-8	0.97%
		1,394	13-14	0.65%

** BCVA ≤ 20/40 in the worse eye; †BCVA ≤ 20/40 with one potential cause: (1) esotropia, exotropia, or vertical tropia at 4 m fixation, or esotropia or vertical tropia at 0.5 m; (2) anisometropia ≥2.00 SER; and hyperopia ≥6.00 SER; ‡BCVA <20/40 for the worse eye, inter-ocular difference ≥2-line, or history of amblyopia treatment. §**Unilateral**: BCVA <20/40 in the worse eye, inter-ocular difference ≥2-line and with ≥1 amblyogenic factors: (1) anisometropic amblyopia: ≥1.00 D, without strabismus; (2) strabismic amblyopia: any heterotropia or history of strabismus surgery without anisometropia or high refractive error; (3) mixed strabismic-anisometropic amblyopia: (1) and (2) were present in combination; (4) stimulus deprivation amblyopia: past or present obstruction of visual axis. **Bilateral**: bilateral BCVA<20/40, with bilateral ametropia (≥4.00 D SER hyperopia ≥6.00 D SER myopia, or ≥2.50 D astigmatism); or with past or present bilateral obstruction of the visual axis. History of amblyopia or treatment. ¶BCVA ≥0.3logMAR, no pathology, ≥ 2logMAR lines inter-ocular difference + presence of an amblyogenic factor.** BCVA ≥0.2logMAR or ≥ 2logMAR lines inter-ocular difference. ††BCVA < 80 ETDRS letters (worse than 0.1logMAR, 6/7.5 Snellen) and ≥two lines difference between the eyes.*

The IES examination included: cover test at 3m and 0.4m, presenting stereoacuity (TNO anaglyph stereo test), and monocular logMAR VA assessment (unaided VA, pinhole VA, Presenting VA), cycloplegic autorefraction and dilated fundoscopy, to facilitate comparisons with other studies. Refer to Chapter six, where the IES methodology is outlined in detail. Based on the above information, and in order to enable comparison with other studies, the IES definition for amblyopia was based on the RESC definition (Xiao *et al.,* 2015) and is presented in section 10.3.

5.3   Dependence on Criterion

As seen in Table 5.1, definitions of amblyopia are diverse. Ohlsson (2005) highlighted the issue, suggesting the result of this definitional vagueness was a continued lack of clarity about the characteristics of amblyopia and its outcomes. Thus, prevalence rates for amblyopia vary greatly for many reasons, including no internationally agreed definition or vision threshold for amblyopia.

Studies that defined amblyopia as vision in worse eye ≥ 0.3logMAR and the percentage of amblyopia found were: Fan *et al.* (2007): 1.2%; Polling *et al.* (2012): 3.1%; Ganekal *et al.* (2013): 2.02%; Donnelly *et al.* (2005): 1.1% and Ohlsson *et al.* (2003):2.5%.

Studies that defined amblyopia as vision in the worse eye ≥0.2logMAR and the percentage of amblyopia found were: Friedman *et al.* (2009): 1.8%; MEPEDS (2008): 2.1%; Pai *et al.* (20102): 1.9% and Ohlsson *et al.* (2001): 1.1%. Studies that defined amblyopia as VA in worse eye ≥0.18logMAR were: Chia *et al.* (2010): 1.2% and Khandekar *et al.* (2009): 1.3%.

Prevalence also varied within a sample when different criteria were applied. For example, Robaei *et al.* (2006) study demonstrated this well when different criteria were

applied, the amblyopia prevalence ranges from 1.8% to 0.2%. Amblyopia was initially diagnosed in 1.8% of the study population, and this included children with a history of amblyopia treatment. When more stringent criteria were applied this result changed as follows: With VA worse than 0.2logMAR (6/7.5 Snellen) in the weaker eye, the prevalence rate was found to be 1.4%; if a two line difference in vision between fellow eyes was applied, the prevalence rate reduced to 0.7%. When the American Association for Pediatric Ophthalmology and Strabismus recommended criteria were used (VA of 20/40 (6/12) or worse plus two or more lines difference between eyes), the prevalence rate was 0.7%.

Chia *et al.*'s (2010) population-based study in Singapore diagnosed 1.2% of their study group with amblyopia. However, 2.8% of the sample met the VA criterion for amblyopia but did not meet the required amblyogenic factors required.

The Multi-ethnic Pediatric Eye Disease Study (2009) and Friedman *et al*. (2009) required the presence of at least one amblyogenic factor (see Table 5.1) (Varma *et al.*, 2006; Friedman *et al.*, 2008). Flom and Neumaier (1966) required an inter-ocular difference in VA between fellow eyes > one line (Flom and Neumaier, 1966).

5.4   Influence of ethnicity

The RESC multicentre study reported considerable variation in the prevalence of amblyopia across the participating ethnic groups: 1.44% in Hispanic, 0.93% in Chinese, 0.62% in Indian, 0.52% in Malay, 0.35% in Nepali and 0.28% in African children (Xiao *et al.,* 2015). The highest prevalence being 1.4% found in Hispanic children and lowest 0.28% in African children (Xiao *et al.*, 2015). Xiao *et al*. (2015) hypothesised a higher prevalence of amblyopia in European and East Asian children might be due to low pigment and its association with strabismus and disordered visual pathways (Guillery, 1996; Wolf, Rubin and Kodsi, 2005).

Ganekal *et al.* (2013), using a similar definition for amblyopia as the RESC, found the prevalence of amblyopia to be 1.1% in the population-based study of 4,020 Indian children aged 5-15 years, which was higher than RESC, which found 0.62% in its Indian cohort (Xiao *et al.,* 2015). The VIP study of American children of mixed ethnicity found the prevalence of amblyopia to be: 2.98% in the Asian population; 3.27% African-American; 3.48% Native American; 5.04% Hispanic and 5.40% in the non-Hispanic White population (Ying *et al.*, 2014). The VIP study used almost identical definitions for amblyopia as BPEDS, MEPEDS and BPEDS/MEPEDS combined, which facilitates comparison (Varma *et al.*, 2006). The prevalence of amblyopia in the African American population was found to be: 3.3% VIP; 0.8% BPEDS; 1.6% MEPEDS and 1.4% BPEDS/MEPEDS combined. The prevalence of amblyopia in the Asian populations using the same age and definition for amblyopia was found to be: 3.0% VIP study; 1.8% MEPEDS and 0.9% The Strabismus Amblyopia and Refractive Error Study in Singaporean children. The prevalence of amblyopia in the Hispanic population was: 5.0% VIP study and 2.8% MEPEDS. Interestingly, the non-Hispanic-White population showed more considerable variation in amblyopia prevalence: 5.4% VIP study; 1.9% BPED; 4% MEPEDS and 3.1% BPEDS/MEPEDS combined. The amblyopia rates were higher for each ethnic group in the VIP study, which could be due to the low socioeconomic status of the Head Start families (VIP study) or poor performance in VA testing by Head Start pre-schoolers (Ying *et al.*, 2014).

The prevalence of amblyopia in Japan was 0.14%; however, the definition of amblyopia used in this study was unclear, and strabismus patients were not included in the group found to be amblyopic, even though 1.28% of the study group were classified as having strabismus. While some of these strabismic participants may have had alternating strabismus, it is unlikely that all reported strabismus was alternating. The study was

retrospective and relied on questionnaires completed by schools (Matsuo and Matsuo, 2005).

Overall, the prevalence of amblyopia appears to be lowest in Korea 0.4% (Lim *et al.,* 2004) and highest in a non-Hispanic White population 5.4% (Ying *et al.*, 2014).

5.4.1 Bilateral versus unilateral amblyopia

Amblyopia can be unilateral or bilateral. Bilateral amblyopia is usually defined as reduced BCVA in both eyes, coupled with form deprivation during the critical period of visual development (Wang *et al.*, 2011). Bilateral amblyopia is reportedly less prevalent than unilateral amblyopia (Pai *et al.,* 2012; Robaei *et al*., 2006a, 2008; Friedman *et al.,* 2009). Friedman *et al.*'s (2009) population-based study found that less than 10% of those with amblyopia were found to have bilateral amblyopia. Pai *et al.* (2012) reported 1.9% unilateral amblyopia and 0.7% bilateral amblyopia prevalence in 1,422 participants aged 30-72 months in the SPEDS. Chia *et al.*'s (2010) study found a bilateral amblyopia prevalence of 0.36% in 3,009 Singaporean participants aged 48-72 months. Aldebasi *et al.* (2015) reported an amblyopia prevalence of 3.9% (3.24% unilateral and 0.66% bilateral) in 5,176 children aged 6-13 years in the Kingdom of Saudi Arabia; refractive error was responsible for 94.6% of amblyopia. Tarczy-Hornoch *et al.* (2011) examined data collected from MEPEDS and BPEDS and found that bilateral reductions in VA were associated with astigmatism ($\geq$1.00 DC), high hyperopia ($\geq$+4.00 D), socioeconomic disadvantage and Hispanic ethnicity.

5.4.2 Right versus left eye

Most studies found no difference in the prevalence of amblyopia in the right versus the left eye (Goh *et al.,* 2005; Robaei *et al.,* 2006a). Two studies found amblyopia was more likely to be present in the left eye and that this difference was statistically more significant in those with anisometropic amblyopia than with strabismic amblyopia

(Woodruff *et al.,* 1994; Repka, Simons and Kraker, 2010). The IES involved examining the prevalence of amblyopia in both the right and left eyes.

5.5   Effect of age on amblyopia prevalence

As amblyopia is considered to be a treatable condition (Holmes and Clarke, 2006; Cotter *et al.*, 2012), in communities with access to amblyopia treatment, the prevalence rates for amblyopia should decrease during the treatment ages (3-9 years). Robaei *et al.*'s (2006) study of children aged six years in Sydney, demonstrates this well as the amblyopia prevalence found was 0.7% but rose to 1.8% when those treated for amblyopia were included. There are many studies which examined whether amblyopia prevalence varies with age and many found that the prevalence of amblyopia did not decrease with age (Oliver and Nawratzki, 1971; Lithander, 1998; Chia *et al.*, 2010; Pai *et al.*, 2012). There were many reported reasons for this: incidence of new rates was equal to or higher than previously diagnosed rates (Oliver and Nawratzki, 1971); VA measurement in younger children was difficult to measure, and many were unable to complete crowded recognition VA tests (Tarczy-Hornoch *et al.*, 2011); Amblyopia was more prevalent in communities that were socially disadvantaged and medically underserved (Preslan and Novak, 1998; Williams et *al.,* 2008b), as found in Tarczy-Hornoch *et al*.'s (2011) examination of data collected from MEPEDS and BPEDS where bilateral decreased VA rates were higher in communities without social insurance.

5.6   Influence of other factors

Robaei *et al*.'s (2006) study of 6-year-olds in Sydney found an association between amblyopia and: gestational age; low birth weight (<2500 grams); pre-term birth (<37 weeks - fivefold higher chance of developing amblyopia); maternal smoking during pregnancy (marginal) and admission to a neonatal intensive care unit. Pai *et al.* (2012)

did not find any significant relationship between these factors in Australian pre-schoolers. A relationship between the families without health insurance, increased the likelihood of having reduced bilateral VA, was observed in Tarczy-Hornoch *et al.*'s (2011) analysis of data collected by MEPEDS and BPEDS. Simon's (2005) review found an association between the prevalence of amblyopia and lower social class. Pai *et al.* (2012) found no significant relationship between place of birth and prevalence of amblyopia.

The IES examined the relationship between amblyopia and gestational period, maternal smoking and socioeconomic status.

5.7 The relationship between amblyopia and strabismus

Inhibitory interactions between neurons processing non-fusible input from fellow eyes results in the fixing eye dominating cortical vision centres and the non-fixing eye suppressing (reduced response) (Wallace *et al.,* 2018). Over 50% of children with esotropia have amblyopia at the time of diagnosis (Birch and Stager, 1985; Dickey *et al.*, 1991). Although strabismus surgery may facilitate amblyopia treatment in some cases; however, many corrected patients with strabismus retain a small angle of strabismus which can result in local foveal suppression hence amblyopia treatment is still indicated postoperatively (Lam, Repka and Guyton, 1993; Repka *et al.*, 2005).

Reported strabismus prevalence in children ranges from 2.3% in 7-year-olds in the UK (Williams *et al.,* 2008a), 2.8% of Australian 6-year-olds (Robaei *et al.*, 2006c), to 3.6% in Asian and 3.4% in non-Hispanic White children in the US (McKean-Cowdin *et al.*, 2013). The highest RESC strabismus prevalence was in Chile at 9.9% (Maul *et al.*, 2000), and the lowest at 0.5% in India (Murthy *et al.*, 2002).

Strabismus was reported to be associated with premature birth and low birth weight in Sydney (Robaei *et al.*, 2006c).

5.8   The relationship between amblyopia and anisometropia

The visual system is geared towards similar refractive status in both eyes; for instance, Qin *et al.* (2005) found that the refractive error for approximately 85% of humans is within 1.00 D for fellow eyes. Anisometropia is a clinically significant difference in refractive error between fellow eyes (Barrett, Bradley and Candy, 2013). Thus, anisometropia is a significant risk factor for amblyopia and is said to be present in half to two-thirds of all cases of amblyopia found; for example, the MEPEDS found the proportion of amblyopes who have anisometropia to be 61% (Borchert *et al.*, 2010). Also, Flom and Bedell (1985) 66% and Aldebasi *et al.,* (2015) found that 77.7% of amblyopia was due to anisometropia. The reasons for the co-occurrence of amblyopia and anisometropia are the subject of much debate and research. Various hypothesis have been postulated for the coexistence of anisometropia and amblyopia: anisometropia causes amblyopia due to monocular blur giving rise to abnormal binocularity; amblyopia causes anisometropia due to failure of the emmetropisation process; or an as yet unknown trigger/anomaly disrupts emmetropisation and cortical function such as undetected micro-tropia or subtle pathology (Barrett, Bradley and Candy, 2013).

While some researchers have defined anisometropia as ≥0.75 D; however, Barrett *et al.* (2013), MacKenzie, (2008) and Shah *et al.* (2009) contested a difference in refractive error ≤+/- 0.75 D could be due to test-retest variability. Therefore, a more reliable definition in epidemiological studies is anisometropia ≥1.00 D (Barrett, Bradley and McGraw, 2004; MacKenzie, 2008; Shah *et al.*, 2009; Barrett, Bradley and Candy,

2013). The IES adopted this definition for anisometropia (≥1.00 D) in line with the NICER study (O'Donoghue *et al.*, 2013).

Anisometropia may be due to differences in AL of the eyes (Tong *et al.*, 2004; O'Donoghue *et al.*, 2013), or it can be refractive (Ingram, 1979; Qin *et al.*, 2005). Huynh *et al*. (2006) and Tong *et al.* (2004) found an association between anisometropia and increased AL. Differences in corneal toricity have been found in individuals with aniso-astigmatism (Huynh *et al.*, 2006; O'Donoghue *et al.*, 2013). Age also plays a part; the incidence of anisometropia appears to diminish rapidly after the period of 12 months old (Atkinson *et al.*, 1996).

5.8.1 Relationship between depth of anisometropia and amblyopia

A relationship between the depth of amblyopia and the degree of anisometropia has been established (Weakley, 2001; Leon, Donahue, *et al.*, 2008). Tarczy-Hornoch *et al.* (2011) found that 59.9% of participants with anisometropia were amblyopic; in addition, a linear relationship between anisometropia magnitude (range 1.00 D to 5.00 D) and the likelihood of reduced VA was found with a 100% of participants with 5.00 D of anisometropia amblyopic (Tarczy-Hornoch *et al.*, 2011). While many studies reported an increased risk of amblyopia with increased amounts of anisometropia, Levi *et al.* (2011) found the risk to be twice as high in anisometropic hyperopes as anisometropic myopes with the same level of anisometropia. Ying *et al.* (2013) found that the higher the degree of anisometropia in its preschool participants, the higher the inter-ocular difference in VA and the poorer the stereo-acuity. Of particular interest, Ying *et al.* (2013) found unilateral amblyopia was apparent with lower levels of anisometropia than previously considered amblyogenic: SER anisometropia or hyperopic anisometropia >+0.50 D; myopic anisometropia <-0.25 D; and cylindrical

anisometropia >0.25 DC. Furthermore, when compared with participants without anisometropia (isometropic), critical findings in Ying *et al.*'s (2013) study of amblyopia in preschool children demonstrated anisometropic participants had a significantly higher percentage of amblyopia (8% vs 2%); higher Inter Acuity Difference (0.07 vs 0.05 logMAR) and poorer stereo-acuity (145 vs 117 arc seconds).

5.8.2 Age amblyopia and anisometropia

The prevalence of anisometropia (inter-ocular difference ≥1.00 D) appears to be relatively high in children aged ≤ six months, stable from ages 12 months until the early teenage years and then increases with the onset of myopia (Barrett *et al.,* 2013). Anisometropia found in early infancy is unlikely to be permanent in the majority of cases (Deng and Gwiazda, 2012). Saunders, Woodhouse and Westall (1995) proposed that unless anisometropia is accompanied by strabismus, it may be unnecessary to correct anisometropia during the first year of life.

Leon *et al.* (2008) screened 199,079 children aged 0-6 years, mean age 3.7 years; the prevalence and depth of amblyopia increased with increasing magnitude of anisometropia. What is more, Leon *et al.* (2008) exposed a marked increase in amblyopia in anisometropic children with increasing age, where the prevalence of amblyopia in the anisometropic group varied from 14% in one-year-olds to 75% in five-year-olds.

Donahue (2006) investigated the relationship between anisometropia (>1.00 D), patient age and amblyopia, which involved examining the patient records of 119,311 children aged 0-7 years. The author observed that younger children with anisometropia had a lower depth and prevalence of amblyopia, adding that by age three years amblyopia had already developed. Donahue (2006) recommended earlier identification of anisometropia, ideally before the age of three years, to retard or possibly prevent the

development of amblyopia. Hence, preschool screening is vital to identify orthotropic anisometropia to prevent amblyopia from developing.

Abrahamsson and Sjöstrand (1996) suggested that a 5.00 D difference in SER is the limit to which the visual system can cope with between one and three years of age; with anisometropia ≥5.00 D the visual system was unable to compensate, and amblyopia developed. For children with anisometropia between 2.00 D and 5.00 D, some children developed amblyopia, and some did not.

5.8.3 Screening for anisometropia

The detection of anisometropic amblyopia in the absence of strabismus is usually later than strabismic amblyopia (Woodruff *et al.,* 1994; Chua and Johnson, 2004; Shah *et al.*, 2009) due to the lack of any obvious physical signs. As previous research has identified a strong association between anisometropia and the development of amblyopia; for instance, in De Vries's (1985) longitudinal study, amblyopia developed in 50% of those with orthotropic anisometropia. Similarly, Abrahamsson *et al.*'s (1990) longitudinal study revealed the presence of amblyopia in 53% of their participants with orthotropic anisometropia, and also 60% of their anisometropic participants became amblyopic. Hence identifying and treating anisometropia, in order to prevent visual impairment due to anisometropic amblyopia is a public health issue (Hartmann *et al.*, 2000). Vision screening is designed to identify orthotropic anisometropia to prevent amblyopia from developing. Newer vision screening technologies such as photo screening (Spot Vision Screener, Welch Allyn) detect amblyogenic factors rather than measured amblyopia and are therefore suitable for preschool children. However, as many of those with amblyogenic factors may not develop amblyopia (Donahue *et al.,* 2003), for children aged ≥ 5-years-old, VA measured monocularly using crowded optotype should be used

in preference to eccentric photo-screening to detect decreased VA (Donahue *et al.,* 2013).

5.8.4 The relationship between anisometropia and ametropia

Several studies have identified a link between anisometropia prevalence and the level of ametropia (Dobson *et al.*, 2008; O'Donoghue *et al.*, 2013). The NICER study identified a link between anisometropia and moderate (≥+2.00 D) hyperopia in children aged 12-13 years, and that anisometropic eyes had a greater AL (O'Donoghue *et al.*, 2013). Similarly, Huynh *et al.* (2006) noted a higher incidence of anisometropia in children with moderate hyperopia when compared to those with mild hyperopia (≥+0.51 D, ≤+2.00 D). The VIP study examined the association of hyperopia with vision disorders and found that there was a significantly higher incidence of anisometropia for children with hyperopia ≥+3.25 D (Huynh *et al.*, 2006; Kulp *et al.*, 2014).

In contrast, Tong *et al.* (2004) and Qin *et al.* (2005) found anisometropia to be more common in participants with myopia. Likewise, Shih *et al*. (2005) discovered a prevalence of anisometropia of 9.3% in Taiwan; this was associated with a high prevalence of myopia. Dobson *et al.* (2008) found anisometropia ≥1.00 D in 15% of the 1,041 Native American school children aged 4-13 years. Dobson *et al.* (2008) found SER anisometropia linked with cylindrical anisometropia in their study, but interestingly, there was a significant group of children who had astigmatic anisometropia without SER anisometropia.

In summary, further analysis of risk factors associated with anisometropia is essential; why similar genetic, demographic and lifestyle variables can affect fellow eyes differently possibly causing differential growth in AL merits investigation due to the association with amblyopia (Barrett, Bradley and Candy, 2013).

The IES examined the relationship between anisometropia prevalence and amblyopia.

5.9 The relationship between amblyopia and refractive error

Hyperopia ≥+3.25 D is associated with amblyopia; the magnitude of hyperopia is associated with increased amounts of amblyopia (Kulp *et al*., 2014).

Correcting moderate hyperopia in the absence of esotropia or reduced VA is not routinely considered for many reasons: financial cost of spectacles; psychological costs associated with wearing glasses; possible interference with the emmetropisation process consigning children to a lifetime of hyperopia (Lambert, 2016). A longitudinal study involving infants born with moderate hyperopia (no strabismus and refractive error between +3.00 D and +3.75 D) found 90% were emmetropic by three years of age and none developed esotropia (Dobson and Sebris, 1989). However, hyperopia >+3.75 D by age three years should be corrected before four years to prevent amblyopia (Donahue *et al.,* 2003). (The relationship between amblyopia and hyperopia is discussed in section 4.1.2.). The IES examined the relationship between amblyopia prevalence and hyperopia. Astigmatism ≥1.00 DC is significantly associated with amblyopia and ideally, should be corrected by aged three years to prevent amblyopia development (Harvey, Dobson and Miller, 2006; Harvey, 2009).

5.10 Form deprivation amblyopia

Ptosis, congenital cataract, early-onset cataract, corneal opacities, nasolacrimal duct obstruction or any orbital inflammation or inter-ocular inflammation or vitreous haemorrhage may lead to visual deprivation amblyopia (Wallace *et al.*, 2018). While form deprivation amblyopia is the rarest form of amblyopia, it is the most challenging to treat (von Noorden, 1981; Barrett, Bradley and McGraw, 2004).

5.11 Amblyopia summary

Amblyopia and amblyogenic factors such as strabismus and refractive errors are the leading causes of vision loss in schoolchildren (Ying *et al.*, 2013). Amblyopia depends on the criteria used to diagnose it. Epidemiological population-based studies have found the prevalence to be somewhere between 0.8% and 3.6% (see Table 5.1). Global estimates for the prevalence of amblyopia in children range from 0.2% (Matsuo and Matsue, 2005) to 4.7% (Drover *et al.*, 2008). Amblyopia can be subdivided into strabismic, anisometropic and combined anisometropic and strabismic (mixed) (Barrett, Bradley and Candy, 2013). Visual deprivation provided by uncorrected ametropias such as hyperopia and astigmatism is reported to be the significant causes of amblyopia (Dobson *et al.*, 2003; Donahue, 2006; Pai *et al.*, 2012). The prevalence of amblyopia appears to be affected by ethnicity (Xiao *et al.*, 2015). In societies where amblyopia is treated, the prevalence falls and seems to be higher in socially disadvantaged communities (Robaei *et al.*, 2008). Amblyopia prevalence is not affected by age post the sensitive period of visual development (Wallace *et al.*, 2018).

While quality of life issues and amblyopia were attributed to amblyopia treatment in the 1958 findings from the British birth cohort where participants were 41 years-old (Rahi, Cumberland and Peckham, 2006) and not the visual disruption. However, ocular pathology is less likely to be an issue at aged 41 years. Life expectancy has increased in most parts of the world and is now higher than 80 years in the UK, Australia, North America, Scandinavia and Japan (https://ourworldindata.org/life-expectancy). With the lifetime risk of blindness or bilateral visual impairment significantly higher for amblyopes due to ocular pathology (in older amblyopes) or trauma (in younger amblyopes) in the non-amblyopic eye (Rahi *et al.,* 2002; Chua & Mitchell 2004), and as people are living longer lives the duration of time with impaired eyesight is also longer. The consequential increased cost to the public health system further goes to emphasise

the importance of addressing eye care conditions in early life. Hence, treating amblyopia in childhood is essential to prevent potential visual disability in later life (Tommila and Tarkkanen, 1981).

The IES defined amblyopia as BCVA $\geq$0.3LogMAR, plus the presence of an amblyogenic factor. The IES examined the relationship between amblyopia prevalence and: ametropia, strabismus, anisometropia, ethnicity, academic performance, socioeconomic status, urban/rural living environment and diet and lifestyle factors.

Chapter 6 describes the methods used in the IES. The testing protocol and instrumentation used are also discussed.

6 SAMPLING AND MEASUREMENT METHODS

6.1 Introduction

The extent of refractive errors in Ireland is not reliably known, and studies to date suggest that there is wide variation in prevalence throughout the world (Dunaway, 2006); hence, epidemiological studies in Ireland are necessary. The protocols employed in the IES reflect the recent international initiatives designed to promote standardised sampling and measurement protocols and facilitate comparison of data across studies (Negrel *et al.*, 2000; Ojaimi *et al.*, 2005; O'Donoghue *et al.*, 2010; Logan *et al.*, 2011).

6.2 Materials and Methods

6.2.1 Ethics

Approval for the study was obtained from the Technological University Dublin (TU Dublin) (formerly known as the Dublin Institute of Technology) Research Ethics Committee. The research adhered to the principles of the Declaration of Helsinki.

6.2.2 The study area, sample identification and sample size

The IES is a cross-sectional study which involved testing 1,626 children's eyes in schools in Ireland. To facilitate follow-on assessments, longitudinal studies, and comparisons with other studies, two age cohorts were selected: 728 schoolchildren aged 6-7 years; and 898 schoolchildren aged 12-13 years of age. Ideally, prevalence studies ought to be population-based. However, door to door recruitment of participants was beyond the scope of the current study due to limited personnel (all data was collected by S. Harrington), budgetary and time restrictions. Hence, in line with the NICER study (O'Donoghue, *et al.,* 2010) and the AES (Logan *et al.,* 2011) a stratified random cluster sampling (with schools forming clusters) procedure was employed to select the target

population. This was considered appropriate in Ireland as education is compulsory for all children from the ages of 6 to 16 years. In contrast, door to door recruitment was carried out in the RESC studies as education was not compulsory in some of the study locations (Negrel *et al.,* 2000).

6.2.2.1 Sample size calculation

The sample size was calculated based on a predicted prevalence of myopia, which was 3-5% for 6-7-year-olds as reported in the NICER study (O'Donoghue *et al.*, 2010), with a 1.00% precision (standard error) considered appropriate. As the study used cluster sampling in the design effect, the intra-class correlation coefficient was considered. The design effect was the ratio of the between-cluster variance to the total variance. For the 12-13-year-old group, a 1.5% precision on a 10% prevalence of myopia. Also, a participation rate of 75% was factored in to allow for non-participation. Hence the sample size was further inflated by 1/participation rate. The assumed participation rate was 75% based on the NICER study. Thus the sample size was inflated by a factor of 1.33. Thus a sample size of 1,500 (700 6-7-year-olds and 800 12-13-year-olds) was calculated. These prevalence levels of myopia came from the NICER study (O'Donoghue *et al.*, 2010). The sampling strategy was developed in conjunction with Professor John Kearney, a lecturer in epidemiology and nutrition in the Biology department at TU Dublin and Dr Jim Stack, a statistician in Waterford Institute of Technology.

6.2.2.2 Selection of participating schools

A stratified random sampling procedure was used to select the study population. Schools were stratified by (a) primary/post-primary status (b) urban/rural status, (c) and socioeconomic (disadvantaged/advantaged) status.

Primary/post-primary status: In Ireland, children attend primary school between the ages of four to 12 years. However, it is not compulsory until the age of six years. The post-primary school (secondary school) cycle generally lasts from five to six years, although it is not mandatory for children to remain in secondary school once they are 16 years old, or have completed three years in post-primary education.

Socioeconomic status: The Irish state supports schools categorised as Delivering Equality of opportunity In School (DEIS) (Anderson, 2006). The IES classified socioeconomic status by DEIS status: DEIS schools were defined as socioeconomically disadvantaged, other schools were designated as advantaged. Twenty one per cent of schoolchildren in Ireland attend DEIS schools (www.education.ie/en/Schools-Colleges/Services/DEIS-Delivering-Equality-of-Opportunity-in-Schools-/).

Urban/rural status: Using postcode (known as Eircode in Ireland) classification of participants' urban rural status was beyond the scope of the present study as many participants did not provide information regarding their home address and all correspondence with participants/legal guardians took place through the schools. Therefore, in line with the NICER study schools were also stratified by urban/rural status. The Irish Central Statistics Office defines urban and rural areas as follows:

"*The term Aggregate Town Area or Urban area refers to settlements with a total population of 1,500 or more. The term Aggregate Rural Area refers to the population outside Aggregate Town areas and includes the population of settlements with a population of fewer than 1,500 persons*" (https://www.cso.ie/en/releasesandpublications/ep/p-cp1hii/cp1hii/bgn/)

In line with the NICER study, areas were categorised as "rural" if the population density was less than ten persons per hectare (10,000 square metres), otherwise urban (O'Donoghue *et al.*, 2010). According the 2016 Irish census 64% of the population

Ireland live in urban environments (https://www.cso.ie/en/releasesandpublications/ep/p-cp3oy/cp3/urr/).

The IES had, therefore, eight strata in all (=2x2x2). Within each stratum, schools were randomly selected from a complete list (sampling frame) of schools provided by the Irish Department of Education and Skills. The random number generator, from the statistical programming language R (R Foundation for Statistical Computing, Vienna, Austria), was used for this purpose. However, for logistical reasons, schools were excluded where the relevant class size fell below 20. This restriction did not apply to DEIS schools, where small class sizes are the norm. A reserve list of schools was generated to be used in case of non-participation by schools in the first list. The approximate locations of participating schools are presented in Figure 6.1. In line with the Growing up in Ireland study the precise location and names of the participating schools cannot be reported in order to preserve participant anonymity (Thornton *et al.,* 2011).Within the selected schools, all children in the appropriate age and year group were invited to participate. Children who did not assent to the instillation of the eye-drops were not excluded from participating; however, their results were excluded from the data analyses.

Figure 6.1 Map of Ireland and Northern Ireland (Peter Hermes Furian, 2015). The approximate locations of the participating schools are denoted by the red triangles.

Ethnicity: for this study participants was categorised by ethnic grouping; based on previous literature of refractive error prevalence, which found refractive error varied with ethnicity (Logan *et al.*, 2011; French *et al.*, 2013a). Participants' ethnicity was assessed by the study coordinator and confirmed by the parent/guardian through self-report. Participants were categorised as either White, Traveller or non-White (black, South Asian and East Asian participants combined). There is a precedence for the categorisation of non-White in papers addressing public health in populations where the population are mainly homogenous (Seddon, Schwartz and Flowerdew, 1983; Horowitz, Brennan and Reinhardt, 2005; Nguyen *et al.*, 2007). According to the 2016 Irish census, 9.9% of children aged between 5-14 years were non-White. According to the Irish census (2016), the Irish population is predominately White (90.1%), the sampling frame was designed to represent refractive error and VI in schoolchildren in Ireland. The potential sample size of East Asian, South Asian, and Afro Caribbean participants were too low to justify their separate sampling. Although the Traveller community originally descended from the White Irish population, they diverged from the settled population approximately 360 years ago. High levels of autozygosity within the Traveller community has implications for disease mapping within Ireland (Gilbert *et al.*, 2017). The Traveller community was formally recognised as an ethnic minority on the 1st of March 2017.

6.2.2.3 Participant recruitment

Participants were 728 children aged 6-7 years in first class in primary school and 898 children aged 12-13 years in the first year in post-primary school. Selected schools were contacted and, with agreement from school principals, an information pack was distributed to parents/guardians of children aged 6-7 years in primary schools and 12-13 years in post-primary schools. Each package contained a letter of invitation outlining the study, an information sheet explaining the testing procedures, a storyboard to better

explain the study to participants, the study questionnaire, and a consent form. (See Appendix 1 for an example of the parental information, Appendix 2 for the child information and storyboard and Appendix 3 has the consent form and parental questionnaire).

With regard to parental consent, detailed information leaflets were provided, along with the opportunity to raise questions and to consider participation (2-3 weeks in advance of the examination day) in the study. Parents were required to confirm their required parental status and or legal guardianship of the child before providing informed consent, which was a pre-requisite to participation in the study. The consent of only one parent/legal guardian was required for participation.

Good practice also required the child's agreement to participate (informed assent), and this was sought independently before the examination. The nature of the child's involvement in the decision-making process was dependent on their age and maturity, as well as on an evaluation of their ability to understand the nature, purpose and implications of what was involved and to make a decision about their involvement. The IES information pack storyboard outlined the IES examination to make the study more accessible to children (see Appendix 3). Child assent was a necessity for inclusion in the study and overrode parental consent when a child decided not to assent. Children were made aware that their participation was entirely voluntary and that they were free to withdraw at any time and without any negative consequences attached to this decision. The researcher explained the purpose of the research to the children in a way in which they could understand, using language which took account of the children's verbal abilities. The researcher ensured the physical setting (classroom or hall in their school) was one in which the participants felt relaxed, and to which they were given time to adapt and become comfortable. The researcher was sensitive in responding to the

children's verbal and non-verbal communications and gave more/less time to the study methodologies as the children dictated. Data collection took place on school premises and within school hours.

Data from eight children who declined eye drops were excluded from the analysis.

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to the programme of research; participants' parents/legal guardians and home school liaison officers were involved in the design of the study, the informational material to support the data collection and school involvement, and assessed the burden of participation from the patient's perspective. For example, the IES study questionnaire was based on the NICER study questionnaire with input from epidemiology, dietetics and focus group feedback. Furthermore, the questionnaire was refined following multi-site focus group user testing, which involved a cognitive walkthrough evaluation in assessing the burden associated with and the time to complete the questionnaire (Polson *et al.*, 1992; Collins, 2003). Following focus group feedback a storyboard which outlined the IES examination was designed to make the study clear to children; the questionnaire was shortened by removing non-essential questions and simplifying the wording of the remaining questions to maximise accessibility; and a statement advising parents/guardians to skip any questions they felt uncomfortable answering was added to the document. At the end of the study, results and findings were provided to all participants.

6.3   Experimental protocol and techniques

All of the IES participants were tested by S. Harrington on school premises, and within school hours, in groups of four to six. It took between 60 to 90 minutes to complete testing on each group. The testing and examination protocol included VA measurements

(presenting, unaided and pinhole), presenting stereo-acuity, ocular motility and alignment evaluation, cycloplegic autorefraction, height and weight measurement, and dilated fundoscopy (see Figure 6.2).

6.3.1 Parental questionnaire

Parents or legal guardians completed a participant and parental eye and health history and a children's lifestyle questionnaire (see Appendix 3). The completed questionnaires and consent forms were collected from the participating schools in advance of data collection.

Examination enrollment

|

Questionnaire completion and collection

|

Uncorrected VA assessment @ 3m and 40cm

|

Acuity with spectacles / Pinhole vision

|

The amplitude of accommodation (Royal Air Force rule)

|

Ocular motility evaluation, pupillary reflexes and a cover test

|

Presenting Stereo-acuity (TNO test), colour vision (Hardy Rand Rittler fourth edition)

|

Instillation of 0.5% Proxymetacaine Hydrochloride, and 1% Cyclopentolate
Hydrochloride 1.0%

|

Height (Leicester scales) and weight (digital scales)

|

Eye dominance (the Dolman method) and hand dominance (demonstration of which
hand used for writing)

|

Fundoscopy (dilated direct ophthalmoscopy)

|

Biometry

|

Auto-refraction

|

Report

Figure 6.2 Ireland Eye Study workflow

6.3.2 Visual acuity assessment

Assessment of monocular distance visions (presenting, unaided, and pinhole), was carried out using the GOOD-LITE Sloan letters logMAR chart for testing at 3m (refer to Figure 6.2). The logMAR chart is a proportionally spaced logMAR chart which features a strict logarithmic progression of optotype line sizes range from 1.00 (6/60) to -0.3 (6/3). A light meter was employed to ensure the test luminance did not fall below 120 cd/m2. Participants were tested monocularly at a distance of 3m (refer to Figure 6.4). This distance was carefully measured before testing, and floor stickers were used to ensure the distance did not alter during the examination day. Visual acuity was recorded using the by-letter scoring system and recorded in logMAR notation. Participants were observed to ensure they were not squinting while reading letters. The right eye was tested first, followed by the left eye and fellow eye occluded using a frame mounted occlude. Similar to the Avon Longitudinal Study of Parents and Children (ALSPAC) (Williams *et al.,* 2003), pinhole acuity was used as a surrogate for BCVA. A recent study demonstrated good agreement between pinhole acuity and best corrected visual acuity and recommended it as a test for VI not correctable with spectacles (Kumar *et al.*, 2019).

Where participants presented wearing spectacles, VA was measured first unaided and then with their spectacles; one of each of the three acuity charts (refer Figure 6.3) was used to examine the right eye ensuring a different chart was used for the left eye to ensure participants had not memorised the letters. When children scored less than < 0.1logMAR (6/7.5 Snellen) (12-13 years) and < 0.2logMAR (6/9 Snellen) (6-7 years) VA was measured monocularly using the pinhole (refer to Figure 6.5).
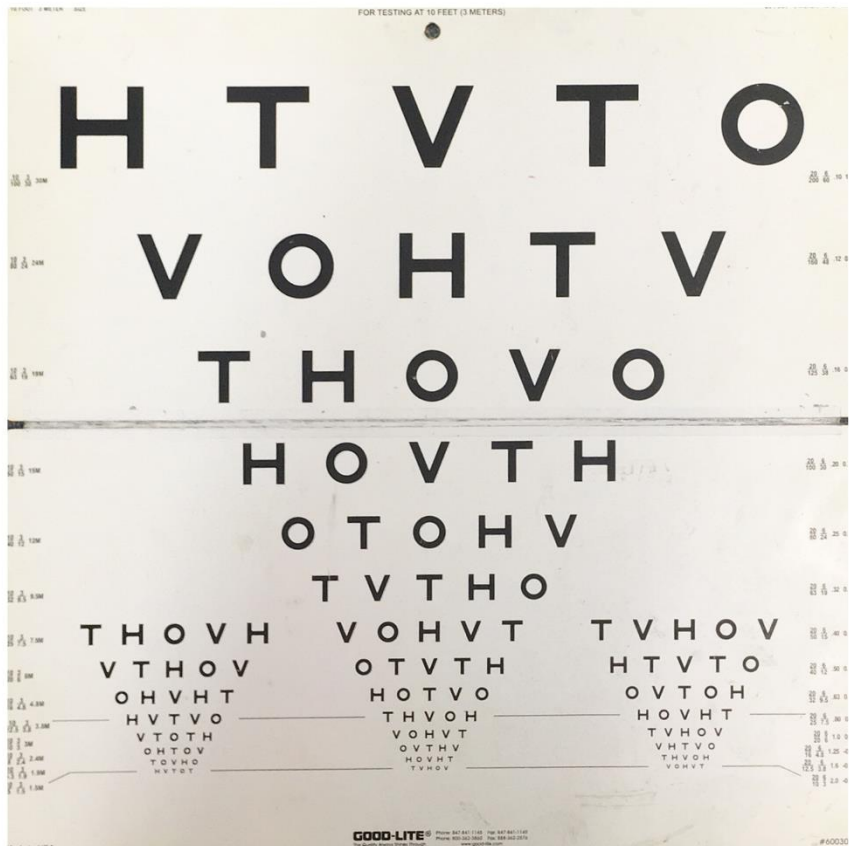
Figure 6.3 The GOOD-LITE Sloan letters logMAR chart for testing at three metres (Author's own, 2015)

Figure 6.4 Participants aged 12 years (left image) and six years (right image) wearing monocular occluder (Author's own, 2015)

Figure 6.5 Pinhole acuity assessment (Author's own, 2015)

Near visual acuities were measured unaided using the Sonsken logMAR near test chart (Novomed limited, Maidstone, ME199AG, UK) card at 40cm (refer to Figure 6.6). The 40cm was measured carefully before testing using the cord attached to the chart. Proportionally spaced logMAR line sizes range from 1.20 (6/126) to 0.0 (6/6).
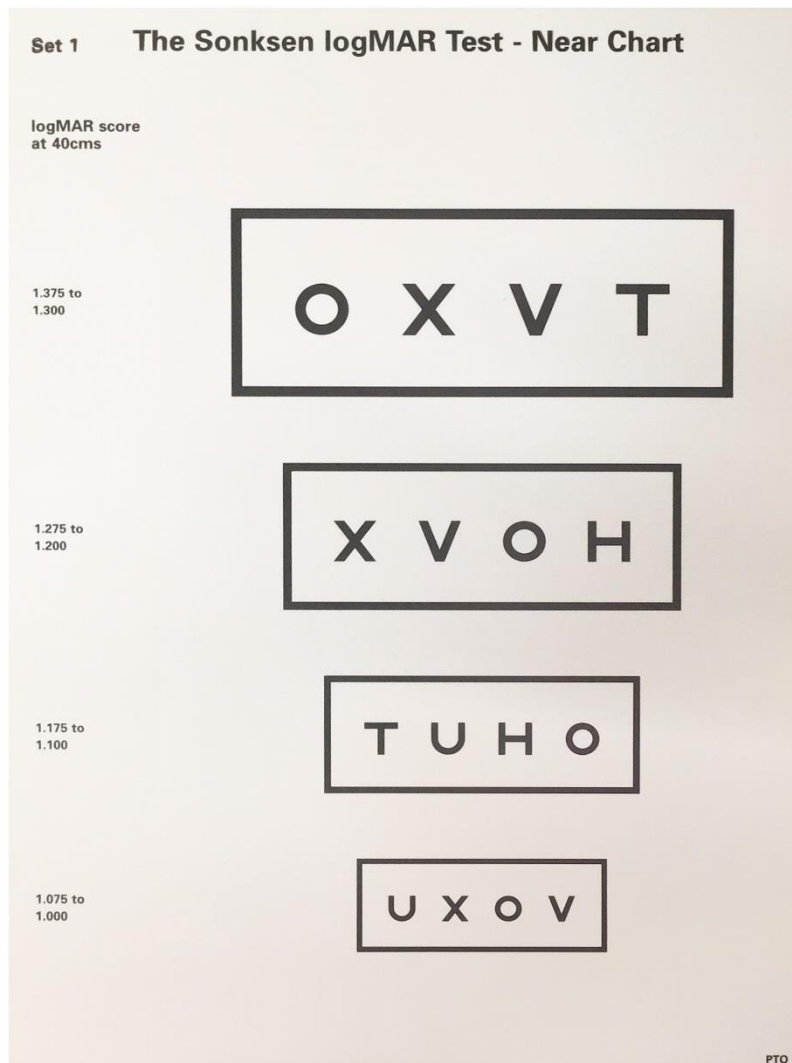
Figure 6.6 The Sonsken logMAR near test chart (Author's own, 2015)

The amplitude of accommodation was measured binocularly using the Royal Air Force rule push up method. Accommodation near point (recorded in dioptres) was measured with the N5 text as the accommodative target and defined as the point on the rule where

the child first indicated blurring of the target. The amplitude of accommodation was not measured monocularly which is a study limitation.

6.3.3 Binocular vision status

Strabismus was identified using the cover-uncover test at both 3m (using the smallest letter on the logMAR chart that could be seen clearly with each eye) and at 40cm (using an appropriately sized fixation target on a Budgie stick) and corneal reflex observation. Strabismus was categorised as esotropia, exotropia and vertical tropia.

Ocular motility evaluation was carried out using a pen torch, followed by pupillary reflexes, Brückner and Hirschberg reflex assessment. Two participants failed motility assessment and were referred to their general practitioner; one of which had orbital rhabdomyosarcoma and the other had a query of Browns syndrome.

Presenting stereo-acuity was measured using the Toegepast Natuurwetenschappelijk Onderzoek (TNO) Anaglyph stereo test (Richmond products, South San Francisco, CA 94080, USA). Previous research found that the TNO stereopsis test has a sensitivity of 100% when screening for amblyopia using a referral criterion of 240 seconds of arc (Walraven and Janzen 1993). The TNO test plates were well illuminated (daylight) and presented squarely in front of the participant (not rotated to the right or the left) at a distance of 40cm. The TNO test consists in total of seven plates, including three screening plates (retinal disparity, 1980 seconds of arc), three quantitative plates (retinal disparities ranging from 15 to 480 seconds) and a suppression test. Once the participants were wearing the required red/green goggles (with spectacles if worn), the seven TNO test plates were presented. Participants who did not appreciate stereo-acuity using the TNO stereo test were retested using Frisby plates (Clement Clarke International limited, Edinburgh Way, Harlow, Essex, UK) before confirming the absence of stereo-acuity. The Frisby Stereo-test consists of three transparent plates of different thickness (6mm,

3mm, and 1.5mm). The plates were presented against a clear background at a distance of 40cm. No special glasses are needed when performing this test as it involves real targets and is, therefore, a test of natural vision. Participants who failed to detect the target on the 6mm plate presented at 40cm were deemed not to have stereo-acuity.

The hand predominately used for writing and drawing was recorded as the dominant hand. To determine ocular dominance the hole-in-card Dolman test was used. The participant held a 30cm light grey square card, with both hands, at arm's length. With both eyes open the subject viewed a target through a 3cm hole. The examiner alternatively occluded each eye to determine which eye aligned with the hole and the target. With the dominant eye covered the participant could not see the target, and in contrast, with the non-dominant eye covered the subject continued to see the target (Wang *et al.,* 2016). This process was repeated three times.

6.3.4 Colour vision assessment

Colour vision testing was carried out binocularly using the Richmond Hardy-Rand-Rittler fourth edition colour vision test, with the habitual prescription in place, at a distance of 70 cm in natural daylight prior to the instillation of cycloplegic eyedrops. The Hardy-Rand-Rittler test combines suitability for non-numerate subjects with the ability to screen for tritan CVDs and good sensitivity (Cole, Lian and Lakkis, 2006). The test consists of four demonstration plates, six screening plates, and 14 diagnostic plates (10 plates for Protans and Deutans; four plates for Tritans). The demonstration plates act as a control; identification of the symbols only requires an understanding of instructions and adequate vision and does not require colour vision. Symbols on the subsequent plates are made up from spots of colours which lie on the protan, deutan or tritan achromatic confusion loci and the colours become increasingly saturated as the test proceeds. Participants who failed to correctly identify and locate any symbols on

any of the six screening plates were tested on the diagnostic plates (pages11-24) to confirm CVD type. Hence the colour vision screening fail criterion was one missed screening plate. All participants correctly identified and located the symbols on the screening plates (plates 1-4).

6.3.5 Participant height and weight

Participant height (in centimetres) was measured using the Leicester height measure MKII (Invicta Plastics limited, Leicester LE3 1UQ, England). Weight (in kilograms) was measured using digital scales Seca 813 (Sönke Vogel, Geschäftsführer, 22089 Hamburg). This instrument featured a step-off facility, once the measurement was taken the instrument display advised the participant to step off, five seconds after the participant stepped off the scales the result was displayed and recorded by the examiner. This ensured that participants did not see the measurement taken. Participants removed shoes for both height and weight measurements (see Figure 6.7). All participants, bar one, were weighed and had their height measured. One 12-year-old participant was a wheelchair user, and it was not possible to take height and weight measurements on the school premises.

Figure 6.7 Leicester height measure and Seca 813 digital scales (Author's own, 2016)

6.4   Refraction

Cycloplegic refraction is the gold standard for epidemiological studies, not only in children but also in adults up to the age of fifty years (Morgan *et al.*, 2015). The standardised use of cycloplegia is essential in studies involving young children where myopia prevalence is low and even small amounts of pseudo myopia will significantly affect prevalence estimates (Morgan, French and Rose, 2020). Cycloplegic refraction is essential for studies addressing associated risk factors (Pan *et al.*, 2012). Without cycloplegia measures of refractive error categories, including spherical equivalent, are unreliable (Zhao *et al.*, 2004). Indeed lack of cycloplegia results in significant misclassification of refractive status even in young adults (Sun *et al.,* 2018). This is particularly important when reporting refractive error prevalence, as to date, there is no reliable way of adjusting measures of refraction without cycloplegia to account for cycloplegia (Fotouhi *et al.*, 2012). Failure to use cycloplegia has been shown to result in

overestimation of myopia and underestimation of hyperopia (Fotedar *et al.,* 2007). For example, a study involving 2,223 Australian 12-year-olds which measured refractive status pre and post instillation of Cyclopentolate Hydrochloride 1% reported that 17.6% of the 12-year-old participants were misclassified as myopic, pre cycloplegia (Fotedar *et al.,* 2007). Similarly, in the Tehran Eye Study, where 3,501 participants were examined pre and post cycloplegia, myopia prevalence was overestimated pre compared to post cycloplegia, in between 4-7% 5-50-year-olds (Fotouhi *et al.*, 2012).

6.4.1 Cycloplegia

In order to produce adequate cycloplegia with minimum systemic side effects, the eye drops protocol was as follows: one drop of topical anaesthetic (Minims Proxymetacaine Hydrochloride 0.5% w/v, Bausch & Lomb, UK), was followed by one drop of Cyclopentolate Hydrochloride (Minims, 1% w/v, Bausch & Lomb, UK) for White participants; non-White participants were administered two drops of Cyclopentolate Hydrochloride 1% five minutes apart. While a single drop of Cyclopentolate Hydrochloride 1% has been reported to produce adequate cycloplegia when compared to using two or three drops (Bagheri *et al.*, 2007), two drops of Cyclopentolate Hydrochloride 1% were found more effective for hyperopic South Asian participants with dark irides (Mohan and Sharma, 2011). Systemic absorption was reduced by advising the participant to close their eyes, post drop instillation, and compressing the lacrimal sac at the medial canthus during and following the instillation of the drops (Shah, Jacks and Adams, 1997). Both Cyclopentolate Hydrochloride 1%, and topical anaesthetic Proxymetacaine Hydrochloride 0.5% are routinely used in optometric practice as they temporarily reduce the participant's ability to focus and cause dilation of the pupil, facilitating more accurate measurements to take place. Studies examining residual accommodation when establishing clinical protocol recommend Cyclopentolate Hydrochloride 1% (Manny *et al.*, 1993). Cyclopentolate Hydrochloride 1% has been

widely employed as the drug of choice for epidemiological studies on refractive error (Negrel *et al.*, 2000; O'Donoghue *et al.*, 2010; Logan *et al.*, 2011).

Proxymetacaine Hydrochloride is a short-acting topical anaesthetic which causes little irritation on instillation (Rosenwasser, 1989). Cyclopentolate Hydrochloride is unstable at pH neutral and is therefore acidified to a pH of 4; this results in considerable discomfort and stinging on instillation. This use of Proxymetacaine Hydrochloride prior to Cyclopentolate Hydrochloride reduced the discomfort, and reflex tearing, thereby facilitating absorption of Cyclopentolate Hydrochloride (Shah, Jacks and Adams, 1997). As Proxymetacaine Hydrochloride is a topical anaesthetic, it may increase the permeability of the cornea thereby facilitating an increased rate of absorption of Cyclopentolate Hydrochloride in the anterior chamber receptor sites (Haddad *et al.*, 2007). Once it was established cycloplegia had been achieved (pupillary reactions non-responsive to light and accommodation amplitude less than 2.00 D on push-up test), at least 20 minutes after instillation of the eye-drops, autorefraction was carried out. The representative value for SER - sphere plus half the cylindrical value - was used in subsequent analysis without any adjustment for accommodation.

6.4.2 Autorefraction

Cycloplegic autorefraction (Dong Yang Rekto ORK 11 Auto Ref-Keratometer, Everview Corp. Seoul, Korea) was used to determine refractive error (Ejimadu, Paul and Efird, 2015). The Dong Yang Rekto ORK 11Ref-keratometer range is -30.00 D to +25.00 D and cylindrical range +10.00 DC to -10.00 DC. When the alignment of the instrument was adequately achieved, the system was automatically activated, which ensured consistency in measurement and removed operator bias in the assessment of clarity of the mires. The calibration was checked at each testing site before commencing data collection using the model eye. Also, automatic checks took place on switching on

the device and after that, after every ten participants. This closed field autorefractor has been used in other studies (Ejimadu and Onua, 2014; Ejimadu, Paul and Efird, 2015). While open-field auto-refractors are preferable when cycloplegia is not used (Gwiazda and Weber, 2004), due to budgetary constraints, the Rekto Autoref Keratometer was used instead of the Shin Nippon which was used in both the AES and NICER study. Therefore, there could be a difference in the results found in the IES when compared to the NICER study and the AES. However, under cycloplegic conditions, the use of close-field autorefractor on refractive outcomes is minimal (Xiong *et al.*, 2017b), therefore, no adjustment was made for residual accommodation in the present study.

On completion of the eye examination, all participants received a pair of post mydriatic disposable sun-spectacles (refer to Figure 6.8).

Figure 6.8 Post mydriatic disposable sun-spectacles (Author's own, 2017)

6.4.3 Biometry

Measuring the eyes ocular components provides critical information regarding myopia progression, and the IOLMaster provides quick, repeatable measurements of both AL and corneal radius (CR) (Santodomingo-Rubido *et al.*, 2002). In addition, the AL/CR ratio has been proposed as a predictor of myopia progression in children (He *et al.*, 2015). Epidemiological studies such as the Singapore Cohort Of the Risk factors for Myopia study, the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study and the Orinda Longitudinal Study in Myopia used A-scan ultrasound biometry to measure the AL and ACD (Saw *et al.* 2002; Zadnik 1993; Kleinstein *et al.*

2003). The NICER study and the AES used the IOLMaster to measure AL, ACD, and keratometry (O'Donoghue *et al.* 2010; Logan *et al.* 2011).

Studies have shown the IOLMaster to be more repeatable than ultrasound for AL measurements (Santodomingo-Rubido *et al.*, 2002). This was also the case with studies involving children (Carkeet *et al.*, 2004; Hussin *et al.*, 2006). There appears to be an agreement in measurements taken by different operators, which are improved with cycloplegia (Kielhorn *et al.*, 2003; Sheng, Bottjer and Bullimore, 2004). The IOLMaster is suitable for use in epidemiological studies, especially those of a longitudinal design, due to its high repeatability. Lam *et al.* (2001) proposed a conversion factor that equates AL to refractive error such that a 1mm change in AL reflects a 3D refractive status shift. Hence, the IOLMaster is useful as a primary outcome measure in the progression of refractive error studies in children (Lam *et al*., 2001). However, Cruickshank and Logan (2018) demonstrated that the mathematical relationship between AL and SER was not linear; longer eyes did not have the same mathematical relationship with AL as shorter eyes. For lower levels of myopia a one mm change in AL had a more profound effect on SER than in higher levels of myopia. Similarly, Strang, Wynn and Bradley (1998) reported the linear relationship between AL and SER changed in high myopia where larger increases in AL were required to produce a one dioptre in refractive error.

The quality of AL measurements with the IOLMaster is influenced by the signal to noise ratio values; therefore, where the signal to noise ratio was less than two; these measurements were excluded and repeated. (Olsen and Thorwest, 2005).

Figure 6.9 Zeiss IOLMaster (Author's own, 2017)

6.4.4   The Zeiss IOLMaster principles of operation

The Zeiss IOLMaster was used to measure AL, ACD and CR (Figure 6.9 displays the IOLMaster in use and Figure 6.10 displays the operating procedure for the IOLMaster based on the Santodomingo-Rubido *et al.* (2002) schematic). The Zeiss IOLMaster uses a non-contact, non-invasive diagnostic imaging technique to measure the eye's AL, CR and ACD, which ensure accuracy and safety. Non-contact methods for optical biometric measures are preferable to contact methods such as ultrasound biometry due to the absence of topical anaesthesia and lack of corneal indentation. The IOLMaster uses a targeting system with a visualisation screen, and a rapid image acquisition system (Baikoff, Jodai and Bourgeon, 2005) and measures are automatic. One examiner (S. Harrington) used the Zeiss IOLMaster 500 (Carl Zeiss, Jena, Germany) to measure the AL, ACD and CR. The supplied accessory "test eye" was used to verify that the IOLMaster was operational and adequately calibrated, and was checked every day in each location before carrying out measurements on participants. Three measures of AL, five ACD readings and three CR readings were taken. The standard deviation for all

biometry readings was checked, and a standard deviation reading of 0.2 D was regarded as problematic, and the measurement repeated.

Axial length measurements: The Zeiss IOLMaster measures AL along the visual axis by the process of partial coherence interferometry; the optical scan uses an external Michelson interferometer (a dual beam version of optical/ocular coherence biometry/tomography). The system is insensitive to longitudinal eye movements as partial coherence interferometry uses the corneal tear film as a reference point. A laser diode produces an infrared laser of wavelength 780nm, with a short coherence length (C_L=160µm); the beam splitter splits the infrared beam into coaxial dual beams; these beams are reflected into the eye by two mirrors (M1 and M2), the separation of these beams is twice the displacement of the mirror (D). Both coaxial beams enter the eye, where reflections take place at the corneal tear film and retinal pigmentary epithelial interfaces; on leaving the eye, the difference in frequency between the coaxial beams is detected by a photodetector after passing through a second beam splitter. Interference between these beam components can take place if their optical path length difference is smaller than the coherence length. When the measurement is taking place, the mirror is moved at a constant speed resulting in a Doppler modulation in light frequency at the photodetector. The displacement of the mirror can be precisely determined and related to the reflected signals detected by the photodetector, allowing measurements of the optical AL to be made (Santodomingo-Rubido *et al.*, 2002). The geometric AL is calculated from the optical AL by considering the refractive index of the eye. The IOLMaster assumes a value for the refractive index of 1.36 for the eye, based on Gullstrand's schematic eye. Individual AL measurements and the mean value are displayed on the visualisation screen. Variations in measurement may occur if there are additional reflections from the internal limiting membrane or the choroid (Vogel, Dick

and Krummenauer, 2001). Only AL measurements with a signal to noise ratio greater than two were used for subsequent analysis.

Corneal curvature measurements: To calculate CR, the IOLMaster reflected six points of light, arranged in a 2.3mm diameter hexagonal pattern on the cornea. The instrument's software measured the separation of opposite pairs of lights and calculated the toroidal surface curvatures from three fixed meridians. The posterior surface of the cornea was calculated as approximately 82.2% of the anterior surface radius. Santodomingo-Rubido *et al.* (2002) found measurements of the corneal curvature to be similar with the IOLMaster to those found with the Javal-Schiotz keratometer (mean difference of mean CR -0.03mm). Connors *et al.* (2002) found that CR measurements using the IOLMaster were repeatable in children.

Anterior chamber depth measurements: Image analysis was also used to measure ACD by calculating the distance between the anterior lens and the corneal surfaces via lateral slit illumination. A seven mm slit was directed at 38° to the visual axis into the anterior chamber of the eye (Santodomingo-Rubido *et al.*, 2002). Image processing of an optical section was formed of the anterior corneal surface to the anterior crystalline lens surface. The instruments camera was aligned with the optical section, and image processing by the instrument's software measured the distance between the anterior surface of the cornea (air to corneal tear film interface) and the anterior lens surface (Carkeet *et al.*, 2004). An average of five measurements for ACD was displayed and the mean used in subsequent analysis. All ACD measurements were taken once it was checked cycloplegia had taken place as ACD measurements taken with a miotic pupil have been reported to be inaccurate. With a miotic pupil, the ACD measurement displayed may be the distance between the anterior iris surface and the anterior corneal surface (Santodomingo-Rubido *et al.*, 2002), and not the ACD.

Assessment of the crystalline lens is not possible with the IOLMaster which is a study limitation. Newer ocular biometers such as the Lenstar 900 (Haag-Streit Diagnostics, UK) have the facility to measure lens thickness and would be preferable in any proposed longitudinal study.

Figure 6.11 shows in school testing set up.
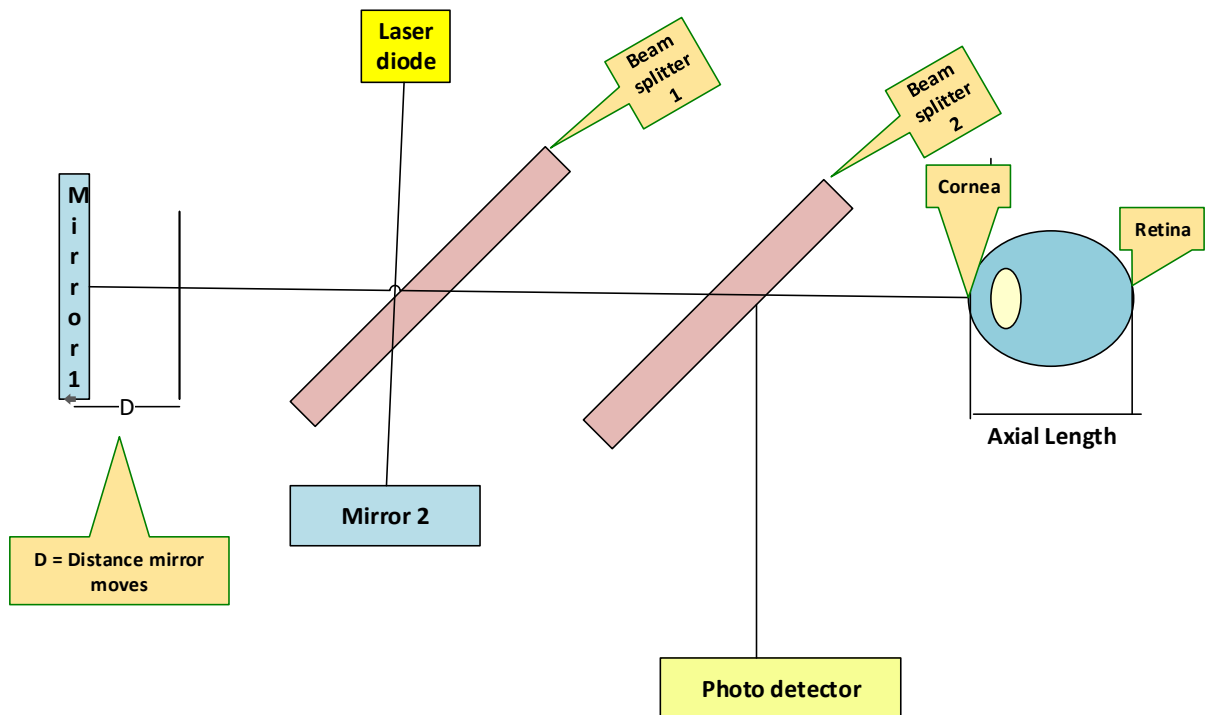
Figure 6.10 Operating principal of the IOLMaster (Author's own, 2019)

Figure 6.11 In school testing set up (Author's own, 2015)

6.4.5 Media/Fundus Examination

Direct ophthalmoscopy examination of the anterior segment and the lens vitreous and fundus and any abnormalities were noted. Ten children failed ophthalmoscopy. One child had orbital rhabdomyosarcoma. Three children had previously undiagnosed congenital cataracts. One child had suspected keratoconus. Three participants appeared to have eye infections. Three participants had retinal lesions which required further examination.

6.4.6 Report and follow up

Subsequent to the examination, parents/legal guardians received a detailed report outlining the tests performed and results recorded. A summary page advising patient management and review was included. Parents/legal guardians were directly contacted, recommending if any follow on treatment was necessary.

6.5   Data management and storage

6.5.1 Data management policy

Protection Measures

Technological University Dublin and its employees, under the Data Protection Act 1988 and the Data Protection (Amendment) Act 2003 are required to safeguard the privacy rights of individuals concerning the processing of personal data. The Data Protection Acts confer rights on individuals as well as responsibilities on those persons processing personal data. This study was compliant with the general data protection regulations which came into force on the 25th May 2018 (Data Protection Act 2018). The European Union General Data Protection Regulations were implemented in Ireland by the data protection Act 2018. Section 42 makes provision for the processing of personal data for scientific research and statistical purposes. Section 54 makes provisions for special categories of personal information for scientific research or statistical purposes.

The Data Protection Act 2018 requires that the processing of all personal data (including special categories of personal data) for scientific purposes, comply with a number of conditions: (1) that suitable and specific measures are taken to safeguard the fundamental rights and freedoms of data subjects; (2) that the personal data is processed in accordance with the conditions outlined in General Data Protection Regulation Article 89; (3) that the processing respects the principle of data minimisation (Article General Data Protection Regulation 5(1)(c)). The suitable and specific safeguards for health research are provided for by the Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations.

6.5.1.1 Participant identities

The IES maintained strict measures to protect patient and participant confidentiality. A personal identification number was generated for each participant. With the exception of

the document that contained the participant's personal information, all other information was distinguished using this identification number to ensure the confidentiality of the participants. The document that contained the participant's personal information was stored and accessed separately from the anonymised data. Access to these data was restricted to the research team and was password protected. In compliance with General Data Protection Regulation Article 89.

6.5.1.2 Data collected and patient records

All data and samples collected were anonymised, identified only by data-link, and stored with very high standards of security. At the end of every testing day, the completed questionnaires were coded and all of the collected data were entered directly into electronic SPSS databases. At the design stage of the study, the aim was to use a digital-first process to avoid introducing errors. However, due to the demands associated with testing young children in groups in school this was abandoned at the early stage in preference to printing out biometric and refractive data, which were later entered to electronic databases. All personal identifying information was stored separately from participants' data and samples and linked using a code that had no external meaning.

6.5.1.3 Data Protection and Encryption

Personal electronic data was subject to appropriate stringent controls, including password protection of all primary and backup data to be held on secure TU Dublin servers. Data files were encrypted and stored in keeping with the Data Protection Act 1988, amended Data Protection Act 2003 and the Data Protection Act 2018. The clinical data will be saved for 11 years or up until the child's 26th birthday, whichever is longer, following HSE (2013) Record Retention Periods Health Service Policy. To date, the

data was only used for the duration of the current study. However, it may also be used for a longitudinal study commencing in 2021.

Hardcopy records: Hard copy records were stored in a locked cabinet, with restricted access.

Confidentiality and anonymity: In Ireland, the Data Protection Acts 1988, 2003, and 2018 regulate research activities including the collection, storing, accessing and disclosing of personal data held in either electronic or manual filing systems by individuals or in general organisational records. Regarding this legislation, which does not expressly specify a particular age threshold for consent, the agreement to allow disclosure of identifiable information on a child research participant must be sought from the child's parent or guardian. However, ethical practice principles require that the child, depending on age and competence, be fully informed of these issues and provides assent where applicable. General Data Protection Regulation (Regulation (European Union) 2016/679 and Directive (European Union) 2016/680), replaces the European Data Protection Directive (95/46/EC).

6.5.2 Protection measures

The measures in place for data management, including the protection of anonymity, permission to access and use personal data, were as follows:

6.5.2.1 Child protection principles

To ensure research procedure was in keeping with current best practice standards of child protection, researchers carried out their work in accordance with the Children First: National Guidance for the Protection and Welfare of Children, published by the Department of Children and Youth Affairs in Ireland (DCYA, 2011). In recognition of national guidelines, TU Dublin developed a Child Protection Policy & Guidelines for Staff (HRP058), which were strictly adhered to throughout the study by each researcher.

The Children First Act was signed into law on the 19th November 2015 (Irish Statute Book 2015, Act 36) and provided a range of key child protection measures. The IES was conducted following the Child First protocols.

6.6 Statistical analysis

The Statistical Package for Social Sciences version 24.0 (SPSS, IBM Corp, Armonk, NY, USA) was used for most analyses. Anonymised study data were entered directly into an SPSS database. A personal code was used for each participant. The statistical programming language R, RStudio version 1.1.456 (R Foundation for Statistical Computing, Vienna, Austria) was used to generate random numbers for the sampling procedure and also to provide prevalence data confidence intervals (CIs). Questionnaires and clinical examination data forms were reviewed for accuracy and completeness in the field. Once data was input to the statistical package SPSS error checking and cleaning was carried out before analysis. Publication permission was obtained during consent, and all published data were anonymised. The consent form provided for this (refer Appendix 2). Throughout, 95% CIs were used. The statistical methodology employed in the five studies (chapter 7 to chapter 11) is described in each section. In summary, the IES involved univariate analysis, bivariate analysis and multivariate analysis of quantitative and qualitative data.

Univariate analyses

Standard 95% CIs were generated for all prevalence data (myopia, hyperopia, etc.). Univariate analysis of the distribution of quantitative data involved: descriptive statistics (mean, standard deviation, variance, interquartile range, skewness (measures the degree and direction of asymmetry of data) and kurtosis (measures the heaviness in the tails of the distribution).

The Kolmogorov- Smirnov test was used to check normality for distributions for the following quantitative data: spherical equivalent refractive data, astigmatism and vision.

Bivariate analyses

Relationships between two categorical variables were investigated using contingency table analysis. Relationships between two quantitative variables were examined using correlation and regression. Analysis of variance and independent samples t-tests were used when one variable was categorical, and one was quantitative. Non-parametric analogues of these tests were also occasionally employed.

Multivariate analyses

Multinomial logistic regression and general linear models/regression analysis were used for analyses involving more than two variables.

In summary, the examination included assessment of VA (presenting, unaided and through a pinhole), cycloplegic auto-refraction, ophthalmoscopy examination to assess the health of the eye, cover test to detect the presence of any strabismus and a stereopsis test.

The NICER study and the AES also followed this model. Therefore, the results will be of interest for comparative purposes. The AES study analysed a multiracial population, and the NICER dealt with a primarily White population (study ongoing).

Chapter 7 reports the study response rate and the prevalence of refractive error and VI in schoolchildren in Ireland.

7 REFRACTIVE ERROR AND VISUAL IMPAIRMENT IN SCHOOLCHILDREN IN IRELAND

7.1 Summary

Aims: To report refractive error prevalence and PVI in schoolchildren in Ireland.

Methods: The IES examined 1,626 participants (881 boys, 745 girls) in two age groups, 6-7 years (728) and 12-13 years (898), in Ireland between June 2016 and January 2018. Participating schools represented a mix of school type (primary/post-primary), location (urban/rural), socioeconomic status (disadvantaged/advantaged). The examination included monocular logMAR presenting VA (with spectacles if worn) and cycloplegic auto-refraction. Parents completed a questionnaire to ascertain participants' lifestyle.

Results: Prevalence of myopia (SER: $\leq$-0.50 D), hyperopia (SER: $\geq$+2.00 D), and astigmatism ($\geq$1.00 DC) amongst 6-7-year-old children was 3.3%, 25% and 19.2% respectively, and amongst 12-13-year-old children, 19.9%, 8.9% and 15.9% respectively. Astigmatic axes were predominately with-the-rule. Prevalence of "better eye" PVI ($\geq$0.3logMAR, with spectacles, if worn) was 3.7% amongst younger and 3.4% amongst older participants. Participants in minority groups (Traveller and non-White) were significantly more likely to present with PVI in the 'better eye'.

Conclusions: The IES is the first population-based study to report on refractive error prevalence and VI in Ireland. Myopia prevalence is similar to comparable studies of White European children, but levels of PVI were markedly higher than those reported

for children living in Northern Ireland, suggesting that barriers exist in accessing eye-care in Ireland.

7.2   Introduction

The WHO and the International Agency for the Prevention of Blindness identified refractive error as the second leading cause of blindness (after cataracts), and proffered presenting VA provides a reliable index of visual disability in a community inasmuch as it includes those with uncorrected refractive error (Resnikoff *et al.,* 2008). Consequently addressing uncorrected refractive error is a WHO Vision 2020 priority (Resnikoff *et al.,* 2008; Naidoo *et al.*, 2016).

Uncorrected refractive errors (myopia, hyperopia and astigmatism) result in reduced educational opportunities and employment options, impacting not only the individual but also the community (Rahi and Gilbert, 2012). Indeed the public health issue of uncorrected refractive error impacts on children's education (Rosner and Rosner, 1997; Williams *et al.*, 2005). What is more, the estimated cost of addressing uncorrected refractive error ($28,000 million US dollars) (Fricke *et al.,* 2012) is considerably less than the estimated global burden and economic cost to society in lost productivity due to uncorrected refractive errors which are conservatively estimated at $269,000 US dollars per year (Smith *et al.*, 2009; Wittenborn *et al.*, 2013). Prior research generally confirms that refractive error prevalence varies globally (Dunaway, 2006).

The IES is the first study to examine the prevalence of refractive error in schoolchildren in Ireland. This study also describes the prevalence of PVI in children aged 6-7-years-old and 12-13-years-old. These data provide the first opportunity to compare children's refractive and visual status in Ireland to that from other areas of the world.

7.3   Methods

Study approval was obtained from the TU Dublin Research Ethics Committee. This research was conducted under the Tenets of Helsinki Declaration of Human Studies (section 6.2.1).

7.3.1 Sampling protocol

The IES sampling protocols are described in detail in section 6.2.2. Stratified random cluster sampling was employed in selecting schools for participation (section 6.2.2).

Within each stratum, schools were randomly selected from a complete list (sampling frame) of schools provided by the Irish Department of Education and Skills. A sample size of 1,500 (700 6-7-year-olds and 800 12-13-year-olds) was calculated.

7.3.2 Ethnicity

The ethnicity of participants was assessed by the study coordinator and confirmed by the parent/guardian through self-report (section 6.2.1). Participants were categorised as either White, Traveller or non-White (black, Asian and Arab subjects combined). According to the 2016 Irish census, 9.9% of children aged between 5-14 years were non-White (refer Table 7.2).

7.3.3 Recruitment

Selected schools were contacted and, with agreement from school principals, an information pack was distributed to parents/legal guardians of children aged 6-7 years in primary and 12-13 years in post-primary schools. Each pack contained a letter of invitation outlining the study, an information sheet explaining the testing procedures, the study questionnaire, and a consent form. Children for whom informed consent and child assent were received were tested on school premises within school hours.

The testing procedures adopted in the IES are detailed in chapter 6; in summary, included the following methods:

1. Assessment of monocular distance visions (with spectacles if worn) using the Good-Lite (Elgin, Illinois) Sloan letters logMAR chart at 3m.

2. Cycloplegic autorefraction was used to determine refractive error. The representative value for SER - sphere plus half the cylindrical value - was used in subsequent analysis.

3. Parents completed a participant and parental history and a children's lifestyle questionnaire.

7.3.4 Definitions

To facilitate comparison with previous studies (Negrel *et al.*, 2000; O'Donoghue *et al.*, 2010; Logan *et al.*, 2011), the RESC protocol was used to define clinically significant myopia and hyperopia. The SER of the right eye was used to classify subjects as myopic (≤-0.50 D SER), hyperopic (≥+2.00 D) or emmetropic (>-0.50 D and <+2.00 D).

Clinically significant astigmatism was defined as 1.00 DC or more. With-the-rule astigmatism was defined as cylinder axes from 1°-15° and 165°-180°; ATR astigmatism as axes 75°-105°, and oblique astigmatism as axes 16°-74° and 106°-164° (Negrel *et al.*, 2000; O'Donoghue *et al.*, 2010; Logan *et al.*, 2011). Astigmatism was defined as myopic when both of the principal meridians were myopic (≤-0.50D); hyperopic astigmatism when both meridians were hyperopic (≥0.50D), and mixed astigmatism when one of the principal meridians was hyperopic and one myopic.

Presenting VI was defined by acuity measures ≥0.3logMAR (6/12 Snellen) with spectacles, if worn, in line with the RESC protocol (Negrel *et al.*, 2000), Presenting VI was reported for the 'better eye' and for 'either eye'.

7.3.5 Statistical methodology

Using the two-sample test for equality of proportions with continuity correction, there was no significant difference in myopia prevalence (p=0.78), hyperopia prevalence

(p>0.99), astigmatism prevalence (p=0.89) and the cylindrical axis of orientation prevalence (p=0.93), between the right and left eyes. Right, and left eye data were strongly correlated for SER (Spearman's rho coefficient = 0.878, p<0.001), astigmatism (Spearman's rho coefficient = 0.383, p<0.001) and presenting vision (Spearman's rho coefficient = 0.795, p<0.001). Hence, the right eye data only are presented.

Risk factors for SER prevalence were identified using multinomial logistic regression, controlling for age group, with emmetropic participants (absence of clinically significant refractive error, SER <+2.00 D to >-0.50 D) as the reference group. When evaluating risk factors for astigmatism, the reference group was participants with astigmatic errors less than 1.00 DC. Risk factors for PVI were examined, utilising those without PVI as the reference group. P-values ≤0.05 were regarded as significant. Throughout, 95% CIs have been used.

7.4   Results

Response rate: Fifty-four per cent of schools on the initial list agreed to participate in this study; additional schools were recruited from the reserve list. School participation rates did not vary significantly with socioeconomic status, urban/rural status or location. A total of 37 schools participated (23 primary schools, 14 post-primary schools) and data collection occurred between June 2016 and January 2018.

Within-school participation rates ranged from 64% to 100%, with an 83.3% average participation rate. Of those invited to participate, parental consent was obtained from 733 participants aged 6-7-years-old (51.8% male; mean age 6.7 years SD0.49) and 901 participants aged 12-13-years-old (56.1% male; mean age 12.8 years SD0.48). All participants successfully completed monocular VA assessment, and 99.3% of 6-7-year-old and 99.7% of 12-13-year-old participants underwent cycloplegic autorefraction and

provided measures for both eyes. Eight participants declined eye drops, and their results were excluded from subsequent analyses.

Figure 7.1 illustrates the non-normal distribution of SER in 2.00 D intervals for both age groups ($p<0.001$, Kolmogorov-Smirnoff test). The distributions show peaks around the mean. SER was positively skewed in 6-7-year-old participants (skew=1.61) and negatively skewed in 12-13-year-old participants (skew= -0.29). In the older age group, the distribution of SER shifts towards less positive values (6-7 years mean±standard deviation (SD) =1.44±1.25D, 12-13 years mean = 0.38±1.61D). There was a considerable variation in SER in both age groups as evidenced by the relatively large standard deviations (refer to Figure 7.1). The difference in mean SER between the two age groups was statistically significant ($p<0.001$, Mann- Whitney test).
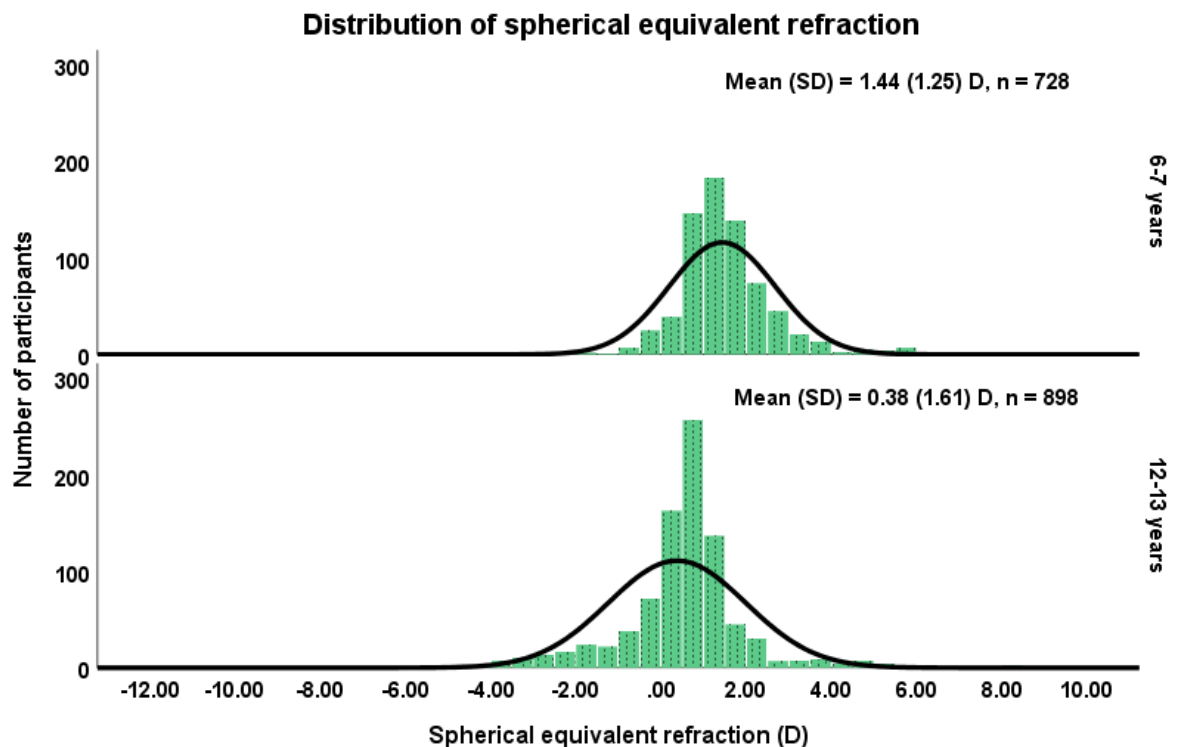
Figure 7.1 Distribution of spherical equivalent refraction in 728 6-7-year-old (top image) and 898 12-13-year-old (bottom image) study participants (right eyes). Each histogram bar represents 0.50D

Figure 7.2 presents SER distribution for the 588 6-7-year-old and 755 12-13-year-old participants who did not have clinically significant astigmatism. There was no significant difference in SER distribution between the 12-13-year-old cohort overall (898 participants) (refer Figure 7.1) and the SER distribution in 12-13-year-olds without clinically significant astigmatism (755 participants) (refer Figure 7.2) (p=0.39, Mann-Whitney test).

This pattern was repeated in the 6-7-year-old participants where no significant difference in SER distribution was found between the 6-7-year-olds overall (728 participants) (refer Figure 7.1) and SER distribution in the 6-7-year-old participants without clinically significant astigmatism (588 participants) (refer Figure 7.2) (p=0.95, Mann- Whitney test).
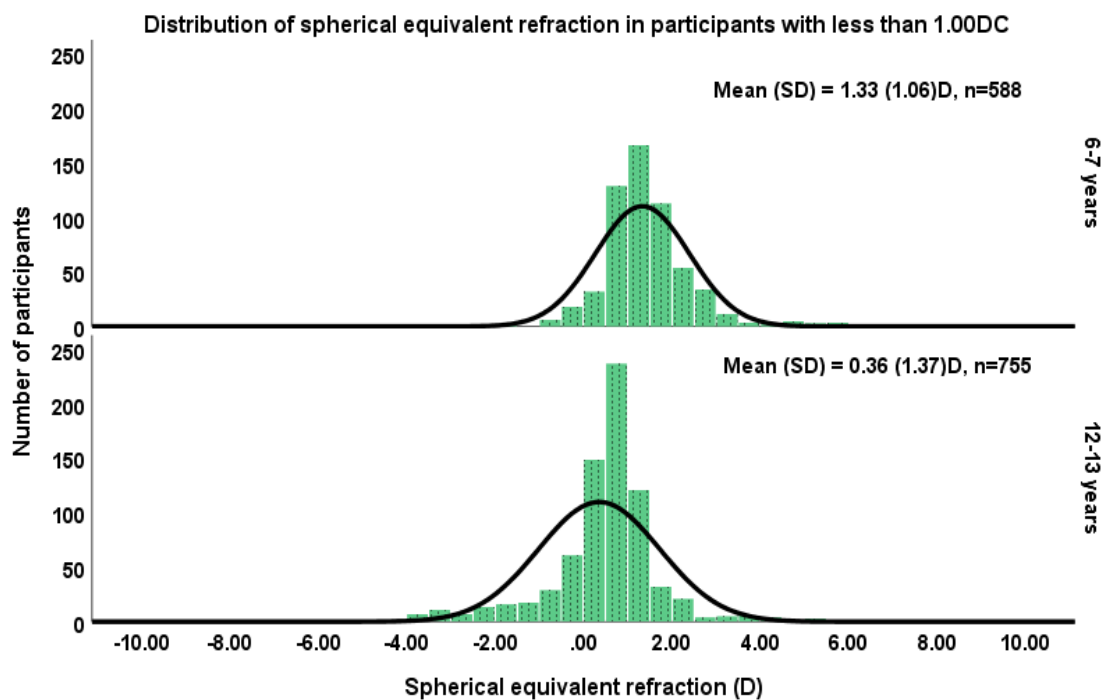
Figure 7.2 Distribution of spherical equivalent refraction (D) in the right eyes of 588 6-7-year-olds (top image) and 755 12-13-year-olds (bottom image) with astigmatism less than 1.00DC in their right eye. Each histogram bar represents 0.50D

Table 7.1 presents the prevalence of clinically significant myopia, hyperopia, astigmatism, astigmatic axis, and PVI plus 95% CIs by age.

Myopia prevalence was significantly higher, and hyperopia prevalence significantly lower, in the older participant group compared with, the younger group, (p<0.001), but no significant difference in astigmatism prevalence between age groups was found. The predominant type of astigmatism was WTR in both age groups.

Table 7.1 Prevalence of refractive error, astigmatic axis, uncorrected visual impairment and presenting visual impairment in 728 participants aged 6-7-years and 898 participants aged 12-13-years

Prevalence	N=728 n	6-7-years % (CIs)	N=898 n	12-13-years % (CIs)
Myopia	24	3.3 (2.2 to 4.9)	179	19.9 (17.4 to 22.7)
Hyperopia	182	25.0 (21.9 to 28.3)	80	8.9 (7.2 to 11.0)
Astigmatism	140	19.2 (16.5 to 22.3)	143	15.9 (13.5 to 18.4)
Astigmatic axis				
WTR	112	80.0 (72.2 to 86.1)	109	77.3 (69.3 to 83.7)
ATR	8	5.7 (2.7 to 11.3)	13	9.2 (5.2 to 15.6)
Oblique	20	14.3 (9.2 to 21.4)	19	13.5 (8.5 to 20.5)
PVI (better eye)	27	3.7 (2.5 to 5.4)	30	3.4 (2.3 to 4.8)
PVI (either eye)	65	8.9 (7.0 to 11.3)	75	8.4 (6.7 to 10.4)

Number of participants in each age group (N); frequency (n); with-the-rule (WTR); against-the-rule (ATR); 95% confidence intervals (CIs).

As SER may influence the prevalence of myopia and hyperopia in populations with significant astigmatism (Dobson *et al.,* 2007), myopia and hyperopia prevalence were also calculated for the 588 6-7-year-old and 755 12-13-year-old participants with <1.00 DC. Myopia prevalence in IES participants without clinically significant astigmatism (6-7 years 2.7% (16/588), 12-13 years 17.5% (132/755)) was not significantly different than amongst the entire study group (refer Table 7.1) (6-7 years p=0.66, 12-13 years p=0.23, 2-sample test for equality of proportions with continuity correction).

Hyperopia prevalence in participants without clinically significant astigmatism (6-7 years 24.3% (143/588), 12-13 years 7.5% (57/755) was not significantly different (6-7 years, p=0.83, 12-13-years p=0.36, 2-sample test for equality of proportions with continuity correction) than hyperopia prevalence in the entire study group (refer Table 7.1). Hence, for the remainder of this thesis myopia and hyperopia prevalence relate to that found in the total study population of 728 6-7-year-old and 898 12-13-year-old participants.

There was no significant difference in PVI prevalence ("better eye" or "either eye") between the younger and older participants. Myopia (83.3% (25/30), p<0.001) and hyperopia (10.0% (3/30), p=0.025) were significantly associated with PVI in the "better eye" amongst older participants. Astigmatism (70.4% (19/27), p<0.001) and myopia (18.5% (5/27), p<0.001) were significantly associated with PVI in the "better eye" amongst the younger age cohort. Astigmatism (61.3% (46/75), p<0.001), myopia (60.3%, (45/75) p<0.001), and hyperopia (25.3%, (19/75) p<0.001) were significantly associated with PVI in "either eye" in the older age group. Astigmatism (64.6%, (42/65) p<0.001) and hyperopia (53.0%, (34/65 participants), p=0.013), were significantly associated with PVI in "either eye" in the 6-7-year-old participants.

7.4.1 Refractive data and demographic profile

In addition to age, the principal demographic study variables in the IES were urban/rural status, gender, ethnicity, and socioeconomic status (refer to Table 7.2).

Multinomial logistic regression examining the relationship between SER and the study demographic variables jointly showed that myopia and hyperopia were significantly related to age group ($p<0.001$) and ethnicity (see section 7.4.2) ($p<0.001$) but not to gender, urban/rural status or socioeconomic status.

The presence of astigmatism was significantly associated with socioeconomic disadvantage ($p=0.02$), and ethnicity (see section 7.4.2) ($p=0.028$), but not gender, urban/rural status, or age.

Table 7.2 Ireland Eye Study principal demographic study variables in 728 6-7-year-old participants and 898 12-13-year-old participants

Demographic variables	N= 728	N=898
	6-7-years n (%)	*12-13-years* n (%)
Gender		
Male	377 (51.8)	504 (56.1)
Female	351 (48.2)	394 (43.9)
Living environment		
Urban	368 (50.5)	751 (83.6)
Rural	360 (49.5)	147 (16.4)
Socioeconomic status		
DEIS	245 (33.7)	108 (12.0)
Non-DEIS	483 (66.3)	790 (88.0)
Ethnicity		
White	582 (79.9)	708 (78.8)
Traveller	65 (8.9)	86 (9.6)
South Asian	22 (3.0)	15 (1.7)
East Asian	21 (2.9)	30 (3.3)
Black	31 (4.3)	49 (5.5)
Arab	7 (1.0)	10 (1.1)
Non-White		
South Asian, East Asian, Black and Arab combined	81 (11.1)	104 (11.6)

Number of participants in each age group (N); frequency (n).

Presenting VI in the "better eye" was associated with urban living (p=0.006), socioeconomic disadvantage (p=0.015) and ethnicity (see section 7.4.2) (p=0.007), but not gender or age. Presenting VI in "either eye" was associated with urban living (p=0.017) and socioeconomic disadvantage (p=0.049), but not ethnicity, gender, or age.

7.4.2 Relationship of refractive error to ethnicity

Table 7.3 presents the prevalence of myopia, hyperopia and astigmatism, plus PVI prevalence, by ethnic group. Both myopia and hyperopia prevalence were significantly related to ethnicity ($p < 0.001$), with a significantly higher prevalence of myopia and lower prevalence of hyperopia in the non-White group (refer Table 7.3). Astigmatism prevalence was markedly higher in non-White participants ($p = 0.007$). The prevalence of PVI in the 'better eye' was substantially higher in Traveller and non-White participants ($p = 0.007$).

Table 7.3 Prevalence of myopia, hyperopia, astigmatism and presenting visual impairment in 6-7-year-old and 12-13-year-old White, Traveller and Non-White participants

	White 6-7-years N=528 %(CIs)	White 12-13 years N=708 %(CIs)	Traveller 6-7-years N=65 %(CIs)	Traveller 12-13 years N=86 %(CIs)	Non-White 6-7 years N=81 %(CIs)	Non-White 12-13 years N=104 %(CIs)
Myopia	1.9 (1.0 to 3.5)	17.4 (14.7 to 20.4)	4.6 (1.2 to 13.8)	17.4 (10.4 to 27.5)	12.3 (6.4 to 21.9)	39.4 (30.1 to 49.5)
Hyperopia	25.8 (22.3 to 29.6)	9.5 (7.3 to 11.8)	35.4 (24.2 to 48.3)	11.6 (6.2 to 20.8)	11.1 (5.5 to 20.5)	3.8 (1.2 to 10.1)
Astigmatism	17.9 (14.9 to 21.3)	15.1 (12.6 to 18.0)	26.2 (16.4 to 38.8)	11.6 (6.1 to 20.8)	23.5 (15.1 to 34.4)	25.0 (17.3 to 34.6)
Astigmatic axis						
WTR	78.8 (69.5 to 86.0)	74.3 (64.7 to 82.1)	76.5 (48.0 to 92.2)	80.0 (44.2 to 96.5)	89.5 (65.5 to 98.2)	88.5 (68.7 to 96.9)
ATR	6.7 (3.0 to 13.9)	11.4 (6.3 to 19.5)	5.9 (0.3 to 30.8)	0.0	0.0	3.8 (0.2 to 21.6)
Oblique	14.4 (8.6 to 23.0)	14.3 (8.5 to 22.8)	17.6 (4.7 to 44.2)	20.0 (3.5 to 55.8)	10.5 (1.9 to 34.5)	7.7 (1.3 to 26.6)
PVI (better eye)	2.1 (1.1 to 3.7)	3.3 (2.1 to 4.9)	13.8 (6.9 to 25.2)	1.2 (0.1 to 7.2)	7.4 (3.0 to 16.0)	5.8 (1.2 to 10.1)
PVI (either eye)	6.4 (4.6 to 8.7)	8.2 (6.3 to 10.5)	21.5 (12.7 to 33.8)	8.1 (3.6 to 6.6)	17.3 (10.1 to 27.6)	9.6 (5.0 to 17.4)

Number of participants in each group (N); 95% Confidence Intervals (CIs), with-the-rule (WTR), against-the-rule (ATR), presenting visual impairment (PVI).

7.4.3 Relationship between astigmatism and ametropia

Astigmatism was significantly associated with hyperopia and myopia (p<0.001). Table 7.4 presents astigmatism prevalence by SER classification where myopia is defined as SER≤ -0.50D, emmetropia as SER >-0.50 and <0.50, low hyperopia as SER >0.50 and <2.00 and moderate hyperopia as SER ≥2.00. Astigmatism prevalence was 33.5% in 6-7-year-olds with moderate hyperopia and 38.8% in 12-13-year-olds with moderate hyperopia. Astigmatism prevalence was 33.3% in myopic 6-7-year-olds and 26.3% in myopia 12-13-year-olds.

Table 7.4 The prevalence of astigmatism (≥1.00 DC) in myopia, emmetropia, low hyperopia and moderate hyperopia in 728 6-7-year-olds and 898 12-13-year-olds

	Myopia SER≤-0.50D n / N (%)	Emmetropia SER>-0.50D and <0.50D n / N (%)	Low hyperopia SER>0.50D and <2.00D n / N (%)	Moderate hyperopia SER>2.00D n / N (%)	Total n / N (%)
6-7 years	8/24 (33.3)	10/52 (19.2)	61/470 (13.0)	61/182 (33.5)	140/729 (19.2)
12-13 years	47/178 (26.3)	16/200 (8.0%)	49/439 (11.2)	31/80 (38.8)	143/898 (15.9)

Number of participants (N); frequency (n); dioptre (D); dioptre cylinder (DC).

Amongst the 140 6-7-year-olds with clinically significant astigmatism, 80.7% (113/140) had hyperopic astigmatism, 14.3% (20/140) had myopic astigmatism, and 5.0% (7/140) had mixed astigmatism. The corresponding numbers for the 143 12-13-year-olds with clinically significant astigmatism were 46.9% (67/143) with hyperopic astigmatism, 37.1% (53/143) with myopic astigmatism, and 16.0% (23/143) with mixed astigmatism.

7.4.4 Profile of spectacle wear in study participants

Table 7.5 presents the profile of spectacle wear in IES participants.

Wearing and not wearing spectacles: The proportion of participants who presented either wearing spectacles (or who had them with them in school but were not wearing them) was 8.8% (64/728) of 6-7-year-olds, and 13.8% (124/898) of 12-13-year-olds; however, of those who reported that they had a current spectacle correction, a proportion did not have their spectacles at school (3.9% (29/728) of 6-7-year-olds and 10.7% (96/898) of 12-13-year-olds). The refractive profile of participants who did not have their spectacles at school was mainly hyperopic (53.6% (16/29)) in the younger cohort, and astigmatic (44.8% (43/96)) or hyperopic (32.3% (31/96)) in the older age cohort (refer to Table 7.5).

Not having spectacles: The prevalence of PVI in the "better eye" or PVI in "either eye", amongst participants who reported no history of spectacle wear, was 3.2% and 7.2% respectively in the younger age group, and 2.1% and 4.4% respectively in the older age group.

Eye examination within the 12 months prior to the study: 77% of the 1,626 IES participants (6-7 years 23.6% (172/728), 12-13 years 23.3% (209/898)) had not had an eye test within the 12 months prior to the IES data collection. There was no significant difference between age groups (p=0.71), genders (p=0.76), or socioeconomic status (p=0.21). However, rural participants (27.3% (137/501)) were more likely to have had an eye test than urban participants (22.1% (244/1106)) (p=0.02). Also, non-White participants (32.0% (56/177)) were more likely than White (22.5% (289/1282)) and Traveller participants (24% (36/148)) to have had an eye test within the 12 months previous to the IES (p=0.02).

Table 7.5 Profile of spectacle wear in 728 6-7-year-old and 898 12-13-year-old participants

Wearing / not wearing spectacles N (%)	No PVI n (%)	PVI 'either eye' n (%)	PVI 'better eye' n (%)
6-7years			
No spectacles: 628 (86.3)	583 (92.8)	45 (7.2)	20 (3.2)
Wearing spectacles: 63 (8.8)	50 (79.4%)	13 (20.6)	4 (6.3)
At school without spectacles: 28 (3.9)	22 (78.6%)	6 (21.4)	1 (3.6)
12-13 years			
No spectacles: 675 (69.6)	645 (95.6)	30 (4.4)	14 (2.1)
Wearing spectacles: 124 (13.8)	114 (91.9)	10 (8.1)	1 (0.8)
At school without spectacles: 96 (10.7)	61 (63.5)	35 (36.5)	15 (15.6)

Presenting Visual Impairment (PVI); number of participants (N); frequency (n).

Presenting visual impairment in the 'better eye': Of the 25 participants aged 6-7 years with PVI in the "better eye", 20 reported no history of spectacle wear, four needed an updated spectacle prescription, and one child did not have their spectacles at school. Of the 30 participants aged 12-13-years with PVI in the "better eye", 14 reported no history of spectacle wear; one child needed a spectacle update, and 15 participants did not have their spectacles at school.

Presenting visual impairment in 'either eye': Of the 64 participants aged 6-7 years with PVI in "either eye", 45 reported no history of spectacle wear, 13 required an updated spectacle prescription and six did not have their spectacles at school. Of the 75 participants aged 12-13 years with PVI in "either eye", 30 reported no history of spectacle wear, 10 required an updated spectacle prescription and 35 did not have their spectacles at school.

Of the 22 participants aged 6-7 years without PVI who reported spectacle wear, but did not have their spectacles at school, 14 were hyperopic and eight astigmatic. Of the 61 participants aged 12-13 years without PVI who did not have their spectacles in school, 30 were hyperopic, 21 astigmatic, nine myopic and one child did not have a refractive error as defined by the IES.

A history of spectacle wear was significantly associated with White ethnicity (p=0.038), older age group (p<0.001), and urban living conditions (p<0.001), but not gender or socioeconomic status. Attending school, without their prescribed spectacles, was associated with socioeconomic disadvantage (p=0.008), older age group (p<0.001) and White ethnicity (p=0.016). Table 7.6 presents the mean logMAR presenting VA for all participants and by gender and ethnicity. It also records the relationship between refractive error and presenting VA. Traveller and non-White 6-7-year-olds had significantly poorer presenting acuity compared to White 6-7-year-olds (p=0.006). Participants with refractive error had significantly poorer presenting VA compared to emmetropic participants (p<0.001 logistic regression).

Table 7.6 Presenting visual acuity in participant's right eyes

Presenting visual acuity	Number	Mean logMAR (SD)	Number	Mean logMAR (SD)
	6-7-year-olds		*12-13-year-olds*	
All	728	0.01 (0.16)[*]	898	-0.07 (0.20)
Boys	377	0.01 (0.15)[†]	504	-0.07 (0.21)†
Girls	351	0.01 (0.17)	394	-0.07 (0.19)
White	582	-0.01 (0.14)[‡]	708	-0.07 (0.20)[§]
Traveller	65	0.08 (0.24)	86	-0.07 (0.18)
Non-White	146	0.06 (0.24)	104	-0.04 (0.22)
Emmetropia	522	0.00 (0.17)	639	-0.12 (0.14)
Myopia≤-0.50 DS	24	0.15 (0.20)[**]	179	0.07 (0.29)**
Hyperopia≥+2.00 DS	182	0.04 (0.16)**	80	0.03 (0.21)**
Astigmatism≥1.00 DC[††]	140	0.11 (0.21)**	143	0.06 (0.23)**

Standard deviation (SD).

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[*] Statistically significant difference between age groups (Mann-Whitney U test for comparison of means in non-parametric data)

[†] No statistically significant gender difference (Mann-Whitney U test for comparison of means in non-parametric data)

[‡] Statistically significant ethnic difference (Kruskal-Wallis test for comparison of means in non-parametric data)

[§] No statistically significant ethnic difference (Kruskal-Wallis test for comparison of means in non-parametric data)

[**] Statistically significant difference in presenting vision compared to those without refractive error (Mann-Whitney U test for comparison of means in non-parametric data)

[††] Bonferroni post-hoc analysis revealed no difference between Myopic, hyperopic and mixed astigmatism (Kruskal-wallis test for comparison of means in non-parametric data with combined) Astigmatism here refers to astigmatism type combined.

7.5   Discussion

The present study utilised robust protocols, in line with previous studies, and achieved relatively high within-school participation rates (88%), ensuring a representative sample set of the demographic profile in schools in Ireland. Forty-six percent of selected schools from the initial sampling list were unable to facilitate collection of data: school principal concerns on the use of eye drops, unavailability of space or diary clashes with other school-based programmes were given as reasons for non-participation. However, the requisite number of schools was achieved from the reserve list covering the urban/rural, socioeconomic disadvantaged/advantaged and primary/post-primary strata. For example, as per the 2016 Irish census, 63% of the population in Ireland live in urban areas (www.cso.ie/en/releasesandpublications/ep/p-cp3oy/cp3/urr/), which is similar to the IES where 68.8% of the present study participants were based in urban schools. Moreover, in 2016, 21.1% (183,000 of 868,629) of schoolchildren in Ireland attended one of the 825 DEIS schools (640 of which are primary schools and 185 post-primary) (www.education.ie/en/Schools-Colleges/Services/DEIS-Delivering-Equality-of-Opportunity-in-Schools-/). The percentage of IES participants attending DEIS schools was 21.7% (353/1,626 participants). With regard to ethnicity, 9.9% of 5-15-year-old children in Ireland are Non-White, which is similar to the IES where 11.4% (185/1626) of participants were Non-White. Therefore, the demographic, social and ethnic profile of the IES participants' closely aligned with the population in Ireland.

Using similar protocols and methodology, the myopia prevalence in schoolchildren in Ireland (6-7 years 3.3%, 12-13-years 19.9%) for the period June 2016 to January 2018, was comparable to that reported in the UK NICER study which took place between 2006 and 2008 in Northern Ireland (6-7years 2.8%, 12-13 years 17.7%) (O'Donoghue *et al.,* 2010), and the AES which took place in Birmingham (UK) in 2006 (AES: 6-7 years

5.7%, 12-13 years 18.6%) (Logan *et al.*, 2011). Myopia prevalence was also similar to that found in Poland (6-7 years 2.0%, 12-13 years 18.6%) (Czepita, Zejmo and Mojsa, 2007), and Australia (6 years 1.6%, 12 years 12.8%) (Robaei *et al.*, 2005b; Robaei *et al.*, 2006d), and significantly lower than that reported in China (5 years 5.7%, 15 years 78.4%) (He *et al.*, 2004). In agreement with the majority of other studies, a significantly higher myopia prevalence was found in 12-13-year-olds than 6-7-year-olds. An exception to this was the RESC study in South Africa where a relatively low and stable myopia prevalence was found with age (7 years 2.5%, 13 years 3.4%) (Naidoo *et al.*, 2003).

Similar to the AES (South Asian: 6-7 years 10.8%, 12-13 years 36.8%, black: 6-7-years 11.4%, 12-13 years 27.5%) (Logan *et al.*, 2011), a markedly higher myopia prevalence was found amongst non-White participants in the present study (6-7 years 12.3%, 12-13 years 39.4%) in the IES. The IES myopia prevalence in the non-White ethnic groups was as follows: East Asians: (6-7 years 14.3%, 12-13 years 46.7%), South Asians (6-7 years 9.1%, 12-13 years 40.0%), and black (6-7 years 16.1%, 12-13 years 34.7%). Dobson *et al.* (2007) reported the use of SER can overestimate myopia prevalence in populations with a high astigmatism prevalence, such as found in their study of 819 3-4 year-old Tohono O'odham children where astigmatism ≥1.00DC was 49.7% (Dobson *et al.,* 2007). Furthermore, there is limited research addressing the relationship between changes in myopia progression and the presence of astigmatism (O'Donoghue *et al.,* 2015). However, despite these limitations SER has been used in the present study in line with previous studies such as the NICER study, the AES, the SMS and RESC studies to facilitate comparisons of refractive error prevalence. Also, no significant difference in myopia prevalence was found in the present study when participants with clinically significant astigmatism were removed from the analysis.

The IES hyperopia prevalence (6-7 years 25%, 12-13 years 8.9%) was broadly in line with Northern Ireland (6-7 years 26%, 12-13 years 14.7%) (O'Donoghue *et al.*, 2010), higher than Australia (6 years 13.2%, 12 years 5.0%) (Robaei *et al.*, 2005b; Robaei *et al.*, 2006d), Poland (6-7 years 13%, 12-13 years 9.4%) (Czepita, Zejmo and Mojsa, 2007), and China (5 years 17%, 15 years 0.5%) (He *et al.*, 2004). The IES hyperopia prevalence at 6-7 years was higher amongst the Traveller (35.4%) and White (25.8%) participants when compared to non-White (11.1%) ethnic groups. Although hyperopia prevalence was lower at 12-13 years amongst White (9.5%) and Traveller (11.6%) participants, it was still significantly higher than that of non-White (3.8%) participants.

The IES astigmatism prevalence (6-7 years 19.2%, 12-13 years 15.9%) was similar to that found in Northern Ireland (6-7 years 24%, 12-13 years 20%) (O'Donoghue *et al.*, 2011), higher than Australia (6 years 7.6%, 12 years 9.4%) (Robaei *et al.*, 2005b; Robaei *et al.*, 2006d), and considerably lower than that reported by Dobson for Native American children (5-16 years 42%) (Dobson, Miller and Harvey, 1999). Similar to Dobson, the IES found astigmatism to be associated with socioeconomic disadvantage and hyperopia. The predominant cylindrical axis of astigmatism was WTR (6-7 years 80.0%, 12-13 years 77.3%), similar to Dobson's report (98.0%) (Dobson, Miller and Harvey, 1999). The NICER study reported the predominant cylindrical astigmatism axes to be oblique (6-7 years 76%, 12-13 years 59%) (O'Donoghue *et al.*, 2011). Astigmatism type was predominately hyperopic in both age groups (6-7 years 80.7%, 12-13 years 46.9%). Similarly, Dobson *et al.* (2007) found mostly hyperopic astigmatism (60.1%). Myopic astigmatism was higher in the 12-13-year-olds (37.1%) than in the 6-7-year-olds (14.3%) which was unsurprising as myopia prevalence was significantly higher in the older age cohort than in the younger age cohort. Also, phase two of the NICER study demonstrated myopia progression was significantly associated with WTR astigmatism (O'Donoghue *et al.*, 2015).

The RESC, NICER study and SMS have well established the association between PVI and refractive error (He *et al.*, 2004; Robaei *et al.*, 2006b; O'Donoghue *et al.*, 2010). Internationally, PVI is accepted as providing an indicator of visual disability in society (Resnikoff, 2008), and the IES found a relatively high prevalence of PVI in the "better eye" of the younger participants (3.7%) compared with the closest comparator, the NICER study (1.5%) (O'Donoghue *et al.*, 2010). The level of PVI in the "better eye" was higher than that reported in Australia (1.5%) (Robaei *et al.*, 2005), and lower than that detected in China (10.3%) (He *et al.*, 2004). Participants from minority groups (Traveller and non-White) in particular were more likely to present with bilateral VI in the IES (Traveller: 6-7 years 13.8% and 12-13 years 1.2%, non-White: 6-7 years 7.4%, 12-13 years 5.8%). As 71.4% of younger participants and 40.0% of older participants with PVI in the IES were previously uncorrected, simple spectacle correction would address a considerable proportion of childhood PVI in the study population. However, the IES found a substantial number of participants who demonstrated VI despite wearing refractive correction because their spectacle correction required updating. Moreover, the majority of IES participants (77%) had not had an eye examination within the 12 months prior to the study. Likewise, Zhang *et al.*'s (2009) '*See well to learn well* 'project reported inaccurate spectacle prescriptions to be commonplace and recommended annual refractions to address this issue.

The present study demonstrates an association between socioeconomic disadvantage and PVI, which was not reflected in the NICER study. Economic barriers have been cited as the primary reason for non-attendance to eye care services or the failure to purchase spectacles (Schneider *et al.*, 2010). In the UK (where the NICER study was conducted) participants are entitled to free eye examinations and spectacle correction. This benefit is not available to all participants in Ireland and participants from the non-White and Traveller communities may have particular difficulty in accessing eye care

for financial and other reasons. The 'All Ireland Traveller Health Study' identified waiting lists, embarrassment and lack of information as the main barriers to Travellers in accessing health services (Moore *et al.,* 2010). Societal factors which may influence access to eye care include family responsibilities, parents' inability to leave work to attend eye care appointments with their child, and a lack of awareness of the importance of vision checks within the community (Schneider *et al.*, 2010).

It is not clear why participants with PVI who had a history of spectacle wear did not bring their spectacles to school, but such participants were more likely to be socioeconomically disadvantaged and in the older age group. The present study did not explore the reasons for participants not having spectacles at school, but issues such as cost of spectacle repair and replacement may be a factor and children's increasing concern over self-image as they age, may also impact. A recent Irish study reported that parents viewed childhood myopia as a cosmetic disadvantage, a potential expense and an optical inconvenience and they were less concerned about the health risks associated with myopia (McCrann *et al.*, 2018). The NICER study reported almost 24% of participants did not bring their prescribed spectacles to school (O'Donoghue *et al.*, 2010), and in Saudi Arabia, children reported they did not wear their spectacles due to parental disapproval, spectacle discomfort, visual appearance, and peer pressure (Aldebasi, 2013). The reasons underpinning a failure to wear prescribed spectacles merits further investigation to inform the development of an eye health awareness programme addressing spectacle wear and strategies to reduce vulnerability amongst children who require spectacles to see clearly or maintain ocular alignment.

In contrast to Zhang *et al.* (2010) and Choi *et al.* (2016) no association between refractive error and urban/rural dwelling was found in the present study. However, in Ireland most post-primary schools are situated in towns and urban settings and children

living in rural environments travel to school in state-funded school buses. Consequently, the number of rural participants in the older age cohort was low in the present study.

7.6   CONCLUSION

The IES is the first study to report on refractive error prevalence and VI in school-children living in Ireland. The IES demonstrates that myopia prevalence is similar to that reported in comparable studies in Western Europe. However, levels of PVI are markedly higher than those reported for children living in Northern Ireland, and there is a previously unreported disparity between children needing and wearing appropriate spectacles in Ireland, indicating sub-optimal uptake of eye care services. Further research is required in order to explore and address individual and societal barriers to optimal vision in Ireland.

Chapter 8 reports risk factors associated with myopia in schoolchildren in Ireland.

8 RISK FACTORS ASSOCIATED WITH MYOPIA IN SCHOOLCHILDREN IN IRELAND

8.1 Summary

Aims: To examine demographic and social factors associated with myopia in schoolchildren in Ireland.

Methods: The IES protocols and methodology is described in detail in chapter 6. The analysis in this chapter involves quantitative data (VA, SER, height, weight) collected during in-school testing and qualitative analysis of the study questionnaire (The mean question response rate was 97.6%) completed by the participant's parents or legal guardians in advance of data collection.

Results: Myopia prevalence was significantly higher in 12-13-year-olds (OR =7.7, 95% CIs: 5.1 to 11.6, p<0.001), and significantly associated with non-White ethnicity (OR=3.7, 95% CIs: 2.5 to 5.3, p<0.001).

Controlling for age-group and ethnicity, myopia prevalence was also significantly linked with height (p<0.001), and higher in participants in the following groups: using screens>3 hours per day (OR=3.7, 95% CI:2.1 to 6.3, p<0.001); obesity (OR=2.7, 95% CIs: 1.9 to 3.9, p<0.001); sedentary lifestyle (OR=2.9, 95% CIs: 1.9 to 4.4, p<0.001); frequently reading/writing (OR=2.2, 95% CIs: 1.4 to 3.5, p=0.001); less daylight exposure summertime (OR=5.00 95% CIs 2.4 to 10.3, p<0.001); spring season births (OR= 1.9, 95% CIs: 1.1 to 3.3, p=0.02); paternal history of myopia (OR=2.4, 95% CIs: 1.8 to 3.3, p<0.001); and bottle-fed for first 3 months of life (OR=1.7, 95% CIs: 1.3 to 2.5, p=0.02).

Conclusions: The associations found between myopia prevalence in schoolchildren in Ireland and demographic and lifestyle factors suggest that longitudinal research

investigating associations between myopia prevalence and these factors may be beneficial in advising preventative public health programmes.

8.2 Introduction

While for many the presence of myopia is an expense and inconvenience (McCrann *et al.*, 2018) correctable with spectacles or contact lenses, for an ever-increasing minority, myopia is a factor leading to an increased risk of myopia-related VI due to myopic macular degeneration, retinal detachment, myopic maculopathy, choroidal neovascularisation, staphyloma, myopic retinoschisis, cataract, glaucoma, and reduced peripheral vision (Wong *et al.*, 2014; Nagra *et al.*, 2018) (see section 3.2.1 for more detail on pathological myopia). Myopia is a recognised growing health issue in East and South East Asia in particular, where large-scale measurement and monitoring first began in the 1980s, with a very high prevalence (80 to 90%) in school leavers (Seet *et al.*, 2001). The global myopia prevalence was estimated at two billion in 2010 and predicted to rise to five billion (half the projected world's population) by 2050 (Holden *et al.*, 2016). Of further concern, one in ten of the world's population is estimated to be pathologically myopic (SER≤-5.00D) (Holden *et al.,* 20116).

Previous studies demonstrated myopia risk factors for schoolchildren include: family history (Low *et al.*, 2010), outdoor activity (Low *et al.*, 2010) congested living conditions (Choi *et al.*, 2017), ethnicity (Saw, 2006), socioeconomic status (Tideman *et al.*, 2017), obesity (Tideman *et al.*, 2017), intensive near work (Saw *et al.*, 2002; Tideman *et al.*, 2017), and body stature (Dirani, Islam and Baird, 2008). Myopic children were reported to be late and light sleepers, as poor sleep quality and later bedtimes are significantly associated with high myopia (Ayaki *et al.*, 2016). There is extensive literature on the aetiology and risk factors associated with myopia; chapter

three presents more detail on myopia prevalence and associated risk factors in schoolchildren in previous studies.

With regard to Ireland, between 5.3% and 10.1% of blindness (VA ≤1.0logMAR, 6/60 Snellen) in adults was reported due to myopia (Munier *et al.*, 1998). Furthermore, the IES reported myopia affecting one in five 12-13-year-olds (chapter seven) (Harrington *et al.*, 2018). As myopia is more prevalent in non-White ethnic groups, and a significant risk factor for ocular diseases (Saw, 2006), and given almost 10% of children in Ireland aged 5-15 years were non-White (2016 Ireland Census), Irish epidemiological studies are essential to inform public health policy in Ireland on the implications of myopia prevalence. In this context, the relationship between myopia prevalence, the degree of myopia and ocular disease have financial consequences as the cost of treating myopia, and its associated co-morbidities can be considerable (Zheng *et al.*, 2013). Thus, to formulate targeted and effective policies to reduce myopia related VI, policymakers must first understand both the extent of the problem, as well as its determinants.

The primary aim of this study was to explore relationships between IES refractive error data (for the period June 2016 – January 2018) and demographic and lifestyle variables, including the increasing use of digital media by schoolchildren. The secondary aim of this study was to compare findings with previous studies, such as the NICER study - the closest comparator with a similar demographic profile, refractive error prevalence, and equivalent study protocols and methodology (O'Donoghue *et al.*, 2015; Harrington *et al.*, 2018). The NICER study data collection took place ten years before the IES, between May 2006 and April 2008 (O'Donoghue *et al.*, 2015).

8.3 Methods

The methodology (see chapter 6) and study response rate for the IES has previously been described (section 7.4). In summary, the IES involved 728 participants aged 6-7-

years-old and 898 participants aged 12-13-years-old. The protocol for data collection included cycloplegic autorefraction (section 6.4.2.) in determining the refractive error. Height (in centimetres) and weight (in kilograms) (section 6.3.3.) and an analysis of questionnaire data (Appendices 3 and 4).

Participants were categorised as either White (1290 participants), Traveller (156 participants) or non-White (black 80 participants, East Asian 51 participants, South Asian 49 participants). Participants were also categorised by urban or rural living status and socioeconomically advantaged or disadvantaged status.

8.3.1 Definitions used

All IES participants with SER $\leq$-0.50D in either eye were classified as myopic; high myopia was defined as SER$\leq$-6.00D (Flitcroft *et al.*, 2019). Please note Harrington, Stack and O'Dwyer (2019) defined high myopia as SER$\leq$-5.00D; however, the recently published International Myopia Institute White paper proposed a set of standards and definitions and thresholds of myopia for epidemiological studies with high myopia defined as SER$\leq$-6.00D. Hence in this thesis, high myopia was defined as SER$\leq$-6.00D.

8.3.2 Statistical methodology

It has been previously reported (chapter 7) that myopia prevalence differed significantly between the two IES age-groups (Harrington *et al.*, 2018). All other reported risk factors associated with myopia in this study were identified using multinomial logistic regression, controlling for age group and ethnicity, with emmetropic (SER $\leq$+2.00 D and $\geq$-0.50 D) participants as the reference group in all analyses. The 5% level of significance has been used throughout, without correction for multiple tests.

8.4 Results

Table 8.1 presents the OR for myopia by age and ethnicity in 728 and 898 study participants. Table 8.2 provides a summary of the OR associated with each significant risk factor of myopia controlling for age group and ethnicity in all analyses. Appendix 4 displays all IES findings, for associations between myopia prevalence and demographic, historical and lifestyle factors.

Myopia (in at least one eye) was found in 27 of 728 (3.7%, 95% CIs: 2.5 to 5.4) participating 6-7-year-olds and 205 of 898 (22.8%, 95% CIs: 20.1 to 25.7) 12-13-year-olds. High myopia was found in two 12-13-year-olds (0.2%, 95% CIs: 0.05 to 0.9), both of which were East Asian. There were no 6-7-year-olds with high myopia. Due to the very small numbers of highly myopic participants in the IES, risk factors associated with high myopia were hard to assess.

Table 8.1 Odds ratio for myopia by age and ethnicity in study participants

Risk Factor (response rate %)	Myopic(n)/total(N)	(%)	Odds Ratio(95% CI)	P value
Age group (100%)				
6-7 years	27/728	(3.7)	Ref	
12-13 years	205/898	(22.8)	7.7 (5.1 to 11.6)	**<0.001**
Ethnicity (100%)				
White	155/1290	(12.0)	0.3 (0.2 to 0.4)	**<0.001**
Traveller	20/151	(13.2)	0.3 (0.2 to 0.5)	**<0.001**
Non-White	57/185	(30.8)	Ref	

Reference category (Ref); Confidence intervals (CI); total number in category (N); frequency (n).

Table 8.2 Odds ratio of myopia, controlling for age group and ethnicity, for socio-demographic and lifestyle risk factors significantly related to myopia in all 1,626 study participants

Risk Factor (response rate %)	Myopic(n)/total(N)	(%)	Odds Ratio(95% CI)	P value
Afterschool activities (98.3%)				
Mainly on phone/screens (sedentary)	50/194	(25.8)	2.9 (1.9 to 4.4)	**<0.001**
Infrequent activity	41/345	(11.9)	1.7 (1.1 to 2.6)	**0.02**
Sporting activities≤ 3 hours/per week	60/463	(13.0)	1.4 (1.0 to 2.1)	0.06
Sporting activities >3 hours per week	74/596	(12.4)	Ref	
Near work time close work (98.2%)				
Most time close work	7/36	(19.4)	3.0 (1.1 to 8.0)	**0.02**
Frequent close work	87/551	(15.8)	2.2 (1.4 to 3.5)	**0.001**
Occasional close work	102/766	(13.3)	1.6 (1.0 to 2.5)	0.06
Little close work	28/243	(11.5)	Ref	
Screen-time (98.5%)				
Less than 1 hour per day	26/313	(8.3)	0.3 (0.2 to 0.5)	**<0.001**
1-3 hours per day	83/707	(11.7)	0.5 (0.3 to 0.8)	**0.001**
More than 3 hours per day	118/582	(20.3)	Ref	
Time outdoors during daylight in summer (98.1%)				
Less than 1 hour per day	17/43	(39.5)	5.0 (2.4 to 10.3)	**<0.001**
1-2 hours per day	47/185	(25.4)	2.7 (1.8 to 4.1)	**<0.001**
2-4 hours per day	97/640	(15.2)	1.6 (1.1 to 2.3)	**0.01**
More than 4 hours per day	65/735	(8.8)	Ref	
Birth season (100%)				
Spring	62/400	(15.5)	1.9 (1.1 to 3.2)	**0.015**
Summer	64/434	(14.7)	1.5 (0.9 to 2.6)	0.12
Autumn	67/442	(15.2)	1.6 (1.0 to 2.8)	0.07
Winter	39/350	(11.1)	Ref	

Risk Factor (response rate %)	Myopic(n)/total(N)	(%)	Odds Ratio(95% CI)	P value
Child factors (98%)				
Breast fed only for first 3 months	98/620	(15.8)	0.9 (0.6 to 1.3)	0.6
Bottle fed only for first 3 months	66/651	(10.1)	0.5 (0.4 to 0.8)	**0.002**
Combined breast and bottle fed for the first three months	54/314	(17.2)	Ref	
BMI group (99.9%)				
Non-overweight	139/1193	(11.6)	0.4 (0.3 to 0.5)	**<0.001**
Overweight	45/249	(18.1)	0.6 (0.4 to 1.0)	**0.04**
Obese	48/136	(35.3)	Ref	
Parental factors (93%)				
Parental myopia				
Father myopic	84/382	(22.0)	2.4 (1.8 to 3.3)	**<0.001**
Father not myopic	117/1130	(10.4)	Ref	

Number of participants (N); frequency (n): 95% confidence intervals (CIs); Reference category (Ref):

body mass index (BMI).

8.4.1 Demographic factors and myopia in the IES

The principal demographic factors in the IES were age-group, ethnicity, urban/rural status, socioeconomic status, and gender.

Multinomial regression analyses examining the relationship of myopia prevalence to these study demographic variables, revealed that age-group ($p<0.001$), and ethnicity ($p<0.001$) were highly significantly related to myopia prevalence, but that urban/rural status ($p=0.66$), socioeconomic status ($p=0.70$), and gender ($p=0.51$) were not.

There was no significant difference in myopia prevalence between the East Asian, South Asian and black participants (6-7 years $p=0.69$, 12-13 years $p=0.45$, overall $p=0.49$). Myopia prevalence (either eye) in East Asian participants (6-7 years 14.3% (3/21), 12-13 years (16/30) 53.3%), South Asian participants (6-7 years 8.3% (2/22), 12-13 years 44.0% (7/15) and black participants (6-7 years 16.1% (5/31), 12-13 years 38.9% (19/49), was significantly higher than in White (6-7 years 2.1% (12/582), 12-13 years 20.2% (143/708), $p<0.001$) and Traveller participants (6-7 years 7.1% (5/65), 12-13 years 18.6% (16/86), $p<0.001$). Due to these findings, the relationships between other variables (lifestyle and social factors) to myopia were investigated, controlling each time for the age-group and ethnicity variables (but not the other demographic variables).

Table 8.3 displays demographic and lifestyle factors stratified by age-group and ethnicity and their relationship with myopia prevalence in the IES. In summary, 12-13-year-olds spent longer reading, writing and on screens and less time outdoors than 6-7-year-olds (all $p<0.001$). Non-White participants spent more time reading, writing, and on screens, less time outdoors and less time engaged in afterschool physical activities than White and Traveller participants (all $p<0.001$).

Table 8.3 Relationship between risk factors associated with myopia stratified by age-group and ethnicity

Weekly activities	White		Traveller		Non-White‡	
Afterschool physical activity *†	*6-7 years*	*12-13 years*	*6-7 years*	*12-13 years*	*6-7 years*	*12-13 years*
	n (%)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*
Mainly on phone/screens (sedentary)§	42 (7.3)	73 (10.5)	5 (7.7)	10 (11.8)	27 (34.6)	37 (37.0)
Infrequent activity	166 (28.2)	96 (13.9)	26 (40)	12 (14.1)	27 (34.6)	18 (18.0)
Sporting activities≤ 3 hours/per week	202 (34.9)	179 (25.9)	19 (29.2)	20 (23.5)	15 (19.2)	28 (28.0)
Sporting activities >3 hours per week	168 (29.1)	344 (49.7)	15 (23.1)	43 (50.6)	9 (11.5)	917 (17.0)
Near work time close work*†						
Most time close work §	16 (2.8)	12 (1.7)	1 (1.6)	1 (1.2)	2 (2.6)	4 (3.9)
Frequent close work	241 (41.9)	216 (31.2)	21 (33.3)	19 (22.2)	22 (28.2)	32 (31.4)
Occasional close work	272 (47.3)	328 (47.4)	28 (44.4)	35 (40.7)	45 (57.7)	58 (56.9)
Little close work	46 (8.0)	136 (19.7)	13 (20.6)	31 (36.0)	9 (11.5)	8 (7.8)
Screen-time *†						
Less than 1 hour per day§	182 (31.6)	67 (9.7)	21 (32.3)	16 (18.6)	19 (24.1)	8 (7.8)
1-3 hours per day	379 (65.8)	543 (78.4)	40 (61.5)	61 (70.9)	53 (67.1)	68 (66.0)
More than 3 hours per day	15 (2.6)	83 (12.0)	4 (6.2)	9 (10.5)	7 (8.9)	27 (26.2)
Daylight exposure summer *†						
Less than 1 hour per day§	6 (1.0)	17 (2.5)	3 (4.7)	5 (5.8)	5 (6.2)	7 (6.7)

Weekly activities	White		Traveller		Non-White‡	
1-2 hours per day	37 (6.4)	85 (12.3)	7 (10.9)	9 (10.5)	19 (23.5)	28 (26.9)
2-4 hours per day	222 (38.5)	286 (41.3)	18 (28.1)	31 (36.0)	38 (46.9)	45 (43.3)
More than 4 hours per day	311 (54.0)	304 (43.9)	36 (56.3)	41 (47.7)	19 (23.5)	4 (23.1)
Birth Season						
Spring§	142 (24.4)	176 (24.9)	11 (16.9)	18 (20.9)	25 (30.9)	28 (26.9)
Summer	150 (25.8)	196 (27.7)	10 (15.4)	26 (30.2)	24 (29.6)	28 (26.9)
Autumn	160 (28.5)	184 (62.0)	22 (33.8)	23 (26.7)	18 (22.2)	29 (27.9)
Winter	124 (21.3)	152 (21.5)	22 (33.8)	19 (22.1)	14 (17.3)	19 (18.3)
Child factors *						
Breast fed only for first three months§	199 (34.6)	290 (42.2)	16 (25.4)	27 (31.8)	34 (45.3)	54 (54.0)
Bottle fed only for first three months	262 (45.6)	267 (38.9)	41 (65.1)	46 (54.1)	19 (25.3)	16 (16.0)
Combined breast and bottle fed	114 (19.8)	130 (18.9)	6 (9.5)	12 (14.1)	22 (29.3)	30 (30.0)
BMI group *†						
Non-overweight§	492 (82.8)	507 (71.6)	51 (78.5)	51 (59.3)	56 (69.1)	45 (43.3)
Overweight	64 (11.0)	117 (16.5)	11 (16.9)	17 (19.8)	11 (13.6)	29 (27.9)
Obese	36 (6.2)	84 (11.9)	3 (4.6)	17 (19.9)	14 (17.3)	30 (28.8)
Parental myopia						
Father myopic§	105 (19.0)	203 (30.9)	14 (23.0)	23 (27.1)	8 (12.3)	29 (32.2)
Father not myopic	449 (81.0)	454 (69.1)	47 (77.0)	62 (72.9)	57 (87.7)	61 (67.8)

* Significant difference with ethnicity, †significant difference between 6-7-year-olds and 12-13-year-olds; ‡ East Asian, South Asian and black participants combined; § reference category; n: number of participants; BMI: body mass index.

8.4.2 Myopia and anthropometry

Controlling for age and ethnicity, myopia prevalence was significantly associated with the following continuous variables: participant height (cm) (p=0.008), BMI (kg/m²) (p=0.001), but not weight (kg) (p=0.053), the odds for myopia being greater in taller participants and those with higher BMI measurements.

The relationship between myopia prevalence and BMI categories was also examined. For this analysis, as per the Childhood Obesity Working Group of the International Obesity Taskforce with cut-offs at half yearly intervals for boys and girls, BMI was divided into three groups: non-overweight (including underweight), overweight, and obese (Cole *et al.*, 2000). These cutoffs were chosen because of their application in the Growing Up in Ireland (Walsh and Cullinan, 2015), and the NICER studies (O'Donoghue *et al.*, 2015).

In the IES, being overweight or obese was associated with the following factors:

- Age-group: 19.1% (139/728) of 6-7-year-olds and 32.7% (294/898) of 12-13-year-olds were overweight or obese (p<0.001);

- Socioeconomic disadvantage: 27.3% (67/243) of 6-7-year-old and 51.9% (56/108) of 12-13-year-old socioeconomically disadvantaged participants were overweight or obese- the corresponding number for advantaged participants was 14.9% (72/483) and 30.2% (238/790) respectively (p<0.001);

- Non-White ethnicity: 17.2% (100/582) of White, 21.5% (14/165) of Traveller and 30.9% (25/81) of non-White 6-7-year-olds were overweight or obese - the corresponding percentages for 12-13-year-olds were 28.4% (201/708), 40.0% (34/86), and 56.7% (59/104) respectively (p<0.001) and

- Female gender: 16.4% (62/377) of 6-7-year-old and 30.8% (155/504) of 12-13-year-old males were overweight or obese, and the corresponding percentage for females was 21.9% (77/251) and 35.3% (139/394) respectively (p=0.03).

Amongst 6-7-year-olds, 3.2% (19/589) of the non-overweight subgroup were myopic; this increased to 3.5% (3/86) of the overweight participants; and 9.4% (5/53) amongst the clinically obese participants. This pattern was repeated in 12-13-year-olds: amongst the non-overweight subgroup, 20.0% (120/603) were myopic, this increased to 25.8% (42/163) of the overweight participants and 32.8% (43/131) amongst the clinically obese participants. Figure 8.1 displays the relationship between myopia prevalence and BMI in IES participants. Multinomial logistic regression analysis, controlling for age and ethnicity, demonstrated that the relationship between myopia prevalence and BMI category was statistically significant ($p < 0.001$). Thus, despite the strong connections of obesity with both age and ethnicity, the statistical evidence from the IES was that myopia prevalence was still significantly associated with obesity, controlling for age and ethnicity.
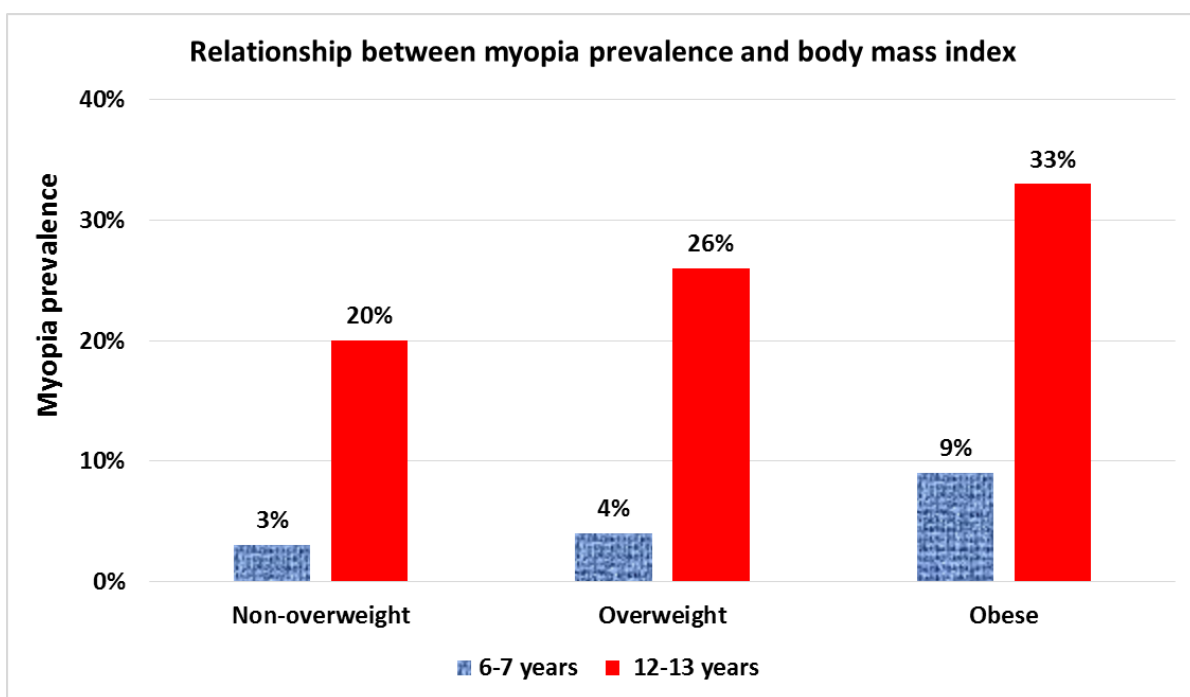
Figure 8.1 Relationship between myopia prevalence and BMI categories in 728 6-7-year-olds (589 non-overweight, 86 overweight, and 53 obese participants) and 898 12-13-year-olds (604 non-overweight, 163 overweight, and 131 obese participants)

8.4.3 Myopia and afterschool leisure activities

Amongst 6-7-year-olds, 9.5% (7/74) with sedentary lifestyles were myopic. This percentage decreased consistently with increased physical activity and dropped to just 2.6% (5/192) for participants mainly involved in after-school physical activities. Hence, myopia prevalence was inversely related to the amount of time engaged in after-school physical activity. This pattern was repeated amongst 12-13-year-olds, where 35.8% (43/120) of participants with sedentary lifestyles were myopic; this decreased to 17.1% (69/404) amongst participants involved in regular after-school physical activities. These differences in myopia prevalence were statistically significant ($p=0.01$, logistic regression controlling for age and ethnicity). Figure 8.2 displays the relationship between myopia prevalence and afterschool activities. The very slight increase in myopia prevalence found amongst 6-7-year-olds in the moderate physical activity subgroup when compared to the light physical activity subgroup was challenging to assess due to the minimal numbers in these subgroups.
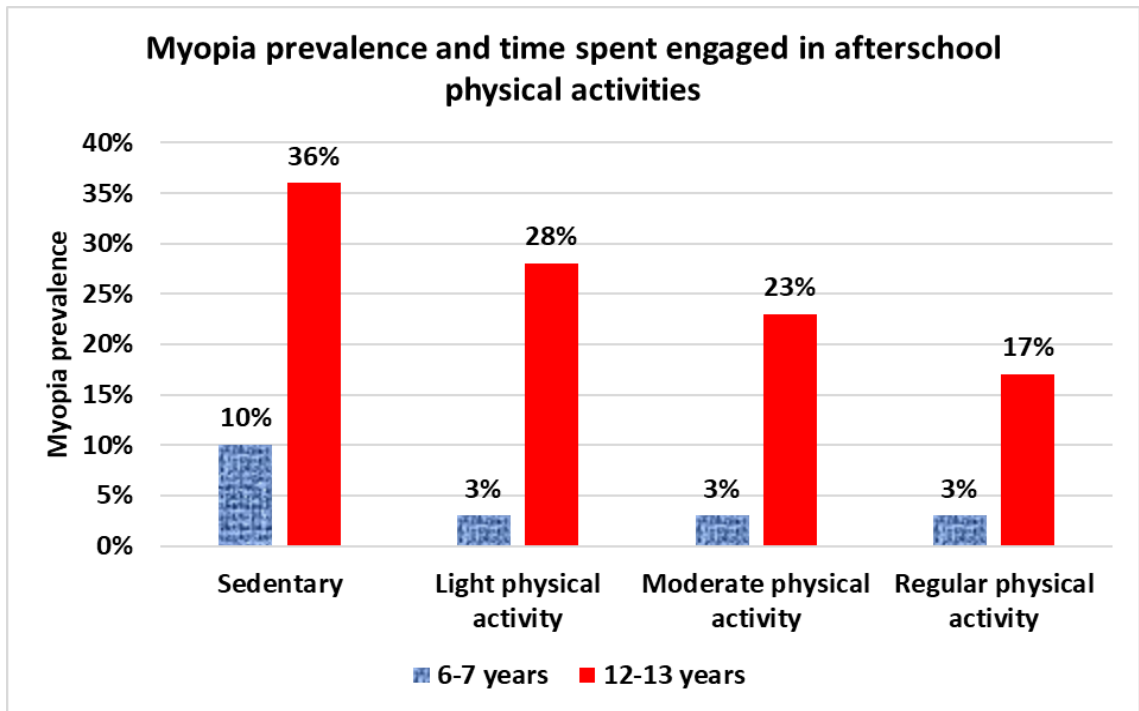
Figure 8.2 Relationship between myopia prevalence and afterschool physical activities in 728 6-7-year-olds (74 sedentary, 219 light physical activity, 236 moderate physical activity, and 192 regular physical activity) and 898 12-13-year-olds (120 sedentary, 126 light physical activity, 227 moderate physical activity, and 404 regular physical activity)

Obesity was significantly related to physical activity in the IES. However, fitting a logistic regression model relating myopia prevalence to the obesity and physical activity categories, jointly, and controlling for age and ethnicity, revealed that both obesity and physical activity remained statistically significant, after controlling for the other. Therefore, in the IES, both obesity and physical activity variables were related to the prevalence of myopia over and above what can be explained by the relationship of these two variables to each other.

8.4.4 Myopia and screen time

Myopia prevalence in the IES increased with increased time engaged in screen technologies in both age groups ($p<0.001$). Amongst 6-7-year-olds, myopia prevalence increased fivefold (3.2% (7/222) in the <1 hour screen time group, 16.0% (4/25) in the

>3hours screen time group). Although the differences were not as pronounced, the myopia prevalence increase was still significant amongst 12-13-year-olds, where myopia prevalence increased from 21.0% (19/91), amongst participants who spent less than one hour per day on screens, to 27.0% (32/119) amongst those who spent greater than 3 hours per day on screens. Figure 8.3 displays the relationship between myopia prevalence and time engaged in screen technologies.
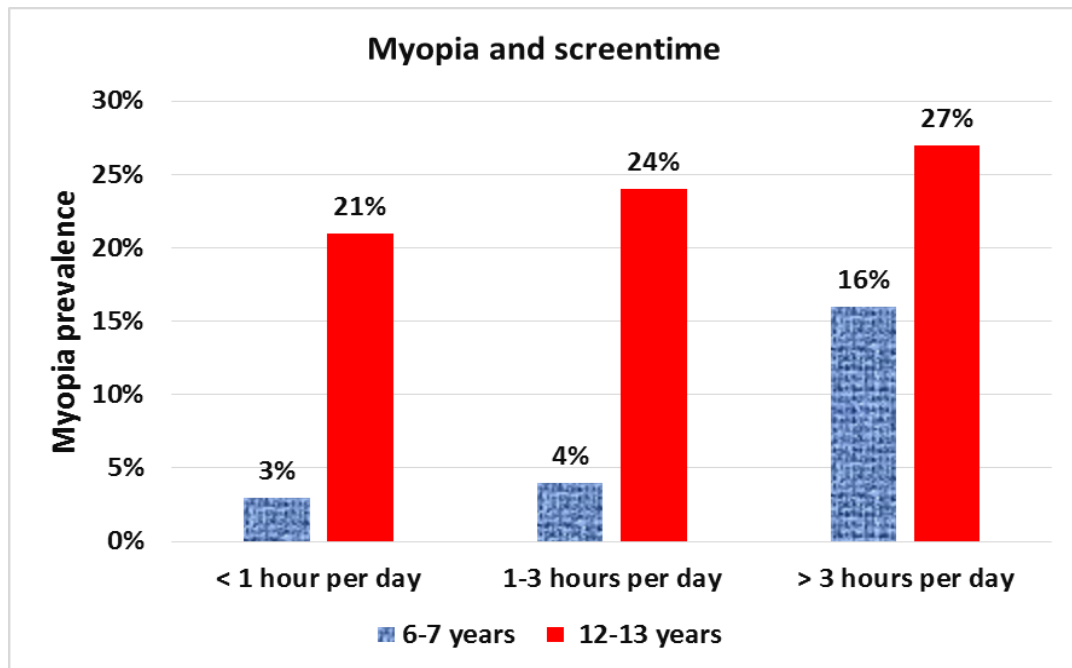
Figure 8.3 Relationship between myopia prevalence and time spent on screens in 728 6-7-year-olds (number of participants in each screen time category: 222 < 1 hour per day, 473 1-3 hours per day, 26 over 4 hours per day), and 898 12-13-year-olds (number of participants in each screen time category: 91 < 1 hour per day, 672 1-3 hours per day, 119 > 4 hours per day)

8.4.5 Myopia and reading/writing

Myopia was closely associated with increased time engaged with reading/writing (p=0.01). Amongst 12-13-year-olds, 41.2% (7/17) of participants who spent most of their leisure time reading or writing were myopic; compared to 28.5% (76/267) of those who frequently spent time reading/writing; 21.6% (91/421) in the group who

occasionally engaged with reading/writing; and only 14.9% (26/175) of those who seldom spent their leisure time reading/writing. Figure 8.4 displays the relationship between myopia and time spent reading/writing in both age cohorts. The minimal differences in myopia prevalence found in the participants aged 6-7-years were difficult to assess due to the very small numbers in these subgroups.

As screen time and time engaged in reading are inherently linked, a logistic regression model relating myopia prevalence to the reading/writing and screen-time categories, jointly (controlling for age and ethnicity), was fitted which revealed that both reading/writing and screen-time remained statistically significant, after controlling for the other. Hence, in the IES, both screen time and reading/writing variables were related to the prevalence of myopia over and above what can be explained by the relationship of these two variables to each other.
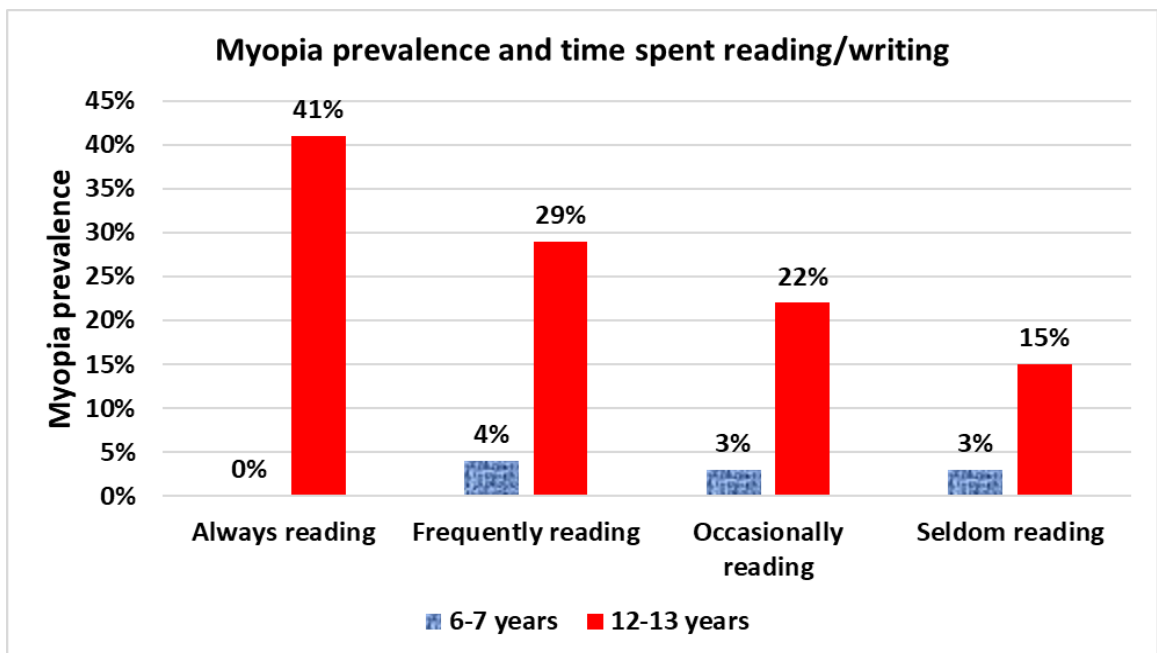
Figure 8.4 Relationship between myopia prevalence and time spent reading or writing in 728 6-7-year-olds (number of participants in each time spent reading/writing category: 19 always reading, 284 frequently reading, 345 occasionally reading, and 68 seldom reading) and 898 12-13-year-old participants (number of participants in each time spent reading/writing category: 17 always reading, 267 frequently reading, 421 occasionally reading, and 175 seldom reading)

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8.4.6 Myopia and daylight exposure

Myopia in the IES was also significantly associated with summer daylight exposure. Myopia prevalence was higher in those spending < 2 hours per day outdoors during summertime (p<0.001). Amongst 6-7-year-old participants myopia prevalence was 14.3% (2/14) in participants who spent less than one hour outdoors during daylight in summer, compared to 2.5% (9/366) in participants who spent more than four hours outdoors per day during daylight. This pattern was repeated in the older age cohort where myopia prevalence was 51.7% (15/29) in participants who spent less than one hour outdoors per day during daylight compared to 15.2% (56/369) myopia prevalence in 12-13-year-olds who spent more than four hours outdoors per day during daylight. Winter daylight exposure was not found to be significantly associated with myopia (p=0.87).

Participants born in spring were more likely to be myopic; 15.5% (62/400) of the myopic participants were born in spring compared to 14.7% (64/434) in summer, 15.2% (67/442) in autumn and 11.1% (39/350) born in winter (p=0.02).

Figure 8.5 displays the relationship between myopia prevalence and time spent outdoors during daylight in summer and myopia prevalence in participants aged 6-7 years and 12-13 years.
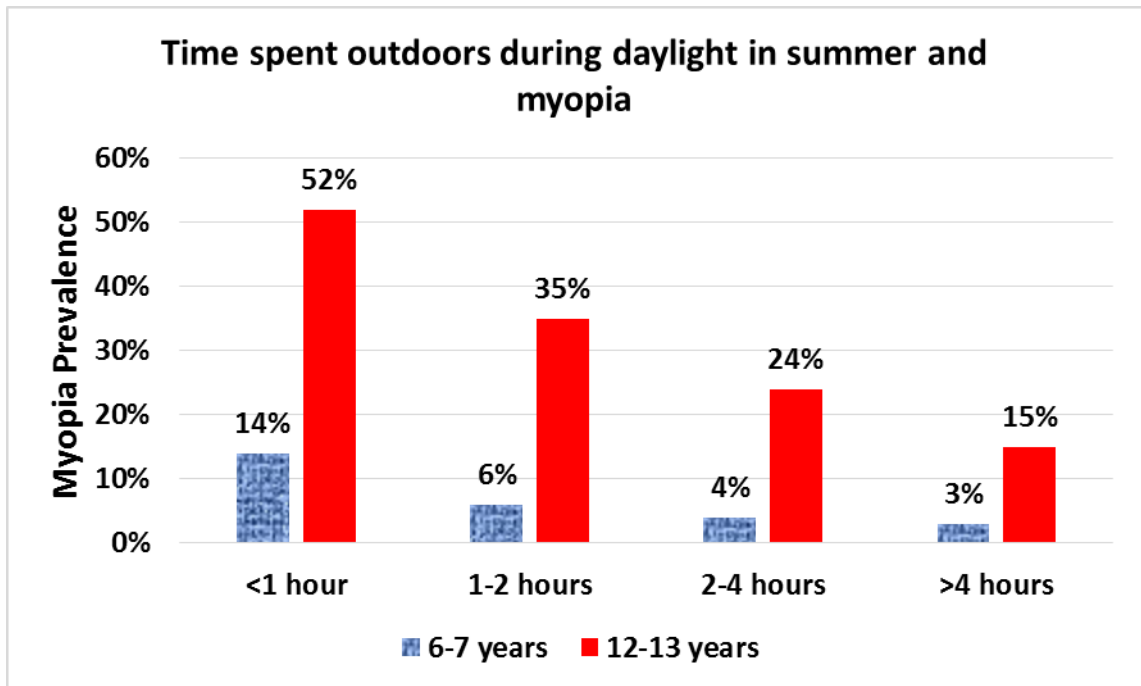
Figure 8.5 Relationship between myopia prevalence and time spent outdoors during daylight in summer in 728 6-7-year-olds (number of participants in each daylight category: 14 < 1 hour, 63 1-2 hours, 289 2-4 hours, and 898 12-13-year-olds, 366 > 4 hours) and 898 12-13-year-olds (number of participants in each daylight category: 29 < 1 hour, 122 1-2 hours, 362 2-4 hours, 369 > 4 hours)

8.4.7 Parental risk factors for myopia

Compared to participants without myopic parents, IES participants with myopic fathers were twice as likely to be myopic (22.0% (84/382) versus 10.4% (117/1130), p<0.001); however, the relationship between a maternal myopia history and myopia in the child was not statistically significant (p=0.27). Also controlling for age and ethnicity, myopia prevalence was not associated with either father's educational level (p=0.62), or mother's educational level (p=0.21).

8.5 Discussion

While epidemiological studies such as the IES can demonstrate a statistical association, they do not determine causation (Flitcroft, 2012). Risk factors associated with childhood myopia in the IES were as follows:

8.5.1 Anthropometry

The association, in the IES, between myopia prevalence and subject height while controlling for age and ethnicity, concurs with a recent study of 7,681 rural Chinese participants aged 5-15-years-old (Qian *et al.*, 2016).

The association, in the IES, between obesity and myopia prevalence is similar to that found in the Netherlands, where myopia was associated with a higher BMI (Tideman *et al.*, 2017). In the IES this relationship remained after controlling for lifestyle. With regard to BMI in Ireland, the Growing Up in Ireland study reported one in four 9-year-olds (26%) as overweight or obese (Walsh and Cullinan, 2015), which is similar to the IES (one in five 6-7-year-olds, and one in three 12-13-year-olds). Furthermore, Quigley *et al.*'s (2019) recent secondary analysis of the Growing Up in Ireland data (9-year-old cohort) found that adiposity and sedentary activity were associated with "*sight problems requiring correction*". The questionnaire response options were as follows: *"treatment with glasses, patch, surgery, laser treatment, other, or no treatment."* The type of refractive error and the level of VA were not investigated.

Conversely, no association was found between myopia prevalence and BMI in Southern Californian subjects aged 5-19 years (Theophanous *et al.*, 2018). However, this retrospective study involved a clinical sample and not a randomly selected population-based sample. Interestingly, the myopia prevalence amongst 12-13-year-old IES participants, who had their eyes examined within the 12 months before IES data collection, was 46.4%, which was broadly in line with that reported in the Southern

Californian 11-13-year-olds (49.4%) (Theophanous *et al.*, 2018). Hence myopic children may be more likely to have their eyes tested.

As BMI in the IES was significantly related to a range of other study variables, the relationship found in the IES between myopia and obesity may be due, in part, to relationships between BMI and these other variables. Nevertheless, when age, ethnicity and after-school physical activity were controlled for in the analysis, the significant relationship between BMI and myopia persisted.

8.5.2 Myopia and time spent outdoors during daylight

The higher myopia prevalence in IES participants born in spring aligns with one Korean study but contrasts with a study of 276,911 Israeli participants which reported higher myopia prevalence within study participants born in summer (Mandel *et al.*, 2008; Lee *et al.*, 2018). Whether increasing myopia prevalence is to do with less daylight exposure or due to activities pursued indoors is a matter for speculation (Ngo *et al.*, 2013).

The association between reduced myopia in IES participants spending increased time outdoors during the summertime concurs with a previous study in Boston (Gwiazda *et al.*, 2014), which is of interest since daylight time varies significantly throughout the year in New England as it does in Ireland. Notably, time outdoors >2.5 hours per day, during daylight, has been reported to postpone the onset of myopia, and slow the myopic shift in refractive error (Wu *et al.*, 2018). However, results regarding the effects of daylight exposure on myopia progression are equivocal (Xiong *et al.*, 2017a; Wu *et al.*, 2018). The mechanisms underpinning daylight exposure's protective effect against myopia are unclear; increased depth of focus plus low accommodative demand associated with time spent outdoors have been proposed as possible biological mechanisms related to this reduction of myopia (Xiong *et al.*, 2017a). Whether, as discussed in section 3.6, this is entirely due to the flat dioptric topography of the visual

field outdoors, which appears to be a strong signal to slow eye-growth, or due to increased light levels outdoors is inconclusive (Flitcroft, 2012).

As higher light levels have been shown to postpone myopia onset, there is likely to be a minimum desired indoor light level for myopia prevention (Zhou *et al.*, 2017).

The close link found between circadian rhythms and eye growth (Flitcroft, 2012; Nickla, 2013), and decreased sleep quality with later bedtimes in highly myopic children (Ayaki *et al.*, 2016), further reinforces the part light exposure plays in refractive error development in children. Therefore, circadian timing and time of day of school hours may be essential factors to consider when addressing myopia control at a public health level.

The lack of any relationship between myopia prevalence and outdoor activities during the winter months is unremarkable in Ireland at a time of year when daylight hours are limited to seven to eight hours. In Ireland, the school day is between five to seven hours, which coincides with daylight hours. Hence, it was challenging to assess the influence of daylight exposure on refractive status during the winter months as few participants reported spending more than four hours per day outdoors during winter.

8.5.3 Afterschool leisure activities

Similar to the Generation R study in Rotterdam (Netherlands), IES participants who engaged in increased afterschool physical activities were found to be significantly less likely to be myopic than those with sedentary lifestyles (Tideman *et al.*, 2019). Furthermore, this significance remained after controlling for BMI in the IES. Consequently, longitudinal research on whether engaging in afterschool physical activities or not engaging in screen-based activities to prevent myopia progression is crucial.

8.5.4 Near work activities

Researchers have consistently reported an association between time engaged in near work activities and myopia, which aligns with the IES study (Saw *et al.*, 2002; Tideman *et al.*, 2017).   However, investigation of the use of screen-based technologies within the classroom and after school is new and its effect on the progression of refractive error is an open question. In the Netherlands, myopia was significantly associated with time spent watching television but not with computer use (Tideman *et al.*, 2017). However, as smartphone use has increased from 75% to 97% in Irish people aged <25years (Howard and Hughes, 2016) researching the effects of these portable screens on the growing eye is now essential. Children are increasingly less likely to use desktop computers or televisions with most accessing online media and entertainment content via screens that are more easily transportable (Ponti *et al.*, 2017). For example, mobile media use in American 2-4-year-olds increased from 34% in 2011 to 80% in 2013; in the UK 51% of infants aged 6-11 months use touch screens daily (Ponti *et al.*, 2017). Screen-based technologies are not responsible for the myopia epidemic in East Asia, which began in the 1980s before the advent of smartphones (Seet *et al.*, 2001), however, the ubiquitous use of smartphones and other media devices may increase the time children engage in near work, thereby reducing the time spent outdoors during daylight. The relationship between increased time on screens and increased myopia prevalence in the IES may be due to several confounding factors. For example, the high accommodative demand associated with using smartphones at short working distances; cumulative blue light exposure (Oh *et al.*, 2015); coupled with dim lighting, resulting in dilated pupils and the consequent increased peripheral image defocus (Flitcroft, 2012), plus reduced time outdoors, may lead to increased risk of myopia onset, or progression in susceptible children.

The lack of any relationship between myopia and urban living in Ireland is unsurprising, as there is little difference in living conditions between urban and rural dwelling when compared to Asia, where crowded living conditions and constricted living space were reported risk factors for myopia development and progression (Choi *et al.*, 2017).

Likewise, the association between socioeconomic status and myopia, found in a Singaporean study, was not mirrored in the IES (Saw *et al.*, 2002). However, in line with Saw *et al.,* (2002) the IES found time engaged in near work to be associated with myopia, possibly highlighting the differences in socioeconomic advantage/disadvantage globally (Galobardes, Lynch and Smith, 2007). In Ireland, all children have access to books and publically funded education, which may not be the case in some countries (Rosner and Ortiz-Ospina, 2018).

8.5.5 Family history

The IES association between myopic participants and parental myopia is in agreement with previous studies (Low *et al.*, 2010; Tideman *et al.*, 2017). However, myopia prevalence in the IES was strongly associated with myopia in the father and not with myopia in the mother; this merits further investigation. As a parental history of myopia was self-reported via the IES questionnaire, the question as to the accuracy of self-reported refractive error category ought to be considered (Breslin, O'Donoghue and Saunders, 2013), although, research has found, the self-reported reason for the use of optical correction was accurate for myopia (89.1%) (Cumberland, Chianca and Rahi, 2016).

Considering a family history of myopia was strongly associated with early onset myopia in Chinese preschool participants (aged <72 months), genetic factors may play a more prominent role, than environmental factors, in early-onset myopia (Low *et al.*, 2010). Conversely, the very low myopia prevalence found in IES participants aged 6-7 years (3.7%), and the scarcity of high myopia in the IES (0.2%), suggests that genetic factors

may play less of a role in myopia prevalence in Ireland. Due to the very small numbers of myopic 6-7-year-olds in the IES risk factors associated with myopia in the younger age cohort were hard to assess. Longitudinal studies will be more revealing in this regard.

8.6   Summary and conclusion

In summary, the IES results demonstrate that obesity, more time spent on screens and near visual tasks, coupled with less time spent engaged in physical activities may increase the risk of myopia in schoolchildren. In agreement with other studies, reduced time spent outdoors was associated with myopia. Also, the 12-13-year-olds extra-curricular activities were more myopogenic than the 6-7-year-olds. Non-White participants, in particular, reported spending spent less time outdoors and more time doing near work than White and Traveller participants.

However, many of the environmental risk factors associated with myopia in the IES may be interrelated; moreover, the statistical adjustment may not altogether remove the influence of one risk factor over another. Furthermore, in considering the IES results, it is essential to stress the cross-sectional nature of the data, the analysis is, therefore, descriptive addressing association and not causal pathways. Notwithstanding these caveats, one clear message from the IES findings is that public health education programmes addressing the importance of daily outdoor activities, managing children's screen-time and sleep-time may be beneficial to the eye health of schoolchildren in Ireland. More research, including longitudinal studies, examining the broader consequences of the ubiquitous media environment, in which children are growing up today, and, in particular, the effect this digital age may have on their health and vision ought to be considered.

Trends in these dynamic and evolving factors need to be monitored over time to identify any changing impact on the progression or reduction in the myopia condition.

Chapter 9 reports on the distribution of ocular biometric measures, and their relationship with refractive status in schoolchildren in Ireland; the association with time spent outdoors during daylight is also addressed.

9 OCULAR BIOMETRY, REFRACTION, AND TIME SPENT OUTDOORS DURING DAYLIGHT IN SCHOOLCHILDREN IN IRELAND

9.1 Summary

Background: Previous studies investigated the relationship between ocular biometry and SER in children; this is the first in Ireland. The effect of ocular biometry and its association with time spent outdoors was also investigated.

Methods: Examination included cycloplegic auto-refraction and non-contact ocular biometric measures of AL, CR and ACD from 1,626 children (see Chapter 6). Time spent outdoors in summer and winter data were as reported in the IES questionnaire (see Appendix 3).

Results: Ocular biometric data were correlated with SER (AL: $r = -0.64$, CR: $r = 0.07$, ACD: $r = -0.33$, AL/CR ratio: $r = -0.79$, all $p<0.001$). Participants aged 12-13-years-old had a longer AL (6-7-years-old 22.53 mm, 12-13-years-old 23.50 mm), deeper ACD (6-7-years = old 3.40 mm, 12-13-years-old 3.61 mm), longer CR (6-7-years-old 7.81 mm, 12-13-years-old 7.87 mm) and a higher AL/CR ratio (6-7-years-old 2.89, 12-13-years-old 2.98), all $p<0.001$. Controlling for age: AL was longer in boys (boys 23.32 mm, girls 22.77 mm), and non-White participants (non-White 23.21 mm, White 23.04 mm); CR was longer in boys (boys 7.92 mm, girls 7.75 mm); ACD was deeper in boys (boys 3.62 mm, girls 3.55 mm, $p<0.001$), and AL/CR ratios were higher in non-White participants (non-White 2.98, White 2.94, $p<0.001$). Controlling for age and ethnicity, more time outdoors in summer was associated with less myopic refraction, shorter AL,

and lower AL/CR ratio. Non-White participants reported spending significantly less time outdoors than White participants ($p<0.001$).

Conclusion: Refractive error variance in schoolchildren in Ireland was best explained by variation in the AL/CR ratio with higher values associated with more myopic refraction. Time spent outdoors during daylight in summer was associated with shorter AL and a less myopic SER in White participants. Strategies to promote daylight/bright sunlight exposure in the wintertime is a study recommendation.

9.2 Introduction

Recent epidemiological studies involving children reported that SER distribution varies with ethnicity (Logan *et al.*, 2011), location (French *et al.,* 2012), and environmental factors such as daylight exposure (Guo *et al.*, 2013; Read, Collins and Vincent, 2015). Longer AL's, and thinner crystalline lens (Wong *et al.,* 2010) are associated with myopic eyes with consequently increased odds of pathological myopia (Saw *et al.*, 2002). Moreover, shorter AL's are associated with hyperopia (Strang, Schmid and Carney, 1998) which may affect visual and educational development due to its association with amblyopia and poorer educational attainment (Williams *et al.,* 2005; Pascual *et al.,* 2014). Of further interest, an association between axial elongation, myopia progression, and reduced time outdoors has been reported in several studies (Guo *et al.*, 2013; Tideman *et al.*, 2019). For example, AL elongation and myopia progression are reportedly slower in summer than in winter in Danish and Chinese children (Donovan *et al.*, 2012; Cui *et al.,* 2013), and young Australian adults (Ulaganathan *et al.*, 2018). Due to the confluence of studies in support of the inverse relationship between light exposure and myopia development (Guo *et al.*, 2013; Read, Collins and Vincent, 2015; Xiong *et al.*, 2017a), there has been a focus by researchers to examine the impact of daylight exposure on children's ocular development. However,

there is a paucity of contemporary population-based age norms for ocular biometric measures in Northern European schoolchildren, and in particular, their relationship with refractive data and environmental factors such as daylight. As daylight is a natural light source, with a continuous spectral power distribution covering the full visible range, its attributes alter with geographical location and season, in particular, day-lengths, and variations in light intensity with fluctuating weather conditions (Adamsson, Laike and Morita, 2017).

Furthermore, seasonal changes in ambient light exposure and AL and SER changes have been previously reported (Read, Collins and Vincent, 2015; Ulaganathan *et al.*, 2018). In this context, understanding the relationships between ocular biometric parameters, refractive status and seasonal light exposure are essential in Ireland where there is considerable variation in day length with shorter day length in winter and longer day length in summer and as significant levels of refractive error exist (Harrington *et al.*, 2018). Notably, the IES (present study) findings for refractive error prevalence were broadly in line with the NICER study in the UK (see chapter 7) (Harrington *et al.*, 2018). In comparison, significantly lower levels of refractive error were reported in the SMS (French *et al.,* 2012).

French *et al.* postulated one reason for the significantly lower myopia prevalence in the SMS might be due to the difference in daylight exposure, as bright sunlight exposure is higher in Sydney, particularly in winter, when compared to Northern Ireland (UK) (French *et al.*, 2012). Epidemiological longitudinal studies reported that time outdoors may prevent or delay the onset of myopia (Jones *et al.*, 2007; French *et al.*, 2013d). Furthermore, clinical trials in Asia found increased time outdoors was associated with a less myopic shift in refraction (Guo *et al.*, 2013b; Wu *et al.*, 2015b; Deng and Pang, 2019). However, the precise biological mechanisms which underpin the protective

effect of time spent outdoors against myopia onset remain unclear; theories include light exposure, depth of focus and dopamine release in the retina (Flitcroft, 2012; Ngo *et al.*, 2013; Chakraborty *et al.*, 2018). More detail on the literature pertaining to time spent outdoors and myopia is presented in section 3.6.

This study is the first to report the distribution of ocular biometric parameters, and their relationship with SER status and time outdoors during daylight in both summer and winter in schoolchildren in Ireland.

9.3   Methods

Chapter 6 presents the IES protocols and methodology in detail. Participation rates are reported in section 7.4. This study protocol included cycloplegic autorefraction, with the representative value for SER used in subsequent analysis.

The Zeiss IOLMaster 500 (Carl Zeiss, Meditec Inc., Jena, Germany) was used to measure the AL (three measurements), ACD (five measurements) and CR (three measurements) (section 6.4.4). Crystalline lens measurements are not presented in the IES as measurement of the crystalline lens was not possible with the IOLMaster. The mean CR was calculated as the average of the steepest and flattest CR. The AL/CR ratio was defined as the AL divided by the mean CR. Parents/legal guardians of participants completed a standardised lifestyle questionnaire (Appendix 3), reporting inter alia, time outdoors during daylight hours in summer and winter; the response options were as follows: less than one hour; one to two hours; two to four hours; or more than four hours.

This study involved 1,441 White participants (White and Traveller participants combined) and 185 non-White participants (See Table 7.2, which presents the IES participants by age-group and ethnicity).

9.3.1 Statistical methodology

Analysis of the distribution of SER, and biometrics involved: descriptive statistics (mean, standard error of mean, standard deviation of the mean, median, range). Measures of skewness and kurtosis were calculated for distributions. Distributions for SER and ocular biometric measures were tested for normality using the Kolmogorov-Smirnov test and were considered normal when $p > 0.05$. (Table 9.1). Linear regression models were constructed to assess the effect of age, ethnicity and gender on the distribution of SER and biometric parameters. Correlations between SER and biometric measures were calculated with Pearson correlation analysis. Linear regression models were created to examine the relationships between biometric parameters and SER while controlling for age, and ethnicity. The regression coefficient (B) and the 95% confidence interval for B were calculated.

Time spent outdoors in summer and winter data satisfied the assumptions required to perform multinomial logistic regression. Controlling for age and ethnicity logistic regression models were applied to examine the relationship between time outdoors during daylight and SER, and time outdoors during daylight and ocular biometric parameters, with participants reporting over four hours outdoors in daylight as the reference category.

The right and left eyes were significantly correlated for SER and ocular biometric measures (Pearson correlation: SER $r = 0.89$, AL $r = 0.95$, CR $r = 0.96$, ACD $r = 0.96$, AL/CR $r = 0.89$, all $p < 0.001$), therefore, results are presented for the right eye only. The 5% level of significance was used throughout and CIs were 95%.

9.4 Results

Table 9.1 presents descriptive statistics, including measures of spread, of SER, and ocular biometric parameters measures by age, gender and ethnicity for study

participants. The distribution for SER was non-normal. Ocular biometric measures were in the main normally distributed for the population overall with some exceptions in subgroups (see the final column in Table 9.1). The SER mean ± standard deviation (SD) in study participants (6-7 years 1.44 ± 1.25 D, 12-13 years 0.38±1.61 D, p<0.001) was previously reported (see Chapter 7 and Figure 7.1). The SER mean ± SD for non-White participants (6-7 years 0.83 ± 1.00 D, 12-13 years -0.64 ± 1.98 D) was lower than White participants (6-7 years 1.51 ± 1.26 D, 12-13 years 0.51 ± 1.51 D, p<0.001), with no gender differences (p=0.09).

The AL mean ± SD was shorter in 6-7-year-olds (22.53 ± 0.79 mm) than in 12-13-year-olds (23.50 ± 0.89 mm) (p<0.001), (Figure 9.1), longer in boys (23.32 ± 0.95 mm) than girls (22.77 ± 0.92 mm) (p<0.001), and longer in non-White participants (23.21 ± 1.11 mm) than White participants (23.05 ± 0.95 mm) (p=0.006).
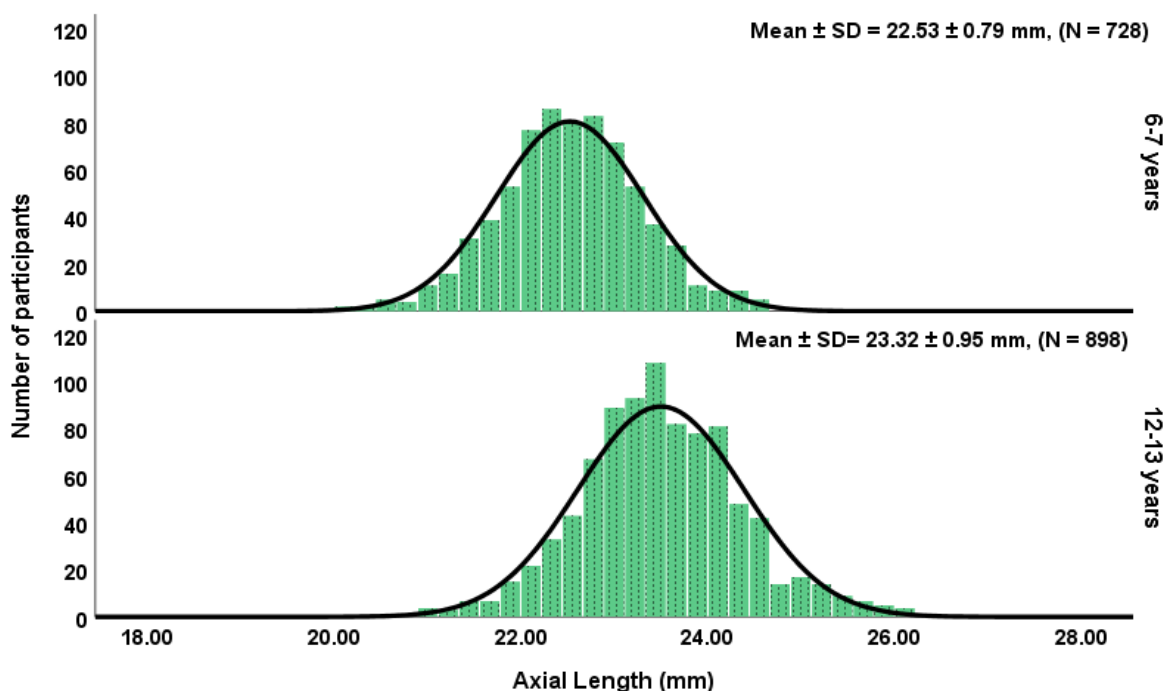
Figure 9.1 Distribution of axial length (mm) in 728 6-7-year-old (top image) and 898 12-13-year-old (bottom image) participants. The mean axial length was significantly longer in the older age group (6-7 years 22.53±0.79mm, 12-13 years 23.32±0.95mm). Each histogram bar represents 0.2mm

The CR mean ± SD was lower in 6-7-year-olds (7.81 ± 0.27 mm) than 12-13-year-olds (7.87 ± 0.26 mm) (p<0.001), (Figure 9.2), lower for girls (7.75 ± 0.25 mm) than boys (7.92 ± 0.26 mm) (p<0.001), with no ethnic differences (p=0.06).
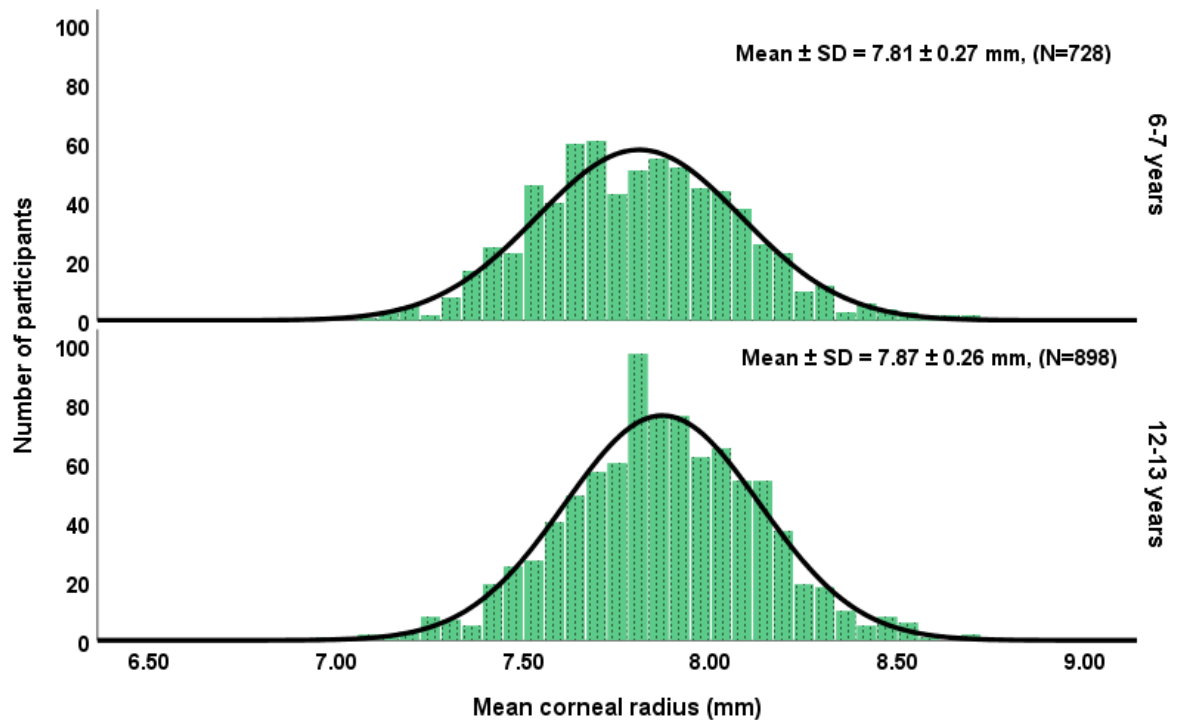
Figure 9.2 Distribution of mean corneal radius in 728 6-7-year-olds (top image) and 898 12-13-year-olds (bottom image). The mean CR was longer in the older age group (6-7 years 7.81±0.27mm, 12-13 years 7.87±0.26mm). Each histogram bar represents 0.02mm

The ACD mean ± SD was shallower in 6-7-year-olds (3.40 ± 0.21 mm) than 12-13-year-olds (3.61 ± 0.11 mm) (p<0.001), shallower in girls (3.55 ± 0.25 mm) than in boys (3.62 ± 0.26 mm) (p<0.001), with no ethnic differences (p=0.13).

The AL/CR ratio mean ± SD was lower in 6-7-year-olds (2.89 ± 0.09) than 12-13-year-olds (2.99 ± 0.11) (p<0.001), lower for White participants (2.94 ± 0.11) than non-White participants (2.98 ± 0.12) (p<0.001), with no gender differences (p=0.30).

Table 9.1 Measures of spread for spherical equivalent refraction, and ocular biometric parameters by age, gender and ethnicity, in study participant's right eyes

	Mean	SEM	SD	Median	Range	Kurtosis	Skewness	K-S
Spherical equivalent (D)					Min, max			
6-7 years (n=728)	1.44†	0.05	1.25	1.25	-4.50, 9.00	6.09	1.62	< 0.001
12-13 years (n=898)	0.38	0.05	1.61	0.50	-10.25, 8.25	5.88	-0.50	< 0.001
Boys (n=881)	0.90‡	0.05	1.52	0.75	-5.00, 8.00	3.73	0.48	< 0.001
Girls (n=745)	0.80	0.06	1.59	0.75	-10.25, 9.00	8.00	-0.52	< 0.001
White (n=1441)	0.96	0.04	1.49	0.75	-5.00, 9.00	4.61	0.56	< 0.001
Non-White (n=185)	0.00§	0.41	1.78	0.25	-10.25, 3.00	7.74	-0.22	< 0.001
Axial length (mm)								
6-7 years (n=728)	22.53†	0.03	0.79	22.52	19.24, 25.73	0.93	-0.15	0.20
12-13 years (n=898)	23.50	0.03	0.89	23.46	20.37, 27.65	0.98	0.25	0.01
Boys (n=881)	23.32‡	0.03	0.95	23.35	19.14, 26.47	0.64	0.01	0.20
Girls (n=745)	22.77	0.03	0.92	22.75	19.69, 27.65	1.56	0.37	0.01
White (n=1441)	23.05	0.03	0.95	23.04	19.69, 26.27	0.38	0.15	0.20
Non-White (n=185)	23.21§	0.08	1.11	23.26	19.14, 27.66	1.64	0.26	0.20

	Mean	SEM	SD	Median	Range	Kurtosis	Skewness	K-S
Corneal radius (mm)								
6-7 years (n=728)	7.81†	0.01	0.27	7.80	7.10, 8.69	0.05	0.27	0.20
12-13 years (n=898)	7.87	0.01	0.26	7.87	6.95, 8.71	0.22	-0.05	0.20
Boys (n=881)	7.92‡	0.01	0.26	7.92	7.10, 8.71	0.08	0.05	0.20
Girls (n=745)	7.75	0.01	0.25	7.75	6.76, 8.68,	0.20	0.11	0.20
White (n=1441)	7.85	0.01	0.27	7.84	7.09, 8.71	0.08	0.12	0.10
Non-White (n=185)	7.80	0.02	0.27	7.83	6.95, 8.45	-0.22	-0.18	0.20
Axial length/Corneal radius								
6-7 years (n=728)	2.89	0.003	0.09	2.89	2.50, 3.24	1.79	-0.36	0.20
12-13 years (n=898)	2.99†	0.004	0.11	2.98	2.59, 3.56	2.11	0.43	0.01
Boys (n=881)	2.95	0.004	0.11	2.95	2.59, 3.39	1.05	0.07	0.01
Girls (n=745)	2.94	0.004	0.11	2.93	2.50, 3.56	2.74	0.63	0.01
White (n=1441)	2.94	0.001	0.11	2.94	2.50, 3.39	1.29	0.15	0.01
Non-White (n=185)	2.98§	0.01	0.12	2.95	2.73, 3,56	3.32	1.28	0.01
Anterior chamber depth (mm)								
6-7 years (n=728)	3.40	0.02	0.21	3.40	2.45, 3.91	3.31	-0.81	0.05
12-13 years (n=898)	3.61†	0.01	0.25	3.62	2.26, 4.33,	2.62	-0.67	0.07
Boys (n=881)	3.63‡	0.01	0.26	3.63	2.26, 4.33	3.84	-0.94	0.02

	Mean	SEM	SD	Median	Range	Kurtosis	Skewness	K-S
Girls (n=745)	3.55	0.01	0.25	3.55	2.45, 4.26	0.70	-0.24	0.02
White (n=1441)	3.60	0.01	0.26	3.61	2.26, 4.33	2.49	-0.67	0.10
Non-White (n=185)	3.54	0.02	0.23	3.53	2.85, 4.08	0.12	-0.13	0.20

D, dioptre; SEM, standard error of mean; SD, standard deviation; mm, millimetre; K-S, Kolmogorov-Smirnov test for normality; min, minimum; max, maximum; n, number of participants; † Significant difference between age groups; ‡Significant difference between boys and girls; §Significant difference between White and non-White participants.

9.4.1 The relationships between spherical equivalent refraction and ocular biometric parameters

The relationships between SER and ocular biometric parameters were examined using linear regression analysis (see Table 9.2).

Table 9.2 The association of ocular biometric parameters and spherical equivalent refraction in 6-7-year-old and 12-13-year-old study participants right eyes

	Pearson Correlation	β Coefficient (95% CI)†	Model R^2	F statistic	P value
6-7 years (White)					
Axial length (mm)	-0.48	-0.77 (-0.88 to -0.66)	0.23	187.71	**< 0.001**
Corneal radius (mm)	0.09	0.42 (0.06 to 0.77)	0.007	5.26	**0.02**
Axial length/Corneal radius	-0.65	-9.34 (-10.10 to -8.48)	0.42	454.01	**< 0.001**
Anterior chamber depth	-0.26	-1.16 (-2.34 to -0.08)	0.05	4.61	**0.04**
12-13 years (White)					
Axial length (mm)	-0.64	-1.12 (-1.22 to -1.03)	0.41	549.36	**<0.001**
Corneal radius (mm)	0.14	0.80 (0.39 to 1.20)	0.02	15.07	**< 0.001**
Axial length/Corneal radius	-0.82	-11.99 (-12.58 to -11.40)	0.67	1575.33	**<0.001**
Anterior chamber depth	-0.34	-1.90 (-2.32 to -1.47)	0.12	77.86	**<0.001**
6-7 years (non-White)					
Axial length (mm)	-0.27	-0.33 (-0.60 to -0.06)	0.06	6.1	**0.02**
Corneal radius (mm)	-0.01	-0.05 (-0.97 to 0.87)	-0.01	0.01	0.91
Axial length/Corneal radius	-0.47	-6.78 (-9.72, -3.85)	0.21	21.19	**<0.001**

	Pearson Correlation	β Coefficient (95% CI)†	Model R^2	F statistic	P value
Anterior chamber depth	-0.07	-0.70 (-5.11 to 3.71)	0.01	0.11	0.74
12-13 years (non-White)					
Axial length (mm)	-0.72	-1.36 (-1.62 to -1.11)	0.52	111.03	**<0.001**
Corneal radius (mm)	0.08	0.54 (-0.89 to 1.98)	0.01	0.57	0.45
Axial length/Corneal radius	-0.86	-13.70 (-15.33 to -12.07)	0.73	277.98	**<0.001**
Anterior chamber depth	-0.32	-2.62 (-4.33 to -0.92)	0.10	9.36	**0.003**

†*In the regression model, spherical equivalent refractive error was the dependent variable, with each biometric variable as an explanatory variable, mm: millimetres.*

Axial length: The scatter diagram and regression line of AL measurement and SER were constructed to investigate the rate of change in AL with SER (Figure 9.3).

An inverse relationship was found between AL and SER (r= -0.64, R^2=0.41, p<0.001). The linear regression equation was represented by:

Axial length mm = 23.41-0.4(SER(D))
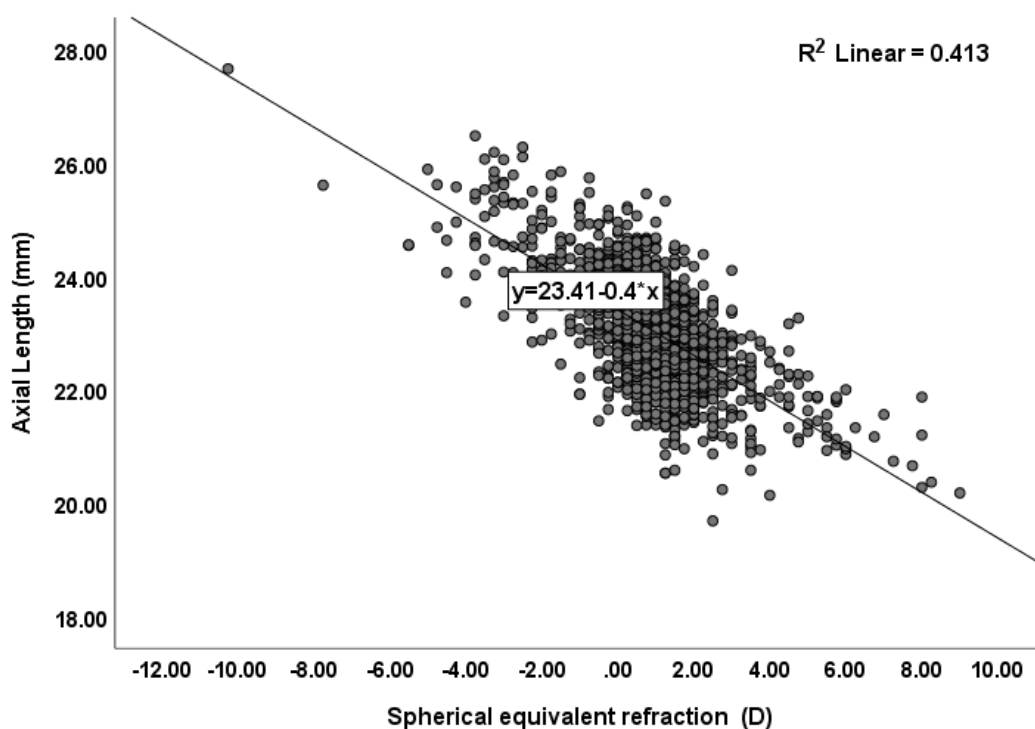
Figure 9.3 A plot of axial length (mm) against spherical equivalent refraction (D) (n=1,626). The line in the scatter plot demonstrates the linear regression equation: axial length (mm) = 23.41 – 0.4 (spherical equivalent refraction (D))

The per-unit change in AL had less impact on SER in 6-7-year-old non-White participants compared to White participants (6-7-years White: β coefficient = -0.77 D, non-White: β coefficient = -0.33 D, p<0.001). The reverse was found in the 12-13-year-olds, whereby the per-unit change in AL had less impact on SER in White participants compared to non-White participants (12-13-year-olds White: β coefficient = -1.12 D,

non-White β coefficient = -1.36 D, p<0.001). For example, in White 6-7-year-olds, AL explained 23% of the variability in SER (R^2=0.23), this dropped to 6% in non-White 6-7-year-olds (R^2=0.06). In contrast, AL explained 41% of the variability in SER (R^2=0.41) in White 12-13-year-olds, which increased to 52% in non-White 12-13-year-olds (R^2=0.52).

Corneal radius: The scatter diagram and regression line of mean CR measurement and SER were constructed to investigate the rate of change in mean CR with SER (Figure 9.4). There was a significant, albeit weak, relationship between mean CR and SER (r= 0.07, R^2=0.005, p=0.005). Overall, mean CR explained only 0.5% of the variation in SER. The linear regression equation was represented by:

Corneal radius (mm) = 7.83 + 0.01 (SER (D))
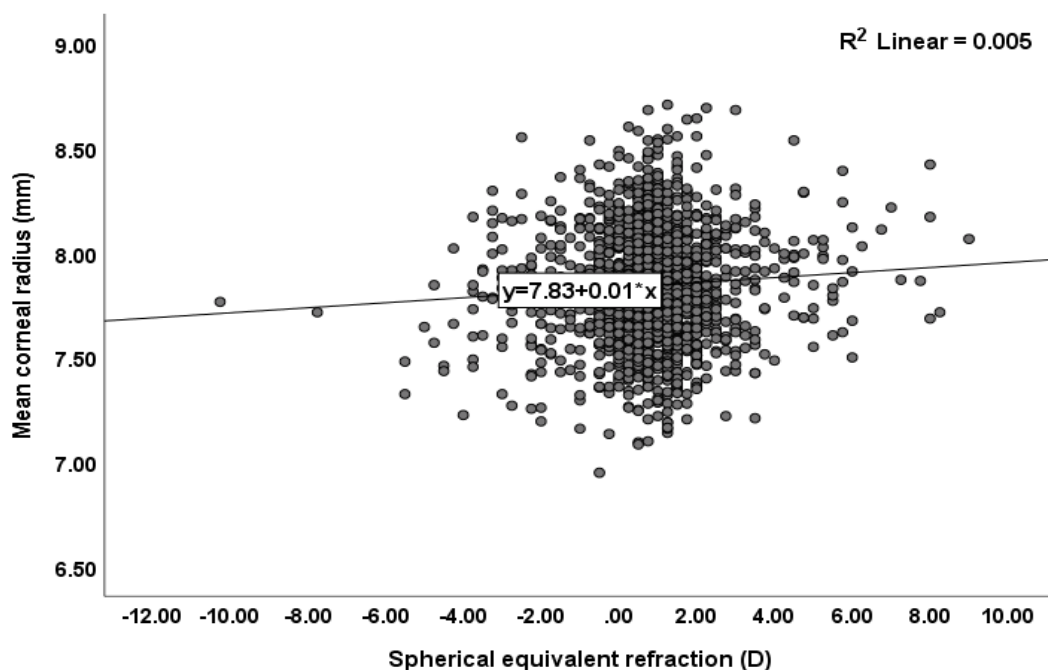
Figure 9.4 A plot of mean corneal radius ((horizontal corneal radius + vertical corneal radius)/2) (mm) against spherical equivalent refraction (D) (n=1,626). The line in the scatter plot demonstrates the linear regression equation: mean corneal radius (mm) = 7.83 + 0.01 (spherical equivalent refraction (D))

Corneal radius was not correlated with SER in non-White participants (see Table 9.2).

Anterior chamber depth: The scatter diagram and regression line of ACD measurement and SER were constructed to investigate the rate of change in ACD with SER (Figure 9.5). The ACD was negatively correlated with SER and overall, explained 11% of the variability in SER (r= -0.31, R^2=0.11, p<0.001). The linear regression equation was:

Amterior chamber depth (MM) = 3.61 – 0.06 (SER (D))
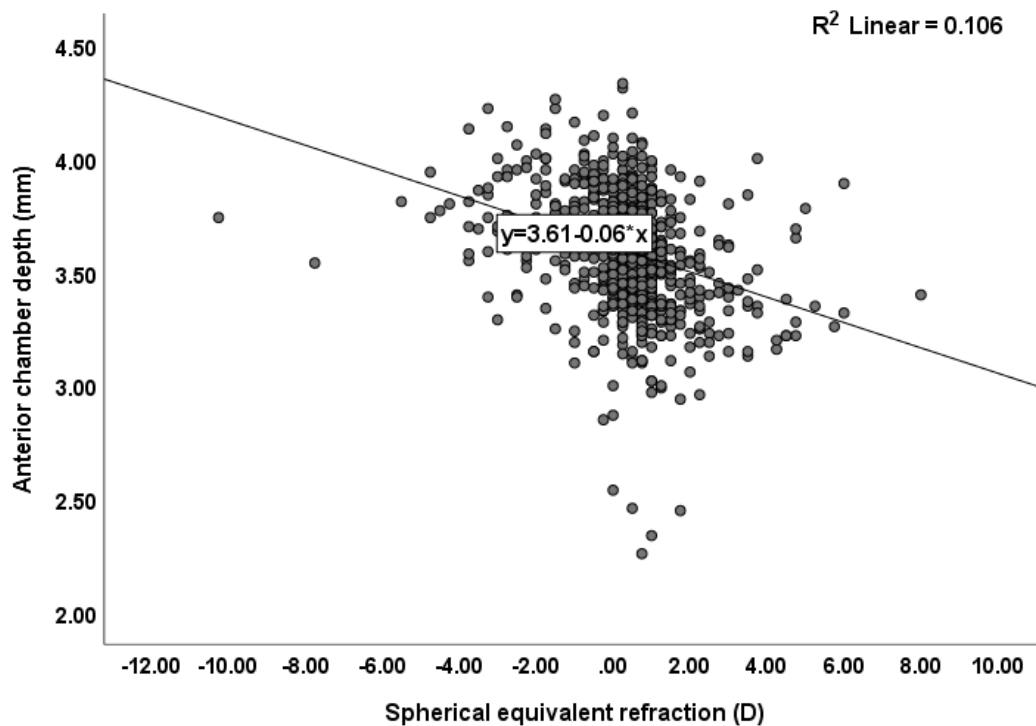
Figure 9.5 A plot of anterior chamber depth (mm) against spherical equivalent refraction (D) (n=1,601). The line in the scatter plot demonstrates the linear regression equation: anterior chamber depth (mm) = 3.61 – 0.06 (spherical equivalent refraction (D))

Axial length/CR ratio: The scatter diagram and regression line of AL/CR and SER were constructed to investigate the rate of change in the AL/CR ratio with SER (Figure 9.6). The AL/CR ratio was strongly correlated with SER (r= -0.79, R^2=0.63, p<0.001). The linear regression equation was:

Axial length / corneal radius ratio = 2.99 – 0.06 (SER (D))
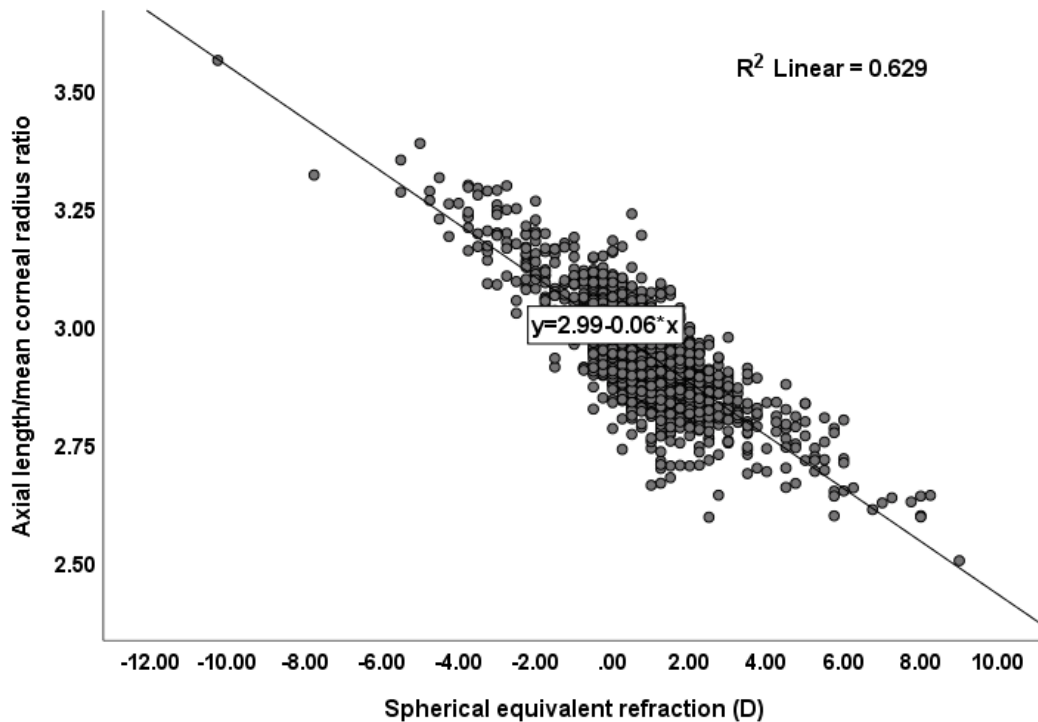
Figure 9.6 A plot of axial length/ mean corneal radius ratio against spherical equivalent refraction (D) (n=1,626). The line in the scatter plot demonstrates the linear regression equation: Axial length/mean corneal radius ratio = 2.99 – 0.06 (Spherical equivalent refraction (D))

The relationship between the AL/CR ratio varied with ethnicity, amongst White 6-7-year-olds the AL/CR ratio explained variance in SER to a greater extent than amongst non-White participants (White 42% versus non-White 21%), however, amongst the older age cohort the reverse was found (White 67% versus non-White 73%).

A linear regression model was calculated to examine the relationship between SER (dependent variable) with covariates AL, CR and ACD jointly while controlling for age and ethnicity. The covariates could significantly predict the SER (r=0.84 and R^2=0.73, F=625.9, p<0.001); 73% of the variance in SER was explained by variation in AL, CR and ACD.

The linear regression equation was represented by:

$SER = 6.32 - 1.91 (AL (mm)) + 4.27 (CR (mm)) + 1.45 (ACD (mm))$

9.4.2 Time spent outdoors during daylight in summer and winter

Participants reported spending more time outdoors during daylight in summer than in winter ($p<0.001$). Participants aged 6-7-years-old spent more time outdoors during daylight than 12-13-year-olds in summer ($p<0.001$) and winter ($p=0.01$). White participants spent more time outdoors during daylight than non-White participants in summer (6-7 years $p<0.001$; 12-13 years $p<0.001$), and winter (6-7 years $p=0.002$; 12-13 years $p=0.001$). Time spent outdoors was not associated with gender during winter ($p=0.11$) or summer ($p=0.053$).

Figure 9.7 displays the percentage of participants in each time outdoors during daylight in summer category by age and ethnicity. Figure 9.8 displays the percentage of participants in each time outdoors during daylight in winter category by age and ethnicity.
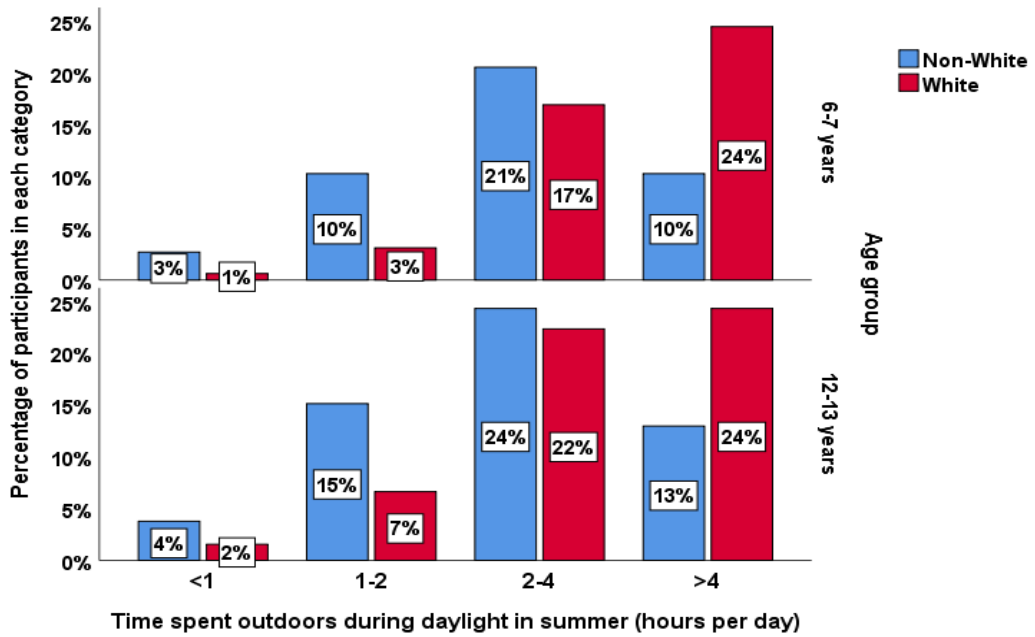
Figure 9.7 The percentage of participants in each category of time spent outdoors in summer, by age group (6-7-years top image, 12-13 years bottom image) and ethnicity (non-White participants blue bars (6-7- years 81 participants, 12-13-years 104 participants), White participant's red bars (6-7 years 647 participants, 12-13-years 794 participants))
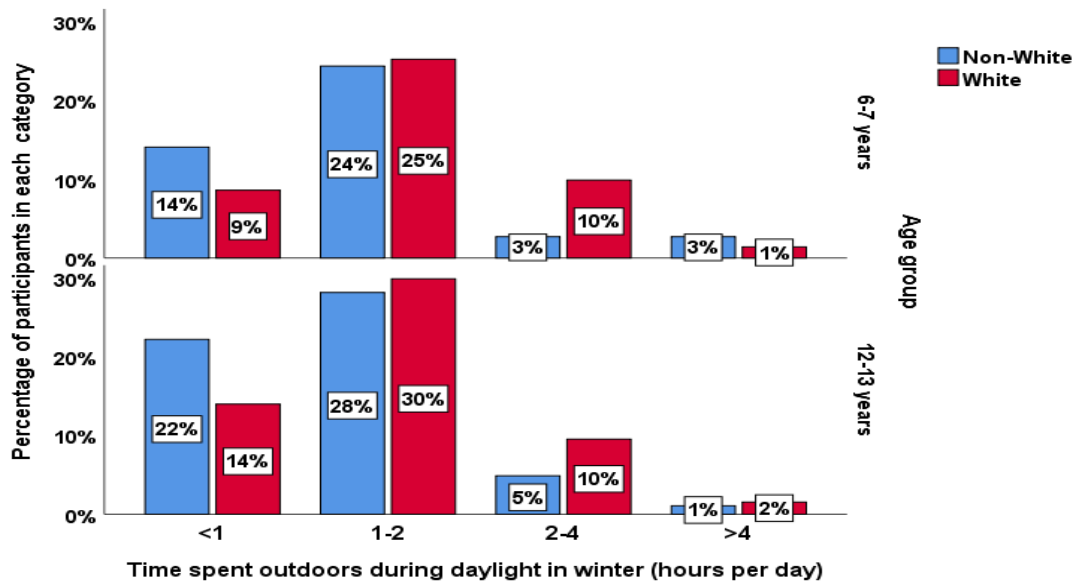
Figure 9.8 The percentage of participants in each category of time spent outdoors in winter, by age group (6-7-years top image, 12-13 years bottom image) and ethnicity (non-White participants blue bars (6-7- years 81 participants, 12-13-years 104 participants), White participant's red bars (6-7 years 647 participants, 12-13-years 794 participants))

9.4.3 The relationship between spherical equivalent refraction, ocular biometry and time outdoors

As time spent outdoors was significantly associated with both age-group and ethnicity, and to investigate further the relationship between time spent outdoors with SER and ocular biometric parameters, general linear models were constructed, controlling for both age and ethnicity in all analyses (Table 9.3).

Table 9.3 The relationship between spherical equivalent refraction, axial length, axial length/corneal radius ratio and time spent outdoors during daylight in summer categories, controlling for age and ethnicity in all analysis

Time spent outdoors †	*B*	SE	95% CIs	*t*	*P* value
Spherical equivalent refraction (D)					
<1 hour	-1.04	0.23	-1.48 to -0.60	-4.60	**<0.001**
1-2 hours	-0.41	0.12	-0.64 to -0.17	-3.36	**0.001**
2-4 hours	-0.11	0.08	-0.26 to 0.05	-1.38	0.167
>4 hours	0[a]	.	.	.	.
Axial length (mm)					
<1 hour	0.31	0.13	0.06 to 0.57	2.29	**0.012**
1-2 hours	0.17	0.07	0.03 to 0.31	2.40	**0.016**
2-4 hours	0.12	0.05	0.03 to 0.21	2.62	**0.009**
>4 hours	0[a]	.		.	.
Axial length/corneal radius ratio					
< 1 hour	0.05	0.02	0.02 to 0.08	3.37	**<0.001**
1-2 hours	0.02	0.01	0.01 to 0.03	2.12	**0.01**
2-4 hours	0.01	0.01	-0.01 to 0.02	1.83	0.068
>4 hours	0[a]	.		.	.

Beta coefficient (B), dioptre (D), millimetre (mm), this parameter is set to zero because it is redundant (a.), standard error (SE), † average daily time spent outdoors during daylight in summer.

Spherical equivalent refraction: participants in the least time outdoors group (< one hour per day), were more myopic by –1.04 D (CIs -1.48 D to -0.60 D, p<0.001), and participants in the 1-2 hours outdoors group were more myopic by -0.41 D (CIs: -0.64 D

to -0.17 D, p=0.001) when compared to participants in the most time outdoors category (more than four hours-per-day). There was no significant difference in SER between participants in the 2-4 hours outdoors category and more than four hours outdoors category (p=0.17).

Axial length: AL was 0.31 mm (CIs: 0.06 mm to 0.57 mm, p=0.01) longer in the least time outdoors cohort; 0.17 mm (CIs: 0.03 mm to 0.31 mm, p=0.02) longer in the 1-2 hours outdoors category; and 0.12 mm (CIs: 0.03 mm to 0.21 mm, p=0.01) longer in the 2-4 hours outdoors per-day category, when compared to participants in the most time outdoors category (more than four hours per day).

Axial length/corneal radius ratio: the AL/CR ratio was 0.05 (CIs: 0.02 to 0.08, p<0.001) higher in the least time outdoors category (less than one hour per day), and 0.02 (CIs: 0.01 to 0.03, p=0.01) higher in the 1-2 hours outdoors per day category when compared to participants in the most time outdoors group (more than four hours per day). There was no significant difference in the AL/CR ratio between participants in the 2-4-hours outdoors category and those in the most time outdoors (p=0.07).

Neither CR *(*p=0.34) nor ACD (p=0.10) was associated with time outdoors during daylight in summer.

While increased time spent outdoors was significantly associated with a less myopic SER amongst 12-13-year-old White participants (p<0.001), in contrast, when analysed separately, time outdoors was not associated with SER amongst non-White participants in either age cohort (6-7 years p=0.42, 12-13 years p=0.52). Figure 9.9 displays boxplots which illustrate the distribution of SER in the various "time spent outdoors" categories in 6-7-year-old and 12-13-year-old White and non-White participants. The mean SER increased with increasing time outdoors in the White 12-13-year-old group.
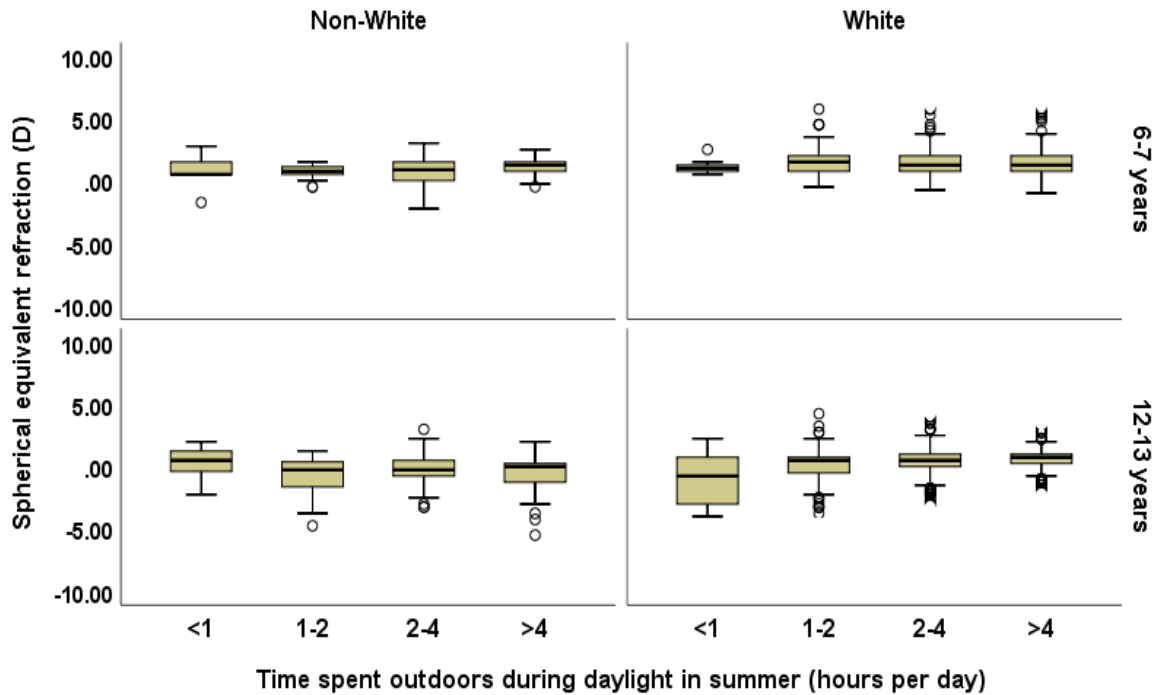
Figure 9.9 Boxplots showing the distribution of spherical equivalent refraction (dioptre) in time spent outdoors during daylight in summer categories

6-7-year-olds (non-White 81 participants top left image and 640 White participants top right image), and 12-13-year-olds (104 non-White participants bottom left image and 778 White participants bottom right image). In White, 12-13-year-olds mean SER was significantly less myopic with increased time outdoors category (bottom right image). From top to bottom the five horizontal bars represent the maximum, 75th percentile, median, 25th percentile the whiskers mark the range of the data with the outliers (<5th percentile or >95th percentile) shown as grey dots. The numbers in each time spent outdoors category are as follows: 6-7-years non-White: 5 <1hour, 19 1-2 hours, 38 2-4 hours, 19 > 4 hours), 6-7-years White: 9 < 1 hour, 44 1-2 hours, 240 2-4 hours, 347 >4 hours. 12-13 non-White: 7 < 1 hour, 28 1-2 hours, 45 2-4 hours, 24 > 4 hours, 12-13 White: 22 < 1 hour, 94 1-2 hours, 317 2-4 hours, 345 > 4 hours.

Similarly, increased time outdoors was associated with shorter AL in White participants ($p<0.001$), but not in non-White participants ($p=0.35$). Figure 9.10 displays boxplots which illustrate the distribution of AL data in each time outdoors category by age and ethnicity categories.
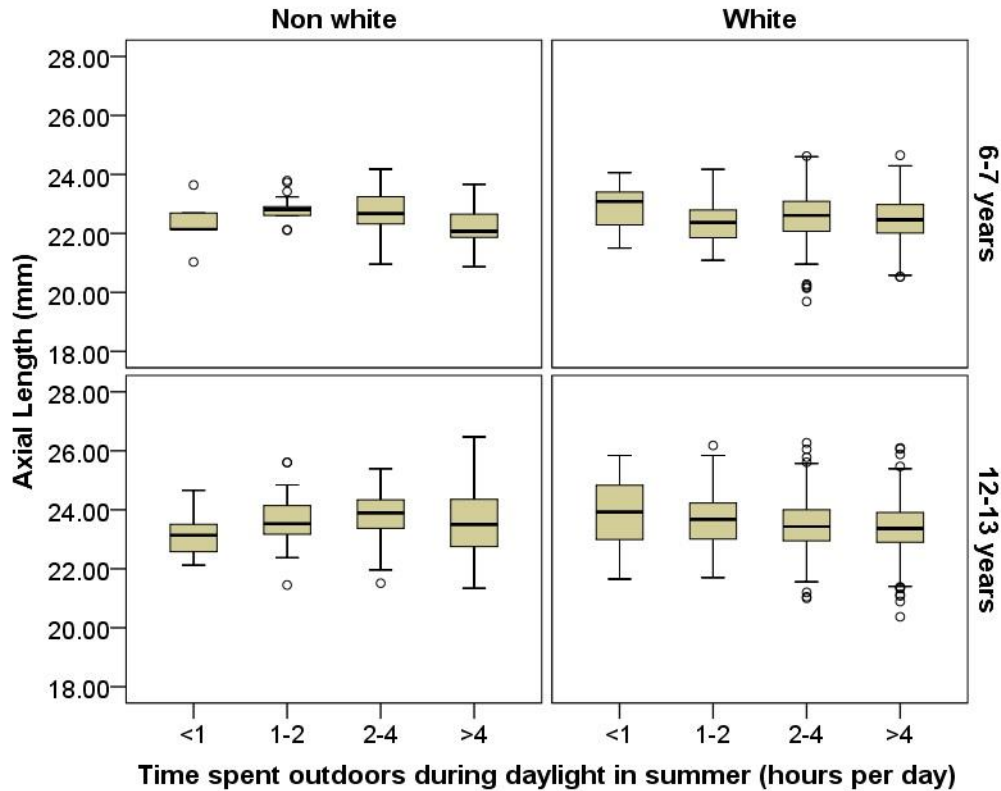
Figure 9.10 Boxplots showing the distribution of spherical equivalent refraction (dioptre) in time spent outdoors during daylight in summer categories

6-7-year-olds (81 non-White participants top left image and 640 White participants top right image), and 12-13-year-olds (104 non-White participants bottom left image and 778 White participants bottom right image. participants top left image and White participants top right image), and 12-13-year-olds (non-White participants bottom left image and White participants bottom right image). In White, 12-13-year-olds mean SER was significantly less myopic with increased time outdoors category (bottom right image). From top to bottom the five horizontal bars represent the maximum, 75th percentile, median, 25th percentile the whiskers mark the range of the data with the outliers (<5th percentile or >95th percentile) shown as grey dots. The numbers in each time spent outdoors category are as follows: 6-7-years non-White: 5 <1hour, 19 1-2 hours, 38 2-4 hours, 19 > 4 hours), 6-7-years White: 9 < 1 hour, 44 1-2 hours, 240 2-4 hours, 347 >4 hours. 12-13 non-White: 7 < 1 hour, 28 1-2 hours, 45 2-4 hours, 24 > 4 hours, 12-13 White: 22 < 1 hour, 94 1-2 hours, 317 2-4 hours, 345 > 4 hours.

The means for SER and ocular biometric parameters are presented by age (6-7 years and 12-13 years), ethnicity (White, non-White) and time outdoors during daylight in summer categories in Table 9.4.

Time spent outdoors during daylight in wintertime was not associated with SER (p=0.49), AL (p=0.64), CR (p=0.33), AL/CR ratio (p=0.71), or ACD (p=0.56).

Table 9.4 Relationship between spherical equivalent, ocular biometric parameters and time spent outdoors during daylight in the summertime in study participant's right eyes

Mean (SE)	Less than one hour	One to two hours	Two to four hours	More than four hours	*P* value	Less than one hour	One to two hours	Two to four hours	More than four hours	*P* value
	White 6-7 years					*Non-White 6-7 years*				
	n=9	n=44	n=240	n=347		n=5	n=19	n=38	n=19	
SER	1.21 (0.21)	1.62 (0.20)	1.53 (0.09)	1.53 (0.06)	0.86	0.70 (0.74)	0.71 (0.14)	0.74 (0.18)	1.16 (0.19)	0.44
AL/CR	2.88 (0.02)	2.86 (0.01)	2.88 (0.01)	2.89 (0.01)	0.36	2.93 (0.04)	2.90 (0.02)	2.92 (0.01)	2.90 (0.04)	0.45
AL	22.65 (0.28)	22.41 (0.10)	22.60 (0.06)	22.47 (0.04)	0.17	22.34 (0.42)	22.58 (0.26)	22.78 (0.12)	22.23 (0.17)	0.12
CR	7.86 (0.08)	7.84 (0.05)	7.84 (0.02)	7.79 (0.01)	0.14	7.62 (0.14)	7.86 (0.04)	7.79 (0.04)	7.67 (0.07)	0.09
ACD	3.28 (0.03)	3.22 (0.20)	3.45 (0.05)	3.35 (0.03)	0.08	3.48 (0.08)	3.44 (0.05)	3.43 (0.05)	3.38 (0.03)	0.80
	White 12-13 years					*Non-White 12-13 years*				
	n=22	n= 94	n=317	n=345		n=7	n=28	n=45	n=24	
SER	-1.14 (0.45)	0.05 (0.17)	0.52 (0.05)	0.72 (0.07)	**<0.001**	0.29 (0.56)	-0.95 (0.38)	-0.57 (0.31)	-0.70 (0.39)	0.52
AL/CR	3.09 (0.52)	3.01 (0.01)	2.99 (0.01)	2.97 (0.01)	**<0.001**	2.93 (0.02)	3.03 (0.02)	3.03 (0.02)	3.04 (0.02)	0.19
AL	24.00 (0.25)	23.70 (0.10)	23.45 (0.05)	23.40 (0.04)	**<0.001**	23.16(0.32)	23.67 (0.17)	23.87 (0.16)	23.57 (0.25)	0.35
CR	7.77 (0.07)	7.87 (0.03)	7.86 (0.01)	7.89 (0.01)	0.12	7.90 (0.06)	7.83 (0.06)	7.88 (0.01)	7.89 (0.01)	0.22
ACD	3.70 (0.05)	3.68 (0.03)	3.63 (0.02)	3.60 (0.02)	0.08	3.38 (0.13)	3.57 (0.05)	3.57 (0.04)	3.60 (0.06)	0.35

SER: spherical equivalent refraction, AL/CR: axial length/corneal radius ratio, AL: axial length, CR: corneal radius, ACD: anterior chamber depth, SE: standard error of the mean, n: number of participants. Significant associations between time outdoors during daylight and spherical equivalent refraction and biometry are highlighted in bold (one-way ANOVA, Bonferroni post hoc tests were run for axial length and SER and the AL/CR for the 12-13-year-old White participants which revealed SER increased, axial length shortened and the AL/CR decreased significantly with each outdoors category. However, there was no significant difference between 2-4 hours and > 4 hours outdoors during daylight for SER (p=0.50) and AL (p>0.99) and AL/CR (p=0.06))

9.5 Discussion

The IES is the first population-based study to analyse the association between SER and ocular biometrics and associations between these parameters with time spent outdoors during daylight in schoolchildren in Ireland. Similar to many previously published studies, the mean SER was significantly more myopic in non-White participants in both age cohorts and negatively associated with AL, with a longer AL related to more negative SER (Rudnicka *et al.*, 2010; Logan *et al.*, 2011; French *et al.,* 2012). For example, the longer AL found in non-White participants in this study, mirrors the AES and the Child Heart and Health Study in England, where South Asian participants had longer AL and a more myopic SER than White participants (Rudnicka *et al.*, 2010; Logan *et al.*, 2011). The extent to which AL explained the variability in SER in this study increased with age (6-7 years 21%, 12-13 years 43%), which concurs with the NICER study (6-7 years 30%, 12-13 years 47%) (French *et al.,* 2012) and Cruickshank and Logan (2018) (6-7 years 37%, 12-13 years 48% and 18-25 years 68%) and contrasts with the SMS (6-7 years 20%, 12-13 years 10%), where a lower prevalence of clinically significant hyperopia and myopia was reported (French *et al.,* 2012). Hence, it may be postulated that refractive errors which develop during childhood may be best explained by variances in AL and this mismatch between AL and the focusing power of the eyes optical components (lens and cornea) becomes more exaggerated with increasing age. While there has been extensive research around the relationship between AL and myopia, the relationship between a shorter AL and a more hyperopic SER found in the IES was strong and aligned with Strang, Schmid and Carney (1998) and Khan (2012).

In agreement with previous studies, the relationship between CR and SER in the present study was, weak (Saw *et al.*, 2002; French *et al.,* 2012). However, the significantly

longer CR found in the older age cohort compared to the younger age cohort in this study contrasts with both the NICER study and the SMS where no difference with age was found (French *et al.,* 2012). When analysed separately there was no significant difference in mean CR with age in the Non-White participants (6-7 years 7.76mm, 12-13 years 7.84mm p=0.08), however in the white participants the older participants had longer CR than the younger age cohort (6-7 years 7.81 mm, 12-13 years 7.88, p<0.001). Previous research generally confirms that most corneal growth takes place in the first two years of life and that corneal radius has reached approximately adult levels by six years of age (Fledelius, & Stubgaard, 1986; Zadnick *et al.,* 2003). Longitudinal research is necessary to investigate when CR stabilises in an Irish population.

Anterior chamber depth in 6-7 year-olds (3.40mm) in the present study was shallower than reported in 6-7-year-old Australian children; where significantly shallower ACD readings were found pre-cycloplegia (3.36mm) when compared to post-cycloplegia (3.54mm) (Ojaimi *et al.*, 2005). As ACD was not measured prior to cycloplegia in this study, findings are likely to be an overestimate of ACD in the natural state. Further analysis of ACD in the Irish population merits investigation due to the association between shallow ACD's with angle closure glaucoma (Schuster *et al.*, 2016). Longer ACD was associated with a more myopic SER in this study; this could be due to longer eyes having deeper ACD although the resultant refractive effect of a longer ACD is towards a less myopic SER (Ojaimi *et al.*, 2005).

The relationship between the AL/CR ratio and SER was linear and negatively associated with SER in the current study. Moreover, the AL/CR ratio best explained the variance in SER, and this relationship strengthened with age. In contrast, a higher mean AL/CR ratio (over 3.00), was reported in Singaporean 7-9-year-olds and associated with a more negative SER (Saw *et al.*, 2002), which more closely aligns with that found in

non-White participants in the present study (6-7 years 2.99, 12-13 years 3.03). In the current study, the lowest mean AL/CR ratio was found amongst 6-7-year-old White participants (2.88) and associated with the highest mean SER (+1.51 D). In comparison, the highest AL/CR ratio was found in non-White 12-13-year-olds (3.03), where the lowest SER was found (-0.61 D). While the AL/CR ratio has received considerable attention with regard to myopia progression in non-White communities (Huang *et al.*, 2016), its association with hyperopia found in Ireland is important and concurs with a previous study involving Saudi Arabian children aged 5-16 years, where the relationship persisted even in hyperopic amblyopic eyes (Khan, 2012). For instance, the AL/CR ratio provides valuable information regarding refractive status (myopia, hyperopia progression), particularly in situations where cycloplegic agents are not appropriate (Huang *et al.*, 2016).

Seventy-three percent of the variance in SER was explained by variation in AL, CR and ACD in the present study. However, the relationship between the crystalline lens and SER was not examined in the present study which is a study limitation. Prior research has demonstrated that the crystalline lens undergoes substantial age related changes in childhood with lens thinning in early childhood (Mutti *et al.,* 2005) and thickening at about age 10 years ((Mutti *et al.,* 1998; Wong *et al.,* 2010; Mutti *et al.,* 2012). Maintaining a precise balance between the AL and combined optical power of the CR and crystalline lens is essential in order to maintain a stable refractive state. Wong *et al.*'s (2010) and Mutti *et al.*'s (2012) longitudinal studies reported loss of compensatory changes in the crystalline lens during childhood axial elongation in participants who became myopic. Hence, longitudinal studies addressing myopia progression ideally ought to include analysis of the crystalline lens.

9.5.1 Effect of time spent outdoors during daylight

Ireland is situated at 53 degrees of north latitude (all study participants were based between 52 and 54 degrees of north latitude, refer Figure 6.1), and day-length varies from a minimum of 7.5 hours in winter to a maximum of 17 hours during summer (*Sunrise and sunset times in Dublin, June 2018*). However, the daily sunshine hours are substantially lower (Refer Figure 9.11 and Figure 9.12), ranging from 1-2 hours in the winter to 5-6.5 hours in the summer (https://www.met.ie/climate/what-we-measure/sunshine). In Ireland, school holidays last between 2-3 months in summer (June, July and August), two weeks in winter (December, January) and two weeks in spring (March, April).
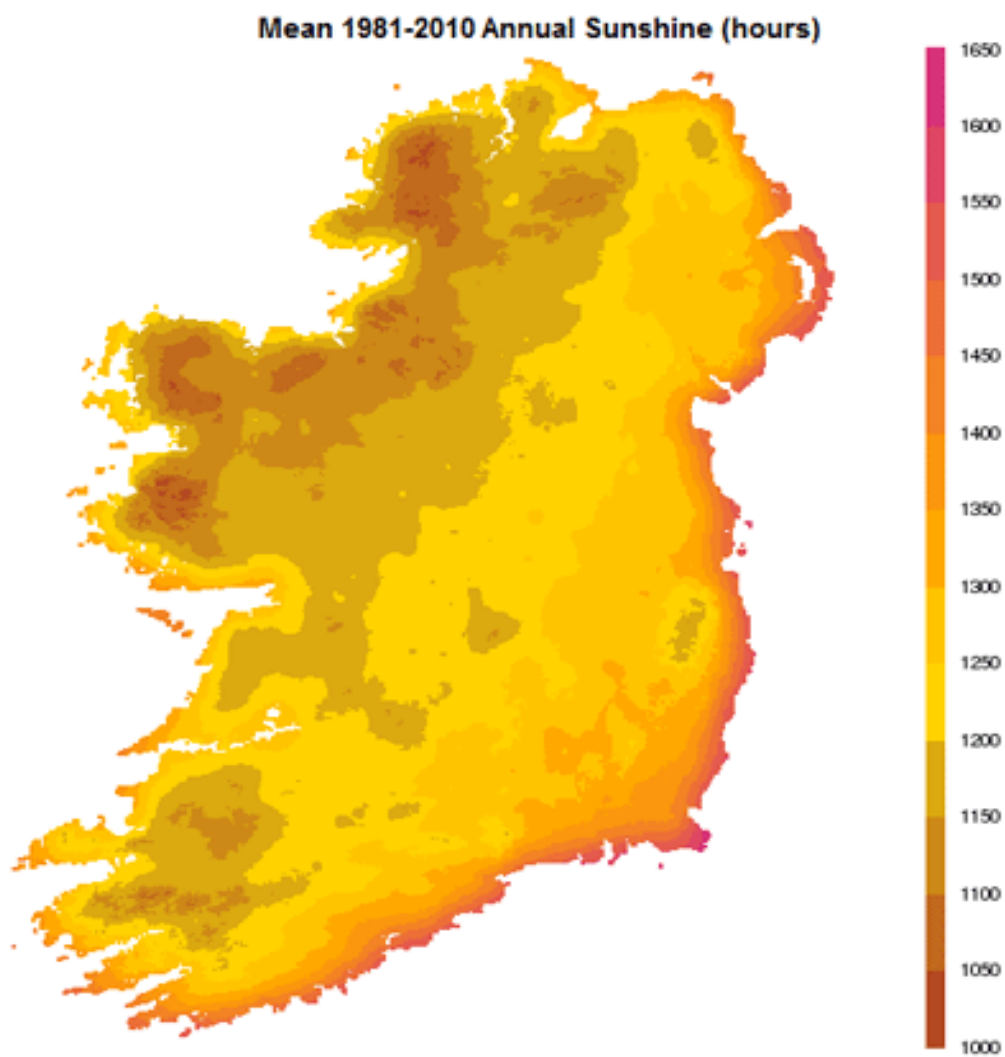
Figure 9.11 Mean annual sunshine hours in Ireland from 1981-2010 (map courtesy of the Irish Metrological service (https://www.met.ie/climate/what-we-measure/sunshine). The number of sunshine hours per year are between 1,100 and 1,600

Seasonal Sunshine

1981-2010 Total Sunshine (hours) Winter

1981-2010 Total Sunshine (hours) Spring

1981-2010 Total Sunshine (hours) Summer

1981-2010 Total Sunshine (hours) Autumn
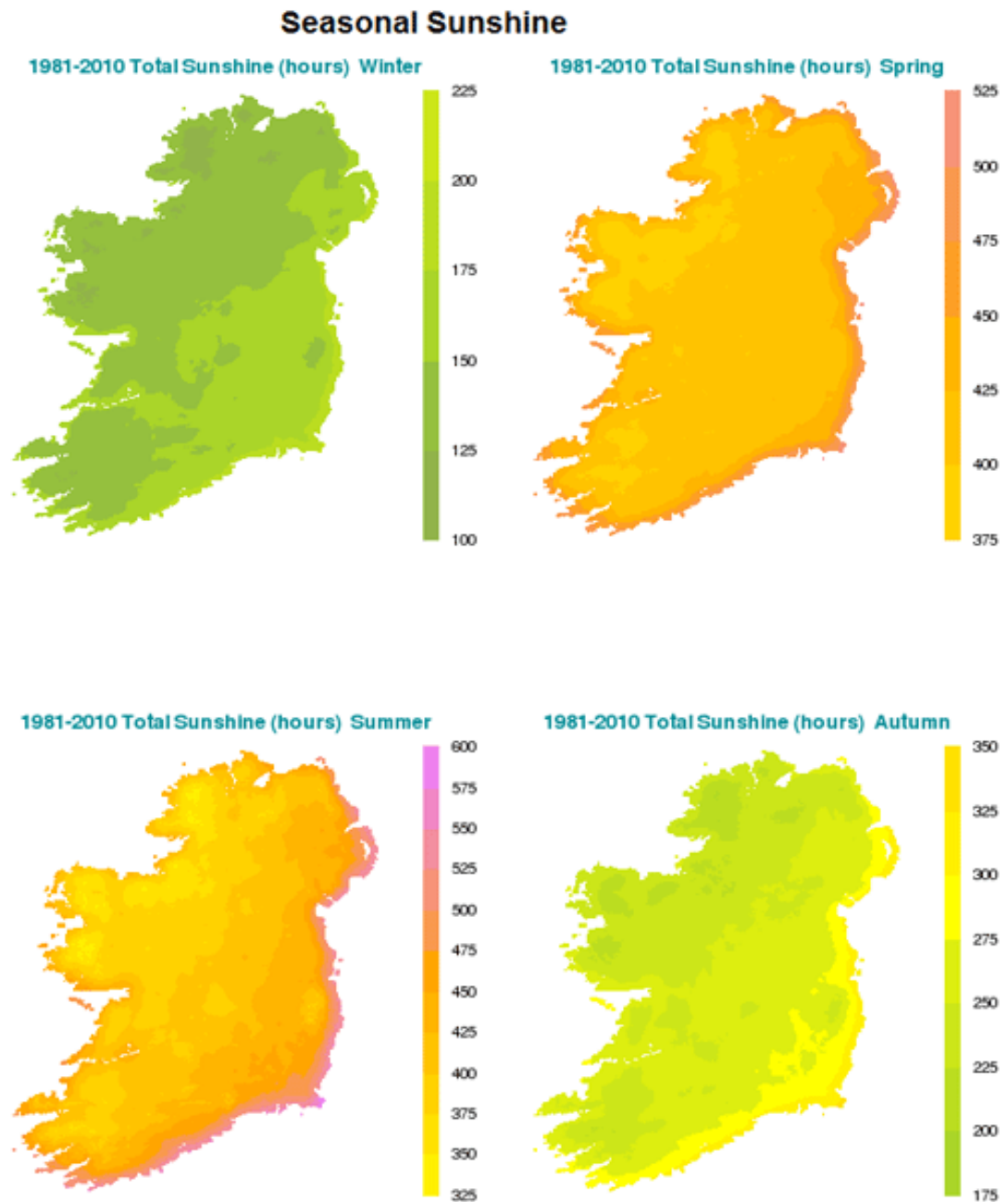
Figure 9.12 Mean seasonal sunshine hours in Ireland from 1981-2010. The months with the most sunshine are May and June with between five to six and a half daily hours sunshine. In December daily sunshine ranges from one hour in Donegal to two hours in the South East (map courtesy of the Irish Metrological service (https://www.met.ie/climate/what-we-measure/sunshine)

The relationship between SER, ocular biometric parameters and time spent outdoors during daylight in winter was not significant, which aligns with previous studies where

daylight hours and sunshine hours were limited during winter (Cui, Trier and Munk Ribel-Madsen, 2013; Gwiazda *et al.*, 2014). Conversely, the relationship between time outdoors and SER during summer was strong, with increased time outdoors associated with a less myopic SER, and shorter AL, in agreement with many studies (Fulk, Cyert and Parker, 2002; Cui, Trier and Munk Ribel-Madsen, 2013; Ulaganathan *et al.*, 2018; Deng and Pang, 2019). In contrast to the Danish study where time outdoors was associated with increased corneal power (Cui, Trier and Munk Ribel-Madsen, 2013), the present study did not find a relationship between corneal curvature and time outdoors in summer.

The current study did not find an association between time outdoors and SER and time outdoors and AL in non-White participants. Notably, non-White participants in the present study reported spending significantly less time outdoors, during both winter and summer, than White participants. Likewise, a recent study reported children in Singapore got on average five hours less light exposure per week than children living in Brisbane, despite 12-hour days in both locations (Read *et al.*, 2018).

The relationship between light exposure and ocular growth is not fully understood, Read *et al.* (2019) demonstrated that daylight/bright light might lead to short term thickening of the choroid; the authors purported choroidal thickness is an important biomarker for myopia progression. Guggenheim *et al.* (2012), proposed sunlight/bright light could trigger retinal dopamine release, which slows axial elongation. Circadian rhythms have been demonstrated in ocular structures with corresponding diurnal variation in ocular biometric measurements (Burfield, Patel and Ostrin, 2018). Hence, ocular diurnal rhythms may be involved in ocular growth regulation (Nickla, 2013). Daylight is a natural 'zeitgeber' (or time cue) for synchronising the internal circadian rhythm, due to temporal fluctuations in daylight intensity and spectral distribution, however, artificial

lighting disrupts circadian rhythms (circadian entrainment) (Fleissner and Fleissner, 2002), which may affect ocular growth (Chakraborty *et al.*, 2018). For example, studies involving chickens and monkeys established that altering the dark/light cycle resulted in significant changes in ocular growth with exposure to bright light during the day providing a protective effect against experimentally induced form-deprivation myopia (Ashby, Ohlendorf and Schaeffel, 2009; Smith, Hung and Huang, 2012). Moreover, light levels indoors, even in rooms with windows, are lower indoors than outdoors (Wildsoet *et al.*, 2019), with an association between the use of light emitting diode lamps and longer ALs reported (Pan *et al.*, 2017). Hence, there may be a minimum level of ambient illumination appropriate to school classrooms to prevent myopia development or progression, for instance, one school-based intervention study increased ambient luminance to > 300 lux on desks and > 500 lux on blackboards, and found that axial elongation was slowed with a less myopic shift in SER in the intervention group when compared to a control group (Hua *et al.*, 2015).

Whether the protective effect of daylight exposure against a more myopic SER is due to being outdoors, during daylight, with consequent choroidal thickening (Read *et al.,* 2019), dopamine release (Guggenheim *et al.,* 2012) and reduced peripheral hyperopic defocus (Garcia *et al.,* 2018), or simply due to not being indoors and engaged in near vision activities, is as yet an area of intense research (Wildoset *et al.*, 2019). Thus, the results in this study support earlier studies that time spent outdoors during daylight is an important modifiable factor (Guo *et al.*, 2013; Li *et al.*, 2015; Read, Collins and Vincent, 2015), also similar to previous studies the present study found that non-White participants may be engaged in a more indoor centric lifestyle (French *et al.*, 2013a; Read *et al.*, 2018). Due to the limited number of non-White participants in this study, further multi-ethnic studies involving larger populations born and living in a Northern European setting are crucial due to the limited day-length in winter, and changeable

weather systems which affect light intensity. In addition, precise quantification of light exposure would be facilitated by the use of wearable devices to objectively measure not only time spent outdoors but also light intensity exposure which would be more revealing than the questionnaire based data involving daylight categories used in the present study (Read, Collins and Vincent, 2014; Ostrin, Sajjadi and Benoit, 2018; Read *et al.*, 2018).

9.6 Conclusion

The distribution of ocular biometric parameters in schoolchildren in Ireland mirrors many other studies involving mainly White children. The AL/CR ratio was highly correlated with SER, and this correlation strengthened with age. Ethnic differences in SER corresponded with ethnic differences in ocular biometry. Of particular interest, compared to White participants, non-White participants had longer AL, corresponding with a more myopic SER. Also, non-White participants spent significantly less time outdoors during daylight than White participants. While study findings are not longitudinal, the age-specific data provide some insights into refractive error patterns and how they change with age. The correlates of these biometric variables and their interactions were variable and multifaceted, and their relationship with SER appeared to strengthen with increasing age. However, longitudinal studies in Ireland examining the association between ocular biometric measures (AL, CR, ACD and the crystalline lens), SER, and time spent outdoors in daylight across seasons will be required to conclude more fully on these findings.

School intervention programmes promoting time outdoors during winter of not less than two hours per day, when daylight hours are limited and coincide with school hours, ought to be considered in schools in Ireland.

Chapter 10 reports amblyopia prevalence and its aetiology in schoolchildren in Ireland. The relationship between amblyopia prevalence and demographic and lifestyle variables are also discussed.

10 AMBLYOPIA PREVALENCE AND ITS AETIOLOGY IN SCHOOLCHILDREN IN IRELAND

10.1 Summary

Purpose: To report amblyopia prevalence and its aetiology in schoolchildren in Ireland

Methods: Chapter 6 describes the study methodology in detail.

Results: Using criteria of pinhole acuity $\geq$0.3logMAR ($\geq$6/12) plus an amblyogenic factor, amblyopia prevalence was identified in 40 6-7-year-olds (5.5%, 95% CIs: 4.0 to 7.5) and 33 12-13-year-olds (3.7%, 95% CIs: 2.6 to 5.2). Controlling for age, amblyopia was associated with socioeconomic disadvantage (OR 2.2 CIs: 1.4 to 3.6, p=0.002), poor spectacle compliance (OR 3.5, 95% CIs: 2.3 to 5.5, p<0.001), and sedentary lifestyle (OR 2.5, 95% CIs: 1.2 to 5.0, p=0.02). Amblyopia was predominately orthotropic and associated with anisometropia and astigmatism in the present study.

Conclusions: Amblyopia prevalence in schoolchildren in Ireland was high compared to other international studies. Uncorrected anisometropia, compliance with spectacle wear and socioeconomic disadvantage were contributing factors in Ireland. Children without obvious visible eye defects were less likely to access eye-care resulting in missed opportunities for intervention where necessary.

10.2 Introduction

Amblyopia is a common cause of preventable monocular (affecting 1%-5% of the population), and in some rare cases, binocular vision loss, in children and is, therefore, a public health concern (Holmes and Clarke, 2006). Amblyopia results from anomalous

visual experience during the critical period of visual development in the early years of childhood (Hubel, Wiesel and LeVay, 1976) and may result from strabismus, refractive error and deprivation (Wu and Hunter, 2006). Furthermore, untreated, amblyopia leads to life-long VI (Webber and Wood, 2005), impacts reading skills (Kelly *et al.*, 2018), and significantly increases the risk of bilateral VI in later life (Rahi *et al.*, 2002). Additionally, amblyopia may affect the quality of life (Carlton and Kaltenthaler, 2011), educational attainment (Chua and Mitchell, 2004) and career choice (Carlton and Kaltenthaler, 2011). In Ireland children are screened for reduced vision (0.2LogMAR or poorer in one or both eyes) at school entry (aged 5 years). Screening coverage is reported at 80% in Ireland (Sloot *et al.,* 2015). Children who fail school vision screening are referred to ophthalmology for follow up treatment (refer to section 1.3.5). See chapter 5 for more detail on previous studies which reported on amblyopia in children.

10.3 Definitions

The definition for amblyopia used in the IES was based on RESC definition for amblyopia (Xiao *et al.*, 2015); amblyopia was defined as BCVA (measured through a pin-hole) $\geq$0.3logMAR ($\leq$6/12 Snellen, 20/40) in at least one eye associated with one or more of the following potential amblyogenic factors: (1) esotropia; exotropia; or vertical tropia at 3 m fixation; or esotropia or vertical tropia at 0.4 m (strabismic amblyopia); (2) anisometropia of $\geq$1.00 D Spherical equivalent refractive error (SER) (anisometropic amblyopia); (3) hyperopia of $\geq$ 6.00 D; myopia of 6.00 D or more, or Astigmatism $\geq$ 1.50 DC; (4) form deprivation (lenticular or corneal opacity or ptosis).

Unilateral amblyopia: If only one eye met the criteria.

Bilateral amblyopia: If both eyes met the criteria separately.

Best corrected visual impairment was vision ≥0.3logMAR (6/12 Snellen) measured through a pinhole.

In order to examine the magnitude of amblyopic VA deficits, based on the BCVA in the amblyopic eye, amblyopia was subdivided into 'moderate' (≥0.4logMAR to 0.6logMAR) or 'severe' (>0.6logMAR) (Wallace *et al.*, 2018).

All refractive errors were measured using autorefraction under cycloplegia and defined as follows; myopia SER≤-0.50 D, hyperopia SER ≥+2.00 D, and astigmatism ≥1.00 DC.

10.4 Methodology

The study methodology was described in chapter six. Risk factors for amblyopia prevalence in this study were identified using multinomial logistic regression, controlling for age group, with participants without amblyopia as the reference group in all analyses. Except where otherwise stated, the p-values reported are for these logistic regression analyses.

The two-sample test for equality of proportions with continuity correction was used to compare prevalence between subgroups. The 5% level of significance has been used throughout.

10.5 Amblyopia prevalence

Table 10.1 displays amblyopia prevalence in the right eye, the left eye, either eye, unilateral amblyopia and bilateral amblyopia in study participants. There was no significant difference in the prevalence of amblyopia in the right eye versus the left eye (6-7 years p=0.80, 12-13 years p=0.63).

The prevalence of bilateral amblyopia was low in both age-cohorts (6-7-years 1.9% and 12-13-years 0.8%) and did not vary with age (p=0.07). Of the 6-7-year-old participants

13 had moderate amblyopia and 11 had severe amblyopia. In the older age cohort three participants had moderate amblyopia and nine had severe amblyopia.

Unless otherwise stated, for the remainder of this chapter, amblyopic means amblyopic in either eye or both eyes.

Table 10.1 Amblyopia prevalence in 728 6-7-year-olds and 898 12-13-year-olds

Amblyopia	*6-7 years (N=728)*	*12-13 years (N=898)*
	n (%) [CIs]	n (%) [CIs]
Right eye	24 (3.3) [2.2 to 4.9]	18 (2.0) [1.2 to 3.2]
Left eye	23 (3.2) [2.1 to 4.8]	22 (2.4) [1.6 to 3.7]
Either eye	40 (5.5) [4.0 to 7.5]	33 (3.7) [2.6 to 5.2]
Unilateral	32 (4.4) [3.1 to 6.2]	26 (2.9) [1.9 to 4.3]
Bilateral	8 (1.1) [0.5 to 2.2]	7 (0.8) [0.3 to 1.7]

Number of participants (N); frequency (n); 95% confidence intervals (CIs).

10.6 Causes of amblyopia

As per the definition for amblyopia adopted in the IES (section 10.3), the relationship between amblyopia and amblyogenic factors is outlined below.

10.6.1 The relationship between amblyopia and anisometropia and strabismus

Table 10.2 presents the prevalence of anisometropia and strabismus in the IES, including all participants, both those with and without amblyopia. There was no

significant difference with age in the prevalence of either anisometropia (p=0.18) or strabismus (p=0.29) in the IES.

Table 10.2 Prevalence of anisometropia, strabismus and mixed aetiology (co-existing anisometropia and strabismus) in all study participants

Anisometropia/strabismus status	*6-7 years (N=728)*	*12-13 years (N=898)*
	n (%) [CIs]	**n (%) [CIs]**
Anisometropia only	51 (7.0) [5.3 to 9.2]	89 (9.9) [8.1 to 12.1]
Strabismus only	28 (3.8) [2.6 to 5.6]	25 (2.8) [1.8 to 4.1]
Anisometropia + strabismus †	16 (2.2) [1.3 to 3.6]	13 (1.4) [0.8 to 2.5]
Neither	633 (87.0) [84.2 to 89.0]	771 (85.9) [83.4 to 88.0]

*Number of participants (N); frequency (n); 95% confidence intervals (CIs)**; mixed aetiology coexisting anisometropia and strabismus †*

Anisometropia only was the primary cause for amblyopia in 27.5% of the 6-7-year-olds, which increased to 51.5% in the older age group; this difference in the primary cause for amblyopia between the age-groups was statistically significant (p=0.04). Strabismus was the primary cause for amblyopia in 12.5% of 6-7-year-olds and 9.1% of 12-13-year-olds. The relationship between strabismus and amblyopia did not vary with age (p=0.93). Amongst the 6-7-year-old participants with amblyopia, 15.0% had mixed aetiology (coexisting anisometropia plus strabismus) amblyopia which was similar to the older age cohort where 15.2% of the 12-13-year-old amblyopic participants had mixed aetiology amblyopia. The relationship between amblyopia and coexisting anisometropia and strabismus did not vary with age (p=0.73). There were two 6-7-year-olds and one 12-13-year-old participant with congenital cataracts which had not been removed.

The relationship between amblyopia and anisometropia and strabismus is presented in Table 10.3.

Table 10.3 Causes of amblyopia in study participants

Ocular outcomes	6-7 years (N=40) n(%)[CIs]	12-13 years (N=43) n(%)[CIs]
Anisometropia	11 (27.5)[15.1 to 44.1]	17 (51.5)[33.9 to 68.8]
Strabismus	5 (12.5) [4.7 to 27.6]	3 (9.1)[2.4 to 25.4]
Mixed anisometropia plus strabismus	6 (0.8) [0.3 to 1.8]	5 (0.6)[0.2 to 1.4]
Refractive error	16 (40.0) [25.3 to 56.6]	7 (21.2) [9.6 to 39.4]
Deprivation	2 (5.0) [0.9 to 18.2]	1 (3.0) [0.2 to 17.5]
Total	40 (100.0)	33 (100.0)

Number of participants (N); frequency (n); 95% confidence intervals (CIs).

10.6.2 The Relationship between Amblyopia and Astigmatism

Of those with amblyopia, 19 (48.7%) of the 6-7-year-olds and 12 (36.4%) of the 12-13-year-olds had astigmatism (≥ 1.50 DC). Multinomial logistic regression, controlling for age, strabismus and anisometropia, showed that astigmatism was significantly related to amblyopia in the IES ($p < 0.001$). When a definition for clinically significant astigmatism of ≥ 1.00 DC was applied, it was found that 26 (65.0%) of amblyopic 6-7-year-olds and 22 (66.7%) amblyopic 12-13-year-olds had astigmatism ≥ 1.00 DC in the affected eye ($p < 0.001$).

10.6.3   The relationship between amblyopia and hyperopia

Amongst amblyopic participants, 61% of 6-7-year-olds and 39.3% of 12-13-year-olds were hyperopic (≥+2.00 D). When the relationship between amblyopia and high hyperopia (≥+6.00 D) was examined, 9.8% of amblyopic 6-7-year-olds and 9.1% of amblyopic 12-13-year-olds had high hyperopia. However, hyperopia (p=0.51) and high hyperopia (p=0.16) were not significantly associated with amblyopia in the IES (multinomial logistic regression controlling for age, anisometropia and strabismus).

10.6.4   The relationship between amblyopia and myopia

Controlling for age, strabismus and anisometropia, myopia prevalence was not associated with amblyopia in either age cohort (6-7 years, p=0.19, 12-13 years, p=0.21). There were no amblyopic 6-7-year-olds with high myopia (SER≤-6.00 D). There was one amblyopic 12-13-year-old with high myopia in their amblyopic eye; high myopia was not associated with amblyopia in the IES (p=0.66, logistic regression).

10.7 Previous treatment for amblyopia

Using the IES parental questionnaire data (questionnaire response: 6-7 years 98.8%, 12-13-years 99.2%), 6.8% (110 participants) (6-7 years: 5.8% (42 participants) and 12-13 years: 7.6% (68 participants) reported a previous history of amblyopia treatment; however, of these, a number remained amblyopic (6-7-years: 11 participants (1.5%), 12-13 years: 20 participants (2.2%)). Four (0.5%) 6-7-year-old participants previously treated for amblyopia had BCVA worse than 0.6logMAR in their amblyopic eye; one of which had BCVA worse than 0.6logMAR in both eyes. Amongst the 12-13-year-old participants who reported a previous history of amblyopia treatment, ten (1.1%) had BCVA worse than 0.6logMAR in their amblyopic eye. Hence, treatment may have been started too late or compliance with treatment may be an issue for these ten severely amblyopic participants.

Table 10.4 Amblyopia treatment history in 728 6-7-year-old and 898 12-13-year-old participants

Age (years)	Amblyopia treatment history		
	Successfully treated n(%)[CIs]	Partially/unsuccessfully treated † n(%)[CIs]	No history of treatment n(%)[CIs]
6-7	31 (4.3) [3.0 to 6.0]	11 (1.5) [0.8 to 2.8]	29 (4.0) [2.7 to 5.7]
12-13	48 (5.4) [4.0 to 7.1]	20 (2.3) [1.4 to 3.5]	13 (1.5) [0.8 to 2.5]

Frequency (n); 95% confidence intervals (CIs); still amblyopic†

In the IES four 6-7-year-olds and 12 12-13-year-olds (total 16 (1.0%) participants) reported a history of strabismus surgery (questionnaire response: 6-7 years 98.6%, 12-13 years 98.7%), 10 (0.62%) of which were not categorised as having amblyopia. A previous history of strabismus surgery was not associated with persistent amblyopia in the IES (p=0.08, logistic regression).

10.7.1 Previous history of spectacle wear

Amongst the 40 6-7-years-old amblyopic participants 23 (60.5%) never had spectacles, five (13.2%) did not have their spectacles in school, and 10 (26.3%) were wearing spectacles. Amongst the 33 12-13-year-old amblyopic participants 12 (36.4%) never had spectacles, a further 12 (36.4%) did not have their spectacles in school, and nine (27.3%) were wearing spectacles. Controlling for age, amblyopia was associated with poor spectacle compliance (OR 3.5, 95% CIs: 2.3 to 5.5, p<0.001).

10.7.2 Previous history of an eye examination

The OR for amblyopia amongst 6-7-year-old participants, who did not report having had their eyes tested within the 12 months before data collection, was 3.9 (95% CIs: 2.0 to 7.5, p<0.001). Of the 40 amblyopic 6-7-year-olds, 20 (50.0%) had not attended for an eye examination within 12 months before the IES data collection (questionnaire response: 6-7 years 98.9%, 12-13 years 99.7%). Hence, half of the amblyopic 6-7-year-

old participants had not been reviewed by an eye-care practitioner within 12 months prior to data collection despite being within the sensitive period of visual development.

Of the 33 amblyopic 12-13-year-olds, 21 (66.7%) had not had their eyes tested within 12 months before the IES. The OR for amblyopia amongst 12-13-year-old participants who had not had their eyes tested was 2.8 (95% CIs: 1.7 to 4.5, p<0.001). All of the 16 participants who reported a previous eye surgery had been reviewed by an ophthalmologist/optometrist within 12 months before the IES.

10.7.3   The relationship between amblyopia and stereo-acuity

In total, 81 6-7-year-old participants (11.1%) and 103 12-13-year-old participants (11.5%) had stereo-acuity worse than or equal to 240 arc seconds. The degree of presenting stereo-acuity was positively correlated with pin-hole acuity (Pearson correlation r=0.515, p<0.001). Table 10.5 presents the prevalence of stereo-thresholds using the TNO stereo test, by age-cohort, in IES participants. All amblyopic participants had stereo-acuity worse than or equal to 240 arc seconds. There were additional study participants with abnormal stereo-acuity in both age-cohorts who were not categorised as amblyopic due to the absence of amblyogenic factors or monocular vision better than the study definition thresholds (0.3logMAR, 6/12 Snellen). The presence of microtropia was not checked for in the IES, which is a limitation.

Table 10.5 Prevalence of TNO stereo-thresholds in 6-7-year-old and 12-13-year-old participants

Stereo-acuity	N (%) [CIs]	N (%) [CIs]
	6-7 years	12-13 years
15	77 (10.6) [8.5 to 13.1]	324 (36.1) [33.0 to 39.3]
30	63 (8.7) [6.8 to 11.0]	189 (21.0) [18.5 to 23.9]
60	219 (30.1) [26.8 to 33.6]	153 (17.0) [14.7 to 19.7]
120	248 (34.1) [30.7 to 37.7]	129 (14.4) [12.2 to 16.9]
240	62 (8.5) [6.6 to 10.8]	61 (6.8) [5.3 to 8.7]
480	20 (2.7) [1.7 to 4.3]	11 (1.2) [0.6 to 2.3]
No stereopsis	39 (5.4) [3.9 to 7.3]	31 (3.5) [2.4 to 4.9]
Total	728	898

Number of participants (N); 95% confidence intervals (CIs). The degree of stereo acuity was positively correlated with pin-hole acuity in the right eye in the 6-7-year-olds (r=0.52, p<0.001) and 12-13-year-olds (r=0.48, p<0.001)

10.8 Relationship of amblyopia to study demographic variables

This section reports on the demographic risk factors associated with amblyopia prevalence in the IES. The demographic study variables were: age-group (6-7 years and 12-13 years); urban/rural status; socioeconomic status (measured by attendance at DEIS or non-DEIS schools); gender (male or female) and ethnicity (White, Traveller, and non-White). Table 10.6 shows the multinomial logistic regression results for the relationship of amblyopia to all these demographic variables.

Table 10.6 Relationship of amblyopia to study demographic variables

Parameter Estimates

Amblyopia[a]		B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp(B) Lower Bound	Upper Bound
Yes	Intercept	-3.57	0.48	56.40	1	**0.00**			
	6-7 years	0.37	0.27	1.86	1	0.17	1.45	0.85	2.49
	12-13 years	0[b]	.	.	0	.	.	.	.
	Male	-0.32	0.24	1.75	1	0.19	0.73	0.45	1.17
	Female	0[b]	.	.	0	.	.	.	.
	Disadvantaged	0.59	0.28	4.42	1	**0.04**	1.81	1.04	3.14
	Advantaged	0[b]	.	.	0	.	.	.	.
	Urban	0.44	0.30	2.20	1	0.14	1.55	0.87	2.78
	Rural	0[b]	.	.	0	.	.	.	.
	White	-0.09	0.37	0.06	1	0.81	0.91	0.44	1.88
	Traveller	0.58	0.45	1.63	1	0.20	1.78	0.74	4.29
	Non-White	0[b]	.	.	0	.	.	.	.

a. The reference category is: not amblyopic.
b. This parameter is set to zero because it is redundant.
Variable(s) entered on step 1: Rural/urban, socioeconomic disadvantage, gender, Age-group, Ethnicity. Significance (Sig.), degrees of freedom (df), the beta coefficient (B), confidence intervals (CI).

It is seen in Table 10.6 that socioeconomic disadvantage (p=0.04) was significantly related to amblyopia, and that age group (p=0.17), gender (p=0.19), urban/rural dwelling (p=0.14) and ethnicity (p=0.18) were not. In light of these findings, when examining risk factors associated with amblyopia, logistic regression models were constructed controlling for socioeconomic status in all analyses.

10.8.1 The relationship between amblyopia and socioeconomic status

Controlling for age group, socioeconomic disadvantage was significantly associated with amblyopia in the IES (OR=2.2, 95% CIs: 1.4 to 3.6, p=0.002, logistic regression).

Amongst the 6-7-year-old participants, the prevalence of amblyopia was 7.8% (19/243) amongst those attending DEIS schools compared to 4.3% (21/485) amongst those attending non-DEIS schools. This pattern was repeated in the older age-cohort, where amblyopia prevalence was 7.4% (8/108) amongst disadvantaged 12-13-year-olds compared to 3.2% (25/790) amongst advantaged 12-13-year-olds.

Controlling for age, the OR for bilateral amblyopia amongst socioeconomically disadvantaged participants was 4.4 (95% CIs: 1.5 to 12.8, p=0.006).

Amblyopia prevalence was associated with the father's educational level (OR=5.3, 95% CIs: 2.2 to 12.9, p<0.001, logistic regression controlling for socioeconomic status). Amongst participants with amblyopia, paternal educational level was as follows: first level (primary school only) 12.3% (7/57), second level (post-primary school) 36.8% (21/57) and third level (college or institute of technology qualification) 50.9% (29/57). The corresponding percentages for participants without amblyopia were: 2.9% (37/1292), 34.4% (445/1292), and 62.7% (810/1292) respectively.

Amblyopia prevalence was also associated with the mother's educational level (OR: 4.4, 95% CIs 1.7 to 11.1, p=0.002, logistic regression, controlling socioeconomic status). Amongst study participants classified as amblyopic, maternal educational level was as follows: first level 9.1% (6/66); second level 36.4% (24/66) and third level 54.5% (36/66). The corresponding percentages for participants without amblyopia were 2.6% (36/1405), 29.8% (418/1405) and 67.7% (951/1405) respectively.

Amblyopia was associated with paternal employment status (p=0.01, logistic regression, controlling for socioeconomic status). Amongst amblyopic participants, 22.4% (13/58) of fathers were unemployed; amongst participants without amblyopia, 4.6% (61/1317) of fathers were unemployed. Mothers employment status was not associated with amblyopia (p=0.07, logistic regression, controlling for socioeconomic status).

10.8.2 Other childhood factors associated with amblyopia in previous studies

Controlling for socioeconomic status in all analysis; birthweight (p=0.95, logistic regression); premature birth (p=0.41, logistic regression) and twin birth (p=0.67, logistic regression) were not associated with amblyopia.

10.9 Lifestyle factors associated with amblyopia

Controlling for socioeconomic status in all analysis, screen-time was not associated with amblyopia (p=0.11, logistic regression). However, the amount of time spent engaged in afterschool physical activities was significantly associated with amblyopia prevalence (OR 2.5, 95% CIs: 1.2 to 5.0, p=0.02, logistic regression). Amongst 6-7-year-old amblyopic participants, 20.5% (8/39) were sedentary, 38.5% (15/39) engaged in light activity, 30.8% (12/39) engaged in moderate physical activity, and 10.3% (4/39) engaged in regular physical activity. The percentages for non-amblyopic 6-7-year-olds were 9.7% (66/682), 29.9% (204/682), 32.8% (224/682) and 27.6% (188/682) respectively. Figure 10.1 displays the relationship between amblyopia and the amount of time engaged in afterschool physical activities in 6-7-year-olds.
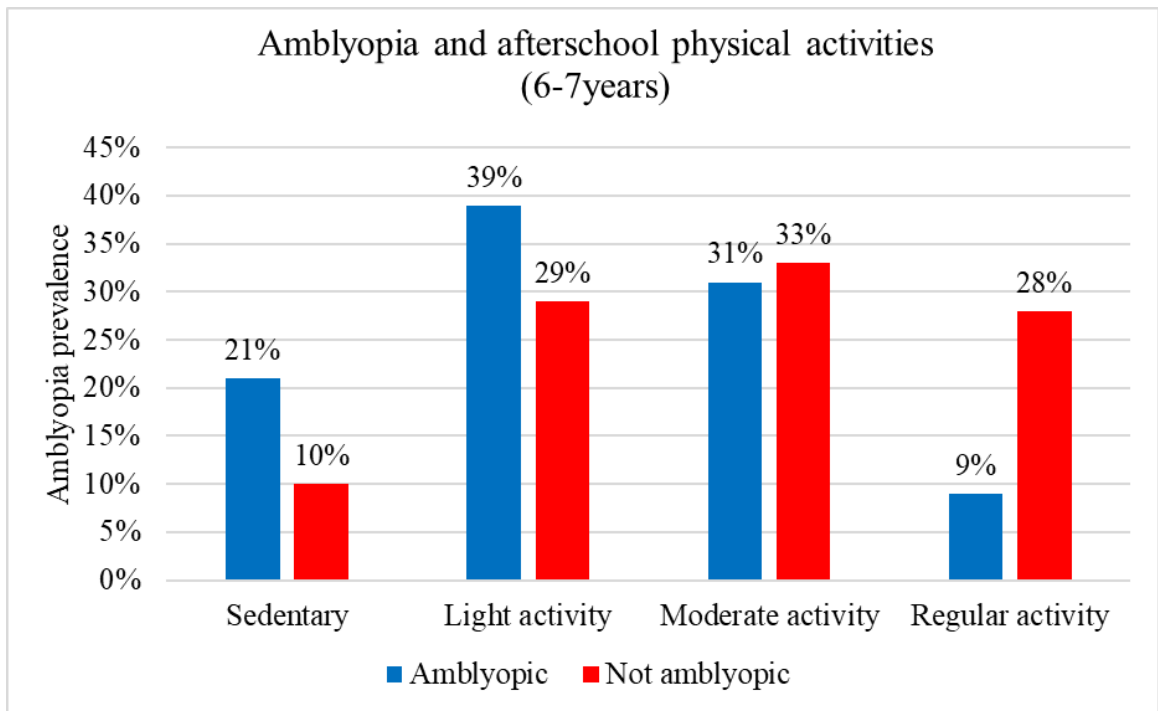
Figure 10.1 The percentage of 6-7-year-olds (N=721) with and without amblyopia in each afterschool physical activity category (sedentary 74 participants, light activity 219 participants, moderate activity 236 participants, regular activity 192 participants)

This pattern was repeated in the 12-13-year-old cohort, where 18.2% (6/33) were sedentary, 24.2% (8/33) engaged in light physical activity, 15.2% (5/33) engaged in moderate physical activity, and 42.4% (14/33) engaged in regular physical activity. The equivalent percentages for the non-amblyopic 12-13-year-old participants were 13.5% (114/844), 14.0% (118/844), 26.3% (222/844) and 46.2% (390/844) respectively. Figure 10.2 displays the relationship between amblyopia and the amount of time engaged in afterschool physical activities in 12-13-year-old participants.
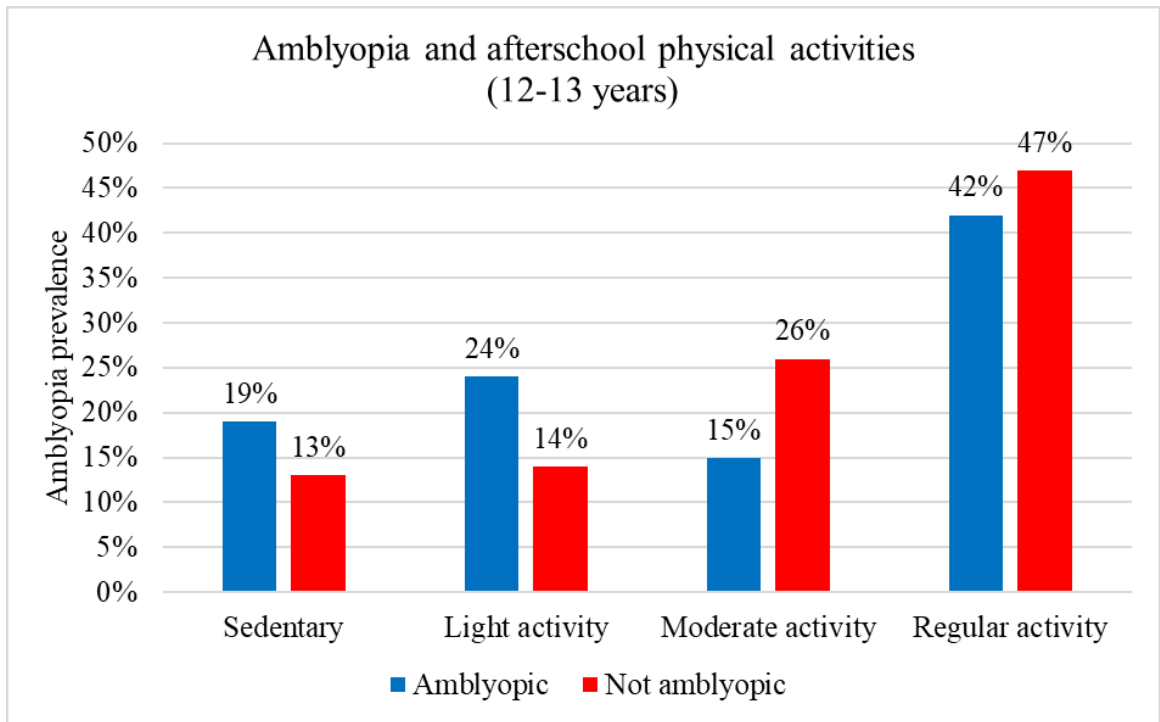
Figure 10.2 The percentage of 12-13-year-olds (N=857) with and without amblyopia in each afterschool physical activity category (sedentary 120 participants, light activity 126 participants, 227 participants, regular activity 404 participants)

Amblyopia was not associated with BMI as a continuous variable (p=0.20, logistic regression) or a categorical variable (p=0.21, logistic regression). Amblyopia was not associated with time spent reading and writing (p=0.39, logistic regression).

10.10 Discussion

This first-time presentation of amblyopia prevalence rates for children in Ireland demonstrates considerable differences in the prevalence of amblyopia between Ireland and other international studies which involved similar methodologies and protocols.

Amblyopia prevalence rates in studies around the world ranged from 0.8% to 3.9% depending on the definitions used and population studied: RESC studies (5-15 years;

0.28% to 1.43%) (Xiao *et al.*, 2015); Australia (6 years: 1.8%, 12 years: 1.9%) (Robaei *et al.*, 2006a; Robaei *et al.*, 2008); Kingdom of Saudi Arabia (6-13 years 3.9%).

10.10.1 Amblyopia and ethnicity

The IES amblyopia prevalence (6-7 years 5.5%, 12-13 years 3.7%) was significantly higher than other studies involving mainly White children such as the Copenhagen Child Cohort 2000 (11-12 years 1.5%) (Hansen *et al.,* 2019), and the Sydney Childhood Eye Study (0.4% which increased to 1.9% when participants previously treated for amblyopia were included) (Robaei *et al.*, 2008). The IES amblyopia prevalence was similar to the VIP study in the US where amblyopia prevalence was 3.0% in Asian and 5.4% in Non-Hispanic White children (McKean-Cowdin *et al.*, 2013) and similar to the VIP study, amblyopia was significantly associated with socioeconomic disadvantage in the IES.

In the RESC, amblyopia prevalence was found to vary significantly across ethnic groups, with the highest prevalence found in Hispanic children (1.4%) and lowest in Nepalese children (0.35%) (Xiao *et al.*, 2015). In contrast, the IES found no difference in amblyopia with ethnicity. However, it must be reiterated that the IES was predominately White (89%), with limited numbers of participants from the other ethnic groupings. As Ireland is becoming more multicultural (9.9% of 5-15-year-olds in the 2016 census were non-White), further research into variations in amblyogenic factors in different ethnic groupings are essential in Ireland. Xiao *et al.* (2015) hypothesised a higher amblyopia prevalence in Europeans, and East Asians may be due to low pigment and its association with strabismus and disordered visual pathways (Guillery, 1996; Wolf, Rubin and Kodsi, 2005). However, a significantly higher amblyopia prevalence was found in predominately White participants in Ireland (6-7 years 5.5%, 12-13 years 3.7%) compared to White Northern Ireland participants (9-16 years 0.8%, seven of 723

participants,(NICER phase two data as BCVA (pin-hole acuity) data were not recorded in the initial phase of the NICER study) (Harrington *et al., 2019*); two areas with similar genetic populations, demonstrating that if any such susceptibility exists, early intervention with prompt treatment and regular follow up can significantly address this possible susceptibility.

10.10.2 The relationship between amblyopia and strabismus

Similar to previous studies amblyopia was associated with strabismus in the IES however the numbers were relatively small when compared to anisometropic amblyopia. The prevalence of strabismus found in the IES (6-7 years 6.0% and 12-13-years 4.2%) was higher than that found in in the UK (7 years 2.3%) (Williams *et al.,* 2008a) and Australia (6 years 2.8%) (Robaei *et al.,* 2006c) and more in line but still somewhat higher than reported in the MEPEDS (3.6% in Asian and 3.4% in non-Hispanic White participants aged 6-72 months) (McKean-Kowdin *et al.,* 2013). The prevalence of strabismus found in the IES was similar to that found in Northern Ireland (9-10 years 5.8%, 15-16 years 4.9%) (Harrington *et al.,* 2019). In the IES, about 10% of amblyopia found was due to strabismus alone. Furthermore, a previous history of strabismus surgery was not found to be associated with amblyopia, indicating that children with strabismus are generally receiving appropriate follow-up treatment within the present system. The majority of amblyopia in the current was refractive (anisometropia and astigmatism) and most amblyopic participants in the current study were orthotropic with no history of spectacles or occlusion therapy. Similarly, the ALSPAC study reported that a majority of amblyopic children at 7.5 years were 'straight-eyed' (Williams *et al.*, 2003).

10.10.3 The relationship between amblyopia and anisometropia

The prevalence of anisometropia in schoolchildren in Ireland (6-7 years 9.2%, 12-13 years 11.3%) and Northern Ireland (12-13 years 9.4%) (O'Donoghue *et al.*, 2013) was similar to that found in Mexico (12-13 years 15.0%) (Ohlsson *et al.*, 2003), albeit relatively high when compared to a considerably lower prevalence found in Sydney where 1.6% of children aged 6 years had anisometropia (Huynh *et al.*, 2006). Studies have shown that anisometropia prevalence is higher in populations with a higher prevalence of ametropia (Weakley, 2001; Afsari *et al.*, 2013). For instance, the strong relationship found in the IES between amblyopia and anisometropia and amblyopia and astigmatism was similar to Dobson's study of Native American children (Dobson *et al.*, 2003, 2008). Barrett, Bradley and Candy (2013) contended there might be inter-individual variability in susceptibility to amblyogenic factors such as anisometropia, strabismus and increasing astigmatism, whereby children with continual or increasing anisometropia and astigmatism are at risk of developing amblyopia; despite similar genetic profile and exposure to environmental factors and in the absence of pathology.

Similar to other studies (Robaei *et al.*, 2006a; Robaei *et al.*, 2008; Chia *et al.*, 2010; Pai *et al.*, 2012), a significant number (6-7 years 22%, 12-13 years 51%) of IES amblyopic children were found to have anisometropia as the only visual anomaly; moreover, between 34% (6-7 years) to 63% (12-13 years) of amblyopic participants were found to have anisometropia and/or strabismus (Harrington *et al.,* 2019). Hence amblyopia prevalence in Ireland was associated with ametropia and anisometropia, which aligns with Shah (2005) and Attebo (1998). Conversely, the NICER study reported an amblyopia prevalence of 0.8% in phase two of the NICER study (participants aged 9-16-year-old) despite anisometropia prevalence rates similar to the IES (O'Donoghue *et al.*, 2013), demonstrating that anisometropic amblyopia can be successfully treated with prompt intervention and compliance with treatment. For example, previous research

demonstrated that the potential for correction of amblyopia and normal visual development is reported to be inversely related to age (Koo, Gilbert and VanderVeen, 2017), with a mean success rate of 75% at age three, 58% at 4-5 years, and 49% at 6-10 years (Epelbaum *et al.*, 1993; Flynn *et al.*, 1999; König and Barry, 2004). Indeed amblyopia and anisometropia can exist without any apparent signs or symptoms in the absence of strabismus due to the absence of any overt signs (Chua and Johnson, 2004). Thus parents of children with orthotropic amblyopia are unlikely to suspect a problem due to the lack of any visible physical signs and this coupled with the fact that these children are generally asymptomatic due to good vision in the non-amblyopic eye generally results in later diagnosis. For example, previous studies reported the mean age of initial presentation in eye clinics for children with strabismus as 3.5 years, whereas in contrast, the mean age for an initial consultation with anisometropia was 6.5 years (Ingram, 1977; Shaw *et al.*, 1988; Woodruff *et al.,* 1994). Attebo *et al.*'s (1998) study of Australian adults reported a mean age of diagnosis with strabismic amblyopia of 7.4 years whereas those adults with anisometropic amblyopia were diagnosed at mean 12.7 years; i.e. outside the critical period for intervention.

Hence anisometropic amblyopia is a public health concern not only in Ireland but also internationally.

10.10.4 Amblyopia and spectacle wear

Prompt treatment of amblyopia with refraction alone has been effective when treating anisometropia and ametropia (Steele *et al.*, 2006; Chen *et al.*, 2007; Cotter *et al.*, 2012), notwithstanding inconsistent reports regarding the impact of prescribing full refraction on the emmetropisation process (Atkinson *et al.*, 1996; Ingram, Gill and Lambert, 2000). In the IES, 17 (five 6-7-year-olds and 12 12-13-year-olds) amblyopic children (including two with bilateral amblyopia) did not have their prescribed spectacles in

school, which may result in poor outcomes for children requiring constant spectacle usage, highlighting the consequences of poor spectacle compliance (Holguin *et al.*, 2006). Also, in the present study, amblyopia was associated with socioeconomic disadvantage. As a result, the cost associated with replacement or repair of spectacles may have been an issue influencing compliance.

In reality, studies have shown, that even when spectacles are provided for free, spectacle compliance can be low (13.4%) (Holguin *et al.*, 2006), to moderate 57% (Pavithra, Hamsa and Madhukumar, 2014). One US (New York City) based intervention program found that when children disproportionally affected from visual dysfunction were supplied with two pairs of spectacles (one held by the teacher), spectacle use rose significantly (Ethan *et al.*, 2010). In comparison, spectacle wear amongst the NICER participants was high, 28.2% amongst participants compared with 12.9% in IES participants; consequently, more research ought to be carried out on why there was greater compliant spectacle wear in Northern Ireland compared to Ireland (Harrington *et al.,* 2019).

10.10.5   Previous history of amblyopia treatment

 The IES data demonstrated that while a significant number of children had been successfully diagnosed and treated for amblyopia, a similar number reported a previous history of amblyopia therapy but were still amblyopic. The reasons why amblyopia treatment was unsuccessful were not explored in the IES. Research suggests recurrence of amblyopia on cessation of treatment is a challenge, with between 13-24% losing two logMAR lines BCVA within 12 months of ceasing treatment (Maconachie and Gottlob, 2015). However, a tapering period of occlusion treatment with careful and prolonged follow up is reported to significantly reduce amblyopia recurrence (Holmes *et al.*, 2004, 2007).

As 54.5% of amblyopic 6-7-year-olds and 66.7% of amblyopic 12-13-year-olds, with a previous history of amblyopia treatment, reported not attending optometry or ophthalmology within 12 months before the IES, it appears that many amblyopic children are being lost to follow up in Ireland, in line with previous studies (Williams *et al.*, 2013). Admittedly, compliance with amblyopia treatment can be challenging (Dixon-Woods, Awan and Gottlob, 2006), and decreases over time (as low as 30% in one jurisdiction) (Preslan and Novak, 1998). Compliance is reportedly higher with a frequent review (Wallace *et al.*, 2013). For example, prior research demonstrated that strategies to improve compliance with amblyopia treatment, whether with spectacle wear alone or occlusion therapy, ought to include the following: scheduling follow-up examination within 2-3 months of initiation of amblyopia treatment and every 3-6 months thereafter, depending on performance at each follow up review (Wallace *et al.*, 2013); involving parents in the daily timing of amblyopia treatment, by setting goals for weekly occlusion targets and allowing parents make decisions about how to achieve those goals (Tripathi *et al.*, 2002). Also, splitting patching hours to facilitate children's educational and afterschool activities and providing children with positive affirmation with reward charts have been found to help (Wang, 2015). Most importantly, to address the gap in understanding, providing parents with verbal explanation (aural and oral) in addition to written information explaining amblyopia treatment can significantly overcome communication barriers (Tjiam *et al.*, 2010). Research conducted in the Netherlands demonstrated that giving amblyopic children storyboards and educational cartoon stories significantly improved compliance with amblyopia treatment and outcomes (Tjiam, 2013).

The situation in Ireland regarding amblyopia treatment is further complicated by the waiting times for follow up appointments, post-failure of school entry vision screening, with waiting lists up to 24 months acknowledged in many areas (Murphy, 2017). Hence,

delays in accessing follow-up examination post a failed school vision screening may also be a factor affecting successful amblyopia treatment, as treatment success rates decrease with increasing age (Scheiman *et al.*, 2005; Holmes, 2011). Access to early and prompt treatment with regular reviews are well documented to increase the likelihood of successful results (Williams *et al.*, 2003; Simons, 2005). Donahue (2006) recommends spectacle correction by age three years in order to prevent amblyopia from becoming established; Leon *et al.* (2008) further reinforced Donahues recommendations. Thus prompt follow up examination is imperative at aged 5-6 years, which is the vision screening age in Ireland. While Clarke *et al.* (2003) stated that a one year delay in commencing treatment did not appear to affect children younger than five years negatively; the authors acknowledged that early treatment was associated with better outcomes. Thus, pre-school screening (age 3-4 years) as recommended by Donohue (2006) and as practised in Denmark where less than 1% amblyopia prevalence was reported (Hansen *et al.,* 2019) ought to be adopted in Ireland where high levels of amblyopia exist.

10.10.6 Bilateral amblyopia

The IES bilateral amblyopia prevalence (6-7 years 1.1% and 12-13 years 0.8%) was low. While the numbers were small, bilateral amblyopia has more severe consequences for these children as they have reduced vision in both eyes (three IES participants were below the legal minimum driving standard). All participants bar one categorised as bilaterally amblyopic were orthotropic, with hyperopic astigmatism, hence, amblyopia may have been prevented with compliant spectacle wear alone (Wallace *et al.*, 2007).

10.10.7 Amblyopia and stereo-acuity

Stereopsis is the highest form of binocular vision (Barrett, 2011), and helpful not only when performing fine motor tasks such as threading a needle or surgery (Bloch *et al.*,

2015), but also relative depth perception, range finding and camouflage breaking (Read, 2015). All of the IES amblyopic children had stereo-acuity worse than or equal to 240 arc-secs as measured using the TNO stereo-test, which is similar to the Sydney Child Eye Study where 68% of amblyopic children had stereo-acuity worse than 120 arc seconds (Robaei *et al.,* 2008). Similarly, Levi *et al.*'s review (2005) concluded that impaired stereoscopic depth perception was the most common visual deficit under normal binocular viewing conditions. Nonetheless, the TNO stereo test, which was used in the present study, has recently been found to overestimate stereo thresholds, for instance, significantly weaker stereo-acuity scores have been reported with the TNO stereo-test when compared to the Randot stereo test (Vancleef *et al.*, 2017), as the TNO test involves depth discrimination and not depth detection and red/green three dimensional spectacles may reduce the binocular confusion associated with Polaroid spectacles. Accordingly, some amblyopic participants may have performed better had alternative stereo-tests been used.

10.10.8 Amblyopia and socioeconomic and gestational factors

Although strabismus, anisometropia and refractive errors are known to be more prevalent amongst pre-term infants (Robaei *et al.*, 2006c), the association found between amblyopia and low birth weight, in Australian schoolchildren, was not echoed in the IES.

The association found, between amblyopia and low income and low socioeconomic status found in other studies such as MEPEDS, BPEDS and ALSPAC study concur with the present study (Majeed *et al.*, 2008; Friedman *et al.*, 2009; McKean-Cowdin *et al.*, 2013). As amblyopia was significantly associated with socioeconomic disadvantage in the IES, either barriers to accessing eye health care may exist amongst socioeconomically disadvantaged children or disadvantaged children may have a more

significant health-care requirement. This a crucial point for policymakers in Ireland as research in the UK (where there is universal free access to eye-care services for all children; see section 1.3.5 for more detail) reported socioeconomically disadvantaged communities less likely to sign-up for school vision screening, when invited, and also less likely to attend high-street optometrists for eye-examinations (Williamson *et al.*, 1995; Majeed *et al.*, 2008).

10.10.9 Amblyopia and afterschool physical activities

Amblyopic participants were significantly less likely to engage in afterschool physical activities than children without amblyopia. The reasons for this were not explored in the IES. Previous research demonstrated reduced participation in physical activities in visually impaired children and adolescents (Aslan, Calik and Kitiş, 2012; Greguol, Gobbi and Carraro, 2015). Equally, Quigley *et al.*'s (2019) found that 'vision problems' were significantly associated with sedentary behaviour in Irish 9-year-olds.

Regarding amblyopia, Suttle *et al.* (2011) and Niechwiej-Szwedo *et al.* (2012) reported amblyopic children having poorer eye-hand co-ordination than non-amblyopic children. As a consequence, amblyopic children may be less likely to engage in team sports where co-ordination and good binocular vision are essential, and the emphasis is not only on aim but also anticipation involving a moving target (Mazyn *et al.,* 2007; Schorer *et al.,* 2013). Khalaj *et al.* (2011) proffered amblyopia impacted on involvement in sport and social activities, with amblyopic participants significantly less likely to participate in sports and social activities when compared to those without amblyopia. Likewise, Packwood *et al.* (1999) found evidence that amblyopia (in the absence of strabismus) was associated with psychosocial difficulties (somatisation) which significantly affected self-image, work and involvement in sport. In contrast Rahi *et al.* (2006) argued the presence of amblyopia impacted little on educational, social and

health and psychological outcomes at a population level over the life course when participants were examined at age 41 years adding that the cost of screening for all levels of amblyopia could not be justified. However, as amblyopic children are more susceptible to vision loss due to injury in the non-amblyopic eye (Harrad and Williams 2003; Rahi *et al.,* 2002; Simons, 2005), they may be less likely to get involved in contact sports.

Grant *et al.* (2014) established that the recovery of binocularity benefits eye-hand coordination speed and accuracy, thereby reinforcing the importance of early detection and treatment of amblyopia. What is more Vella *et al.* (2017) reported bidirectional relationships exist between involvement in sport and adolescent mental health even when controlling for sport type and gender; thus future research exploring the barriers to engagement in afterschool activities for amblyopic children is essential. Analysis of sports based programmes with a view to engaging schoolchildren with VI, including amblyopia, is vital to maximise mental and physical health benefits associated with sports involvement.

10.10.10 Differences in amblyopia prevalence in Ireland and Northern Ireland

Despite similar refractive error prevalence (Harrington *et al.*, 2018) and amblyogenic factors (Harrington *et al.,* 2019), there was a significantly higher prevalence of amblyopia in schoolchildren in Ireland when compared to Northern Ireland. Furthermore, there was a significantly higher prevalence of compliant spectacle wear in Northern Ireland 9-15 year-olds (NICER 28.2%, IES 12.9%, p<0.001). Hence, unlike Ireland, many participants in the NICER study may have been successfully treated for anisometropic amblyopia with compliant spectacle wear alone which is reported to be a successful option for treating anisometropic and refractive amblyopia (Stewart *et al.,*

2004; Steele *et al.,* 2006; Chen *et al.,* 2007). However, why IES amblyopia prevalence was substantially higher than that found in the NICER study is most likely multifactorial. The key differences between children's eye-care in Northern Ireland and Ireland appear to be: better screening coverage (UK>95%, Ireland 80%); the higher per capita ratio of ophthalmologists, optometrists and orthoptists (see section 1.3.5 for more detail), universal free eye examinations with optometrists in Northern Ireland with prompt referral to the hospital eye service if required; early identification of amblyogenic factors with timely provision of spectacles and/or amblyopia treatment if indicated and regular reviews ensuring optimum outcomes and prevention of amblyopia recurrence. Moreover, the cost of eyepatches used for amblyopia treatment is covered by the NHS; however, in Ireland, the onus is on parents to cover this cost. For example, 6.2% (45/723) of NICER phase two participants reported a history of amblyopia treatment, and only 1 participant (0.02%) remained amblyopic (Harrington *et al.,* 2019). Orthoptists, public health nurses, optometrists and ophthalmologists are comparable in Northern Ireland and Ireland with regard to training, qualifications and the functions they undertake, including their role in school-entry vision screening. The differences between the two jurisdictions in terms of public health outcomes, relate to the less comprehensive nature of school-entry vision screening in Ireland (80% compared to >95% in the UK) and the differences in accessing treatment that exist between the two countries (less than six weeks in Northern Ireland compared to 2-4 years in Ireland). Amblyopia is a preventable and treatable condition as identified by Hall and Elliman in "Health for all children" in Northern Ireland, which aligns with "Best health for children revisited" recommendations in Ireland, however, successful treatment outcomes are poorer in Ireland than Northern Ireland despite a similar prevalence of amblyogenic factors.

10.10.11 Provision of paediatric eye care services in Ireland

Half (19/38) of the amblyopic 6-7-year-olds in the current study had not had an eye examination within 12 months prior to data collection which was concerning as all were within the sensitive period where treatment is likely to be successful (Holmes, 2011). As referenced in chapter one, paediatric eye care provision in Ireland is based on a hospital ophthalmology centric structure with little community-based services and very little involvement of optometrists. Unlike the UK, where all children ≤16 years are entitled to a free eye examination and spectacles with a high street optometrist, children in Ireland are not entitled to either a free eye examination or free spectacles with an optometrist. In order to access free eye examinations for children, parents in Ireland are advised by the HSE to attend their general practitioner or public health nurse if they observe eye problems and to be referred to hospital-based ophthalmologists if required (section 1.3.5 provides more detail on paediatric eye care services in Ireland).

10.10.12 School vision screening and follow up in other jurisdictions

The lack or delay of follow-up examinations after failing school vision screenings is not unique to Ireland. Research conducted in five London boroughs (UK), where entry-level school vision screening was carried out, found evidence of parental misconceptions to eye-care and barriers to access existed (Donaldson, Subramanian and Conway, 2018). For instance, only 15% of parents surveyed were aware of school vision screening; furthermore, 33% of parents reported that it was normal for children aged 1-7 years to have a turn in their eyes occasionally; and parents did not want their children to wear spectacles or were worried that spectacles would make their child's vision weaker. Research by school nursing in Rockford Illinois found multiple factors affecting follow-up compliance after failed school vision screenings (Kimel, 2006). While funding and access to care were significant issues (31%), other critical factors included family issues

(all adults working, parent disabled), parental perception to visual problems (29% of families did not believe their child needed a professional examination or not a priority) (Kimel, 2006), and difficulty planning ahead.

On the 15th of July 2000, Kentucky became the first US state to require all children to have their eyes tested before starting public school (Zaba, Johnson and Reynolds, 2003). Following this, when results from school entrance vision screening were compared with comprehensive eye examinations in Kentucky, it was found that comprehensive exams detected eye conditions not picked up in screening (Zaba *et al.*, 2007). Two further US states have since adopted similar legislation (*Frequently Asked Questions III: Children's Vision Law (Missouri)*, 2010).

In contrast, communities with access to prompt state-funded amblyopia treatment for all, such as Australia, which found an amblyopia prevalence of 0.4% in schoolchildren aged 12 years (Robaei *et al.*, 2008); this figure rose to 1.9% when children who had been successfully treated for amblyopia were included, which is still a much lower prevalence than reported in the IES. School vision screening is not routinely carried out in Australia, and the onus is on parents to ensure their children's eyes are examined; eye examinations are state-funded and considerable state resources have been invested in public health education programmes. The Sydney based study reported a reduction in amblyopia prevalence when compared to the Blue Mountains study (also Australian) where 3.9% of the adult participants were diagnosed with amblyopia (Attebo *et al.*, 1998; Robaei *et al.*, 2008). The authors speculated that this reduction in amblyopia prevalence could be due to improved antenatal services and parent education. Similarly, amblyopia prevalence decreased from 2.9% in Danish adults (Vinding *et al.,* 1991) to 1.5% (which dropped to 1.0% when BCVA ≥0.3logMAR was applied instead of BCVA worse than 0.1logMAR) following the initiation of the Danish pre-school screening

programme (Hansen *et al.,* 2019). Correspondingly, Wellesley Cole (1959) reported an amblyopia prevalence of 5.3% on routine examination by the National Health Service of 100,000 individuals at school entry in the UK prior to the commencement of vision screening.

Notwithstanding these findings, the 2018 Cochrane review of vision screening for visual deficits in children and adolescents by Evans, Morjaria and Powell (2018) recommended that where vision screening programmes are being established "*the opportunity to carry out a randomised control trial should not be missed*" adding that the absence of studies comparing vision screening with no vision screening was an evidence gap (Evans, Morjaria and Powell, 2018). However, the ethical implications associated with any such study should not be underestimated. The debate about the value of conducting screening for reduced vision and treating amblyopia persists. Results from the EUSCREEN programme (https://www.euscreen.org/) which involves a comparison of hearing and vision screening programmes in all European Union states using a cost-optimisation model will be interesting in this regard (Sloot *et al.,* 2015).

10.11 Conclusion

The prevalence of amblyopia in the IES was high when compared to other predominately White populations and higher than in the NICER study, despite similar genetic and ocular profile. Thus, compared to Northern Ireland, screening for amblyopia in Ireland may not be sensitive, and amblyopia treatment may be taking place too late to prevent amblyopia development. The results confirm significant inequalities in access to primary eye care for children in Ireland compared to children in Northern Ireland. This inequality is compounded by poor spectacle wear compliance and amblyopia treatment compliance, socioeconomic disadvantage, with many children lost to follow-up in Ireland. The mismatch between service utilisation and clinical need highlight the

inequalities in access to service between Ireland and Northern Ireland. New strategies to improve spectacle compliance are necessary if vision screening programme resources are to be maximised. Hence, public eye health awareness programmes directed particularly at first time parents, schoolchildren, and educators is a study recommendation.

Screening for amblyopia in preschool (Logan and Gilmartin, 2004), to detect amblyogenic factors early is critical when children's eyes are more responsive to treatment. Treating amblyopia in early childhood is essential not only to prevent potential visual disability in later life (Wallace *et al.*, 2018) but also to prevent vision disorders impacting on children's education, social and physical development.

Chapter 11 reports the relationship between vision and school performance in schoolchildren in Ireland.

11 VISION AND SCHOOL PERFORMANCE IN SCHOOLCHILDREN IN IRELAND

11.1 Summary

Introduction: This study explored the association between children's vision and how parents and legal guardians reported their child's school academic progress.

Methods: Chapter six presents the IES protocols and methodology in detail. School performance was reported by the participants' parent/legal guardian as (a) much better than classmates; (b) about the same as classmates; or (c) not as well as classmates (appendix 3).

Results: Controlling for age-group, participants categorised as doing "not as well as classmates" had bilateral presenting distance VI (vision in both eyes ≥0.3logMAR) (OR: 6.7, 95% CIs: 3.8 to 12.7, p<0.001)); bilateral presenting near vision ≥0.3logMAR, (OR: 4.1, 95% CIs: 2.3 to 7.2, p<0.001); amblyopia (pin-hole acuity≥0.3logMAR in the affected eye plus an amblyogenic factor) (OR: 6.00, 95% CIs: 3.5 to 10.3, p<0.001); bilateral amblyopia (pin-hole vision ≥0.3logMAR in both eyes) (OR: 17.2, 95% CIs: 6.7 to 50.0, p<0.001); bilateral astigmatism (≥1DC) (OR: 2.4, 95% CIs: 1.4 to 5.1, p<0.001); reduced stereo-acuity (≥240 seconds of arc) (OR:3.6, 95% CIs: 2.4 to 5.4, p<0.001); poorer accommodation (F=10.8, p<0.001); and higher degrees of astigmatism (F=10.2, p<0.001).

Conclusions: Children reported by their parents or legal guardians as struggling in school were more likely to present with VI. Uncorrected refractive error may impact on children's future educational, health and social outcomes.

11.2 Introduction

Research suggests that up to 80% of what children learn in school is acquired visually (Sylva, 1997; Ehri, 2005; Scheiman and Rouse, 2006), consequently uncorrected refractive error affects children's education (Khalaj *et al.*, 2011). While many studies established an association between myopia and intelligence (Onal *et al.*, 2007; Williams, Miller, *et al.*, 2008), hyperopia has been associated with unsatisfactory educational performance (Stewart-Brown, Haslum and Butler, 2008; Williams, Miller, *et al.*, 2008) and developmental deficits (Atkinson *et al.*, 2002). Furthermore, hyperopia (SER≥ +2.00 D) was found to be strongly associated with self-reported eye-strain and parent-reported reading difficulties in Australian 6-year-old and 12-year-old participants (Ip *et al.*, 2008b). Hence, uncorrected refractive errors result in reduced educational opportunities, which has implications beyond school years affecting employment options, thus impacting not only the individual but also the broader community (Rahi and Gilbert, 2012).

The link between vision and academic performance has been reviewed in many studies which addressed specific aspects of visual function such as VA (Kulp and Schmidt, 1996), stereoacuity (Ponsonby *et al.*, 2013), uncorrected refractive error (Kulp *et al.*, 2016) and inadequate binocular vision status (Christian *et al.*, 2018). However, the influence of reduced vision on educational attainment has not been established (Carlton *et al.*, 2008; Barrett, 2009). Vision appears to be associated with learning in the "learn to read" stage (younger than age eight years) where there is significant demand on the visual system when decoding the text (Chen, Bleything and Lim, 2011). Visual demands change during the "read to learn" stage (older than eight years), for example print size decreases thus increasing visual demand (Legge, and Bigelow, 2011), and fast automatic decoding is required as the emphasis is on comprehension. Besides, amblyopic children read more slowly (Kelly *et al.*, 2015), and take significantly longer

to complete a multiple-choice form despite being provided with the correct answers when compared to a control group (Kelly *et al.*, 2018). Consequently, addressing vision disorders in early childhood is crucial to prevent them from impacting on children's education, social and physical development (Rahi, Cumberland and Peckham, 2006; Wilson and Welch, 2013; Birch *et al.*, 2018). Therefore, the impact of poor presenting vision, on participants' educational performance is a public health issue. The present study examined the relationship between parents/guardians' perception of their children's school academic progress and various aspects of vision.

11.3 Methodology

Sampling, recruitment protocols, participation rates (section 7.4), experimental techniques and methods employed are previously described in detail (see chapter 6). Parents or legal guardians of participants completed a standardised lifestyle questionnaire (Appendix 3), reporting amongst other things, school performance (response rate: 1,613 of 1,626 (99.2%); the response options were as follows (a) much better than classmates (b) about the same as classmates (c) not as well as classmates. Henceforth referred to as above average, average and below average school performance.

11.3.1 Statistical methodology

Multinomial logistic regression analysis, with participants who reported average school performance as the reference category, was carried out to examine the relationship of school performance with categorical variables such as myopia, hyperopia, astigmatism, and amblyopia. The Kruskal-Wallis one-way analysis of variance test was used to compare mean SER (D), astigmatism (DC), amplitude of accommodation (D), stereo-acuity (arc seconds), presenting vision in the distance (logMAR), and at near (logMAR), across the school performance categories with Bonferroni post-hoc analysis

carried out when the relationship between these continuous variables and school performance was significant. Multinomial logistic regression models were also constructed to investigate further the relationship between school performance and vision controlling for socioeconomic status, age, ethnicity and gender. The distribution of presenting vision in participants' right and left eyes was significantly correlated: 6-7-years-old Spearman rho coefficient=0.831, 12-13-years-old Spearman rho coefficient=0.757, overall Spearman rho coefficient=0.796. The distribution of SER and astigmatism were significantly correlated in the right and left eyes (see section 7.3.5). Hence data are presented for the right eye only unless otherwise stated. Amblyopia means amblyopic in either the right eye or the left eye or both.

11.4 Results

Statistical analysis of pre-examination questionnaires and examination results included 722 of the 728 6-7-year-olds (99.2% questionnaire response rate) and 890 of the 898 12-13-year-olds (99.1% questionnaire response rate). Figure 11.1 presents the prevalence of above average (6-7 years 16.5% (120/722), 12-13 years 240/890 (27.0%)), average (6-7 years 73.5% (535/722), 12-13 years 66.9% (595/890)), and below average (6-7 years 9.2% (67/722), 12-13 years 6.2% (55/890)) school performance.

Figure 11.1 Prevalence of above average, average and below average school performance in 722 6-7-year-old (blue bars) and 890 12-13-year-old (red bars) participants

Nine percent (67/722) of 6-7-year-olds and 6% (55/890) of 12-13-year-olds were reported by their parents/ guardians below average academically. Amongst participants reporting below average:

- Sixty-seven percent (42/63) of 6-7-year-olds and 67.3% (37/54) of 12-13-year-olds had not had their eyes examined within 12 months of data collection;

- Thirty-five percent (22/63) of 6-7-year-olds and 17% (9/54) of 12-13-year-olds presented with vision worse than 0.3logMAR in one eye; and

- Fourteen percent (9/63) of 6-7-year-olds and 9% (5/54) of 12-13-year-olds presented with vision poorer than 0.3logMAR in both eyes.

There was no association between socioeconomic status and a history of having had an eye test (p=0.38).

Table 11.1 presents selected ocular outcomes associated with school performance for 6-7-year-old participants and Table 11.2 presents findings for 12-13-year-old participants.

Table 11.1 Significant ocular outcomes associated with school performance in 6-7-year-olds

Refractive and visual status	Above average N=120	Average N=535	Below average N=67	P-value
SER D mean (SD)	1.31 (1.29)	1.46 (1.22)†	1.55 (1.13)	p<0.001
Astigmatism DC mean (SD)	-0.64 (0.6)	-0.58 (0.56)†	-0.91 (0.84)	p<0.001
Presenting vision at 3M(SD) logMAR	-0.01 (0.15)	-0.00 (0.15)‡	0.15 (0.25)	p<0.001
Presenting vision at 40cm(SD) logMAR	0.08 (0.22)	0.07 (0.18)‡	0.23 (0.35)	p<0.001
Pin-hole vision (SD)	0.02 (0.1)	0.02 (0.11)	0.14 (0.23)	p<0.001
Stereo-acuity (secs of arc)	150.4 (217.7)	135.9 (202.6)‡	271.7 (315.8)	p<0.001
Amplitude of accommodation (D)	13.8 (4.2)	13.9 (3.8)‡	11.5 (5.0)	p<0.001
	n (%)	n (%)	n (%)	
PVI 'better eye'(N=27)	5 (18.5)	11 (40.7)	11 (40.7)	p<0.001
PVI 'either eye' (N=65)	13 (20.0)	30 (46.2)	22 (33.8)	p<0.001
No PVI (N=657)	107 (16.3)	506 (77.0)	44 (6.7)	Ref
Myopic (N=26)	6 (23.1)	16 (61.5)	4 (15.4)	p=0.30
Hyperopic (N=233)	35 (15.7)	167 (74.9)	21 (9.4)	p=0.23
Astigmatic (N=180)	25 (13.9)	123 (68.3)	32 (17.8)	p<0.001
Emmetropia (503)	79 (16.7)	383 (74.6)	41 (8.7)	Ref
Amblyopia either eye (N=40)	5 (12.5)	17 (42.5)	18 (45.0)	p<0.001
Amblyopia bilateral both eyes (N=8)	1 (12.5)	3 (37.5)	4 (50.0)	p<0.001
Stereo-acuity<240 arc secs (N=601)	101 (16.8)	464 (77.2)	36 (6.0)	Ref
Stereo-acuity≥240 arc secs (N=121)	19 (15.7)	71 (58.7)	31 (25.6)	p<0.001

†Post-hoc analysis revealed a significant difference between average and above average school performance, ‡Post-hoc analysis showed no difference between average and above average school performance, reference category (Ref), dioptre (D), dioptre cylinder (DC), standard deviation (SD), number of participants (N), frequency (n).

Table 11.2 Significant ocular outcomes associated with school performance in 12-13-year-olds

Refractive and visual status	Above average N=240	Average N=595	Below average N=55	P-value
SER D mean (SD)	0.24 (1.7)	0.42 (1.6)	0.57 (1.4)	p=0.22
Astigmatism DC mean (SD)	-0.52 (0.50)	-0.53 (0.57)	-0.60 (0.58)	p=0.70
Presenting vision at 3M(SD) logMAR	-0.06 (0.23)	-0.08 (0.19)	-0.01 (0.24)	p=0.04
Presenting vision at 40cm(SD) logMAR	0.03 (0.12)	0.03 (0.12)‡	0.07 (0.18)	p<0.001
Pin-hole vision (SD)	-0.1 (0.15)	-0.09 (0.14)	0.0 (0.18)	p=0.07
Stereo-acuity (secs of arc)	87.6 (163.9)	94.8 (189.7)‡	149.4 (252.3)	p=0.004
Amplitude of accommodation (D)	12.2 (3.2)	12.1 (3.8)	11.2 (3.4)	p=0.15
	n (%)	n (%)	n (%)	
PVI 'better eye'(N=30)	7 (23.3)	18 (60.0)	5 (16.7)	p=0.02
PVI 'either eye'(N=75)	21 (28.0)	46 (61.3)	8 (10.7)	p=0.16
No PVI (N=804)	215 (26.7)	545 (67.8)	44 (5.5)	Ref
Myopic (SER≤-0.50D) (N=202)	72 (35.6)	120 (59.4)	10 (5.0)	p=0.007
Hyperopic (SER≥2.00D) (N=102)	32 (31.4)	62 (60.8)	8 (7.8)	p=0.36
Astigmatic (≥1DC) (N=207)	60 (27.6)	142 (65.4)	5 (6.9)	p=0.79
Emmetropic (N=588)	137 (23.3)	415 (70.6)	36 (6.1)	Ref
Amblyopia either eye (N=33)	9 (27.3)	19 (57.6)	5 (15.2)	0.07
Amblyopia both eyes (N=7)	1 (14.3)	2 (28.6)	4 (57.1)	p<0.001
Stereo-acuity<240 arc secs (N=788)	214 (27.2)	530 (67.3)	44 (5.6)	Ref
Stereo-acuity≥240 arc secs (N=103)	27 (26.2)	65 (63.1)	11 (10.7)	p=0.24

†Post-hoc analysis revealed a significant difference between average and above average school performance, ‡Post-hoc analysis showed no difference between average and above average school performance, reference category (Ref), dioptre (D), dioptre cylinder (DC), standard deviation (SD), number of participants (N), frequency (n).

11.4.1 Sociodemographic factors associated with school performance

Logistic regression analysis examining the relationship school performance and sociodemographic factors, with average school performance as the reference category, showed that above-average school performance was associated with older age-group (OR=1.5, 95% CIs 1.1 to 1.9, p=0.006), but not ethnicity (p=0.84), or socioeconomic status (p=0.45) or gender (p=0.81). Below average school performance was significantly associated with socioeconomic disadvantage (OR=2.0, 95% CIs 1.3 to 3.0, p=0.003), male gender (OR=1.7, 95% CIs: 1.1 to 2.5, p=0.01) and Traveller ethnicity (OR=3.0, 95% CIs: 1.3 to 7.0, p=0.008). For instance, 10.7% of socioeconomically disadvantaged participants reported below average school performance compared to 6.6% of advantaged participants (refer Figure 11.2). Appendix 6 presents school performance in all of the participating socioeconomically disadvantaged schools and Appendix 7 presents school performance in all of the participating socioeconomically advantaged schools and Appendix 8 presents school performance in all of the study schools.
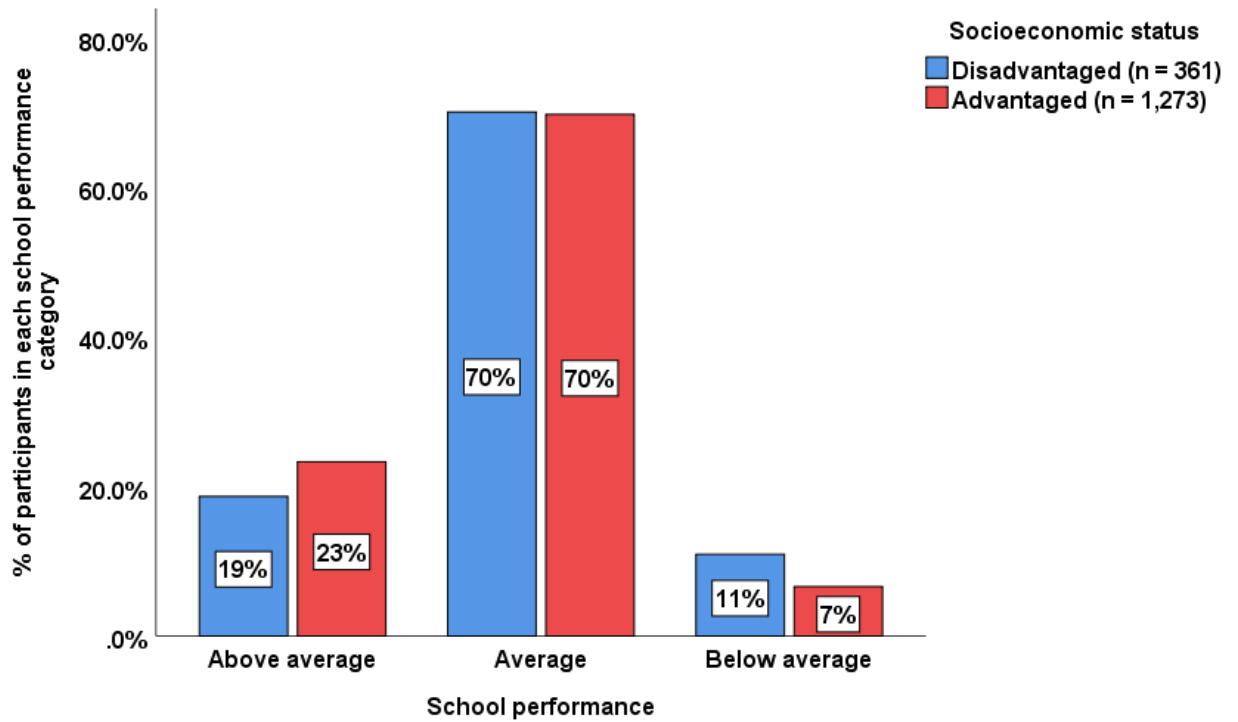
Figure 11.2 Prevalence of above average, average and below average school performance in 361 socioeconomically disadvantaged participants (blue bars) and 1,273 socioeconomically advantaged participants (red bars).

Of the male participants, 7.8% of 12-13-year-olds reported below average school performance compared to just 3.8% of 12-13-year-old females (refer Figure 11.3)
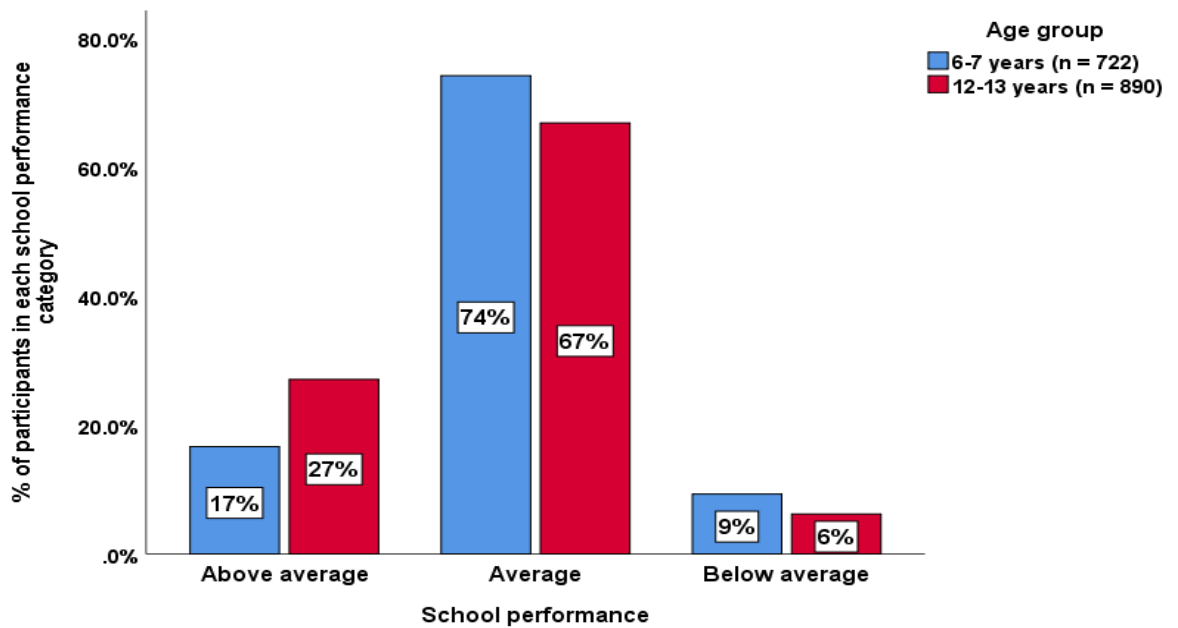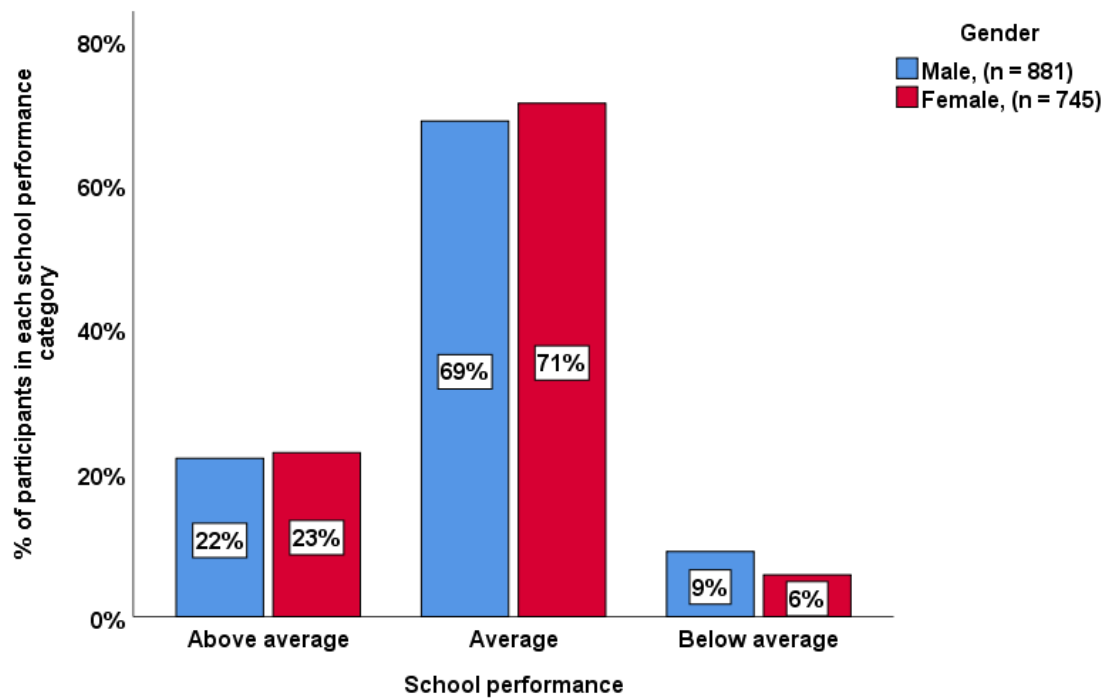
Figure 11.3 Prevalence of above average, average and below average school performance in 881 male (blue bars) and 745 female (red bars) participants

Twenty per cent of 6-7-year-old Traveller participants reported below average school performance compared to 8.1% of White and 7.6% of non-White 6-7-year-olds (refer 11.4).
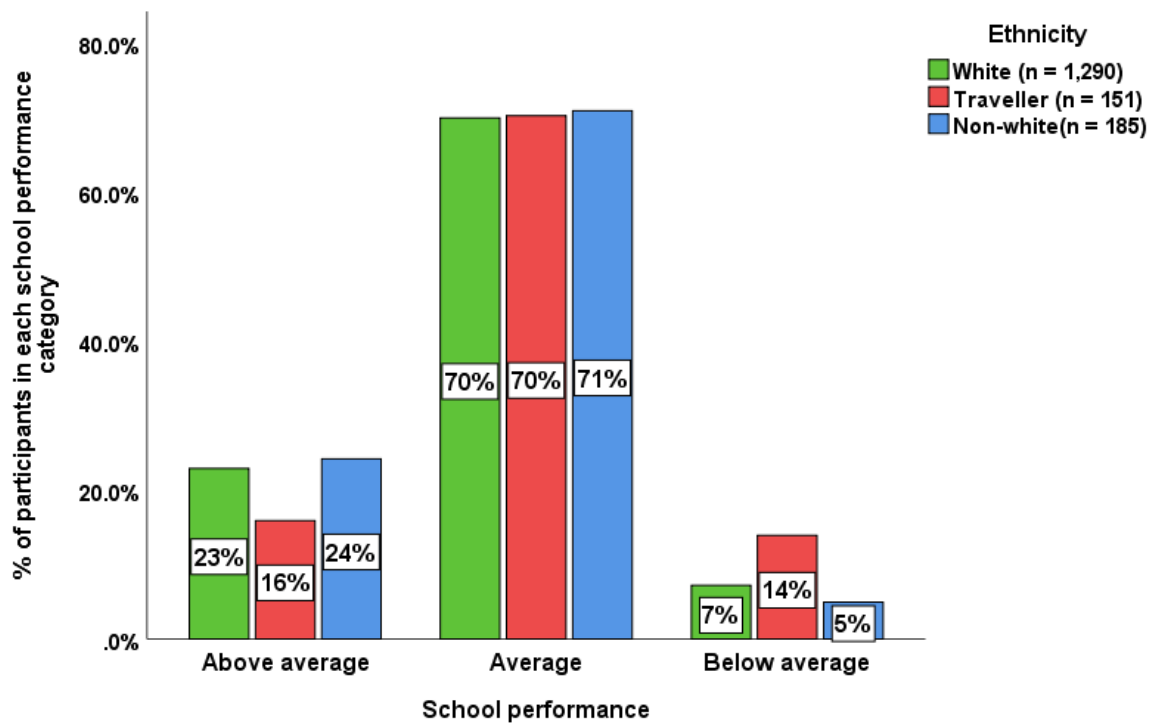
Figure 11.4 Prevalence of above average, average and below average school performance in 1,290 White (green bars), 151 Traveller (red bars), and 185 Non-White (blue bars) participants

Hence logistical regression models were constructed to analyse the relationship between school performance and various aspects of vision controlling for age, ethnicity and gender in all analyses.

11.4.2   Spherical equivalent and school performance

Spherical equivalent distribution varied across the school performance categories amongst the 6-7-year-old participants with a more hyperopic mean± SD SER associated with participants performing below average academically (1.55±1.13 D) when compared to participants in the above average category (1.31±1.29 D) ($p < 0.001$, Kruskal-Wallis test). Bonferroni post-hoc analysis showed participants who performed below average in school had a substantially more hyperopic SER than those who performed about as well as others ($p < 0.001$, one-way ANOVA), who were in turn

significantly more hyperopic than those who performed above average academically (p<0.001, one-way ANOVA). There was no significant difference in mean SER across the school performance categories amongst the 12-13-year-olds (p=0.22).

11.4.3   Astigmatism and school performance

Astigmatism distribution was significantly different across the school performance categories (p=0.001). Participants aged 6-7-years-old who reported below average in school had higher degrees of astigmatism than those with average school performance (p=0.023) and also than participants who performed above average academically (p<0.001). The mean cylindrical correction varied significantly across the school performance categories (p=0.01, Kruskal-Wallis test). Participants who reported below average academic performance had a considerably higher level of astigmatism than participants who performed as well as others (Bonferroni post hoc analysis p=0.03). There was no significant difference in cylindrical correction between the participants who reported above average and participants with average school performance (p=0.93 Bonferroni post hoc analysis). There was no significant difference in mean astigmatism across the school performance categories in 12-13-year-olds (p=0.70) (see Figure 11.5).
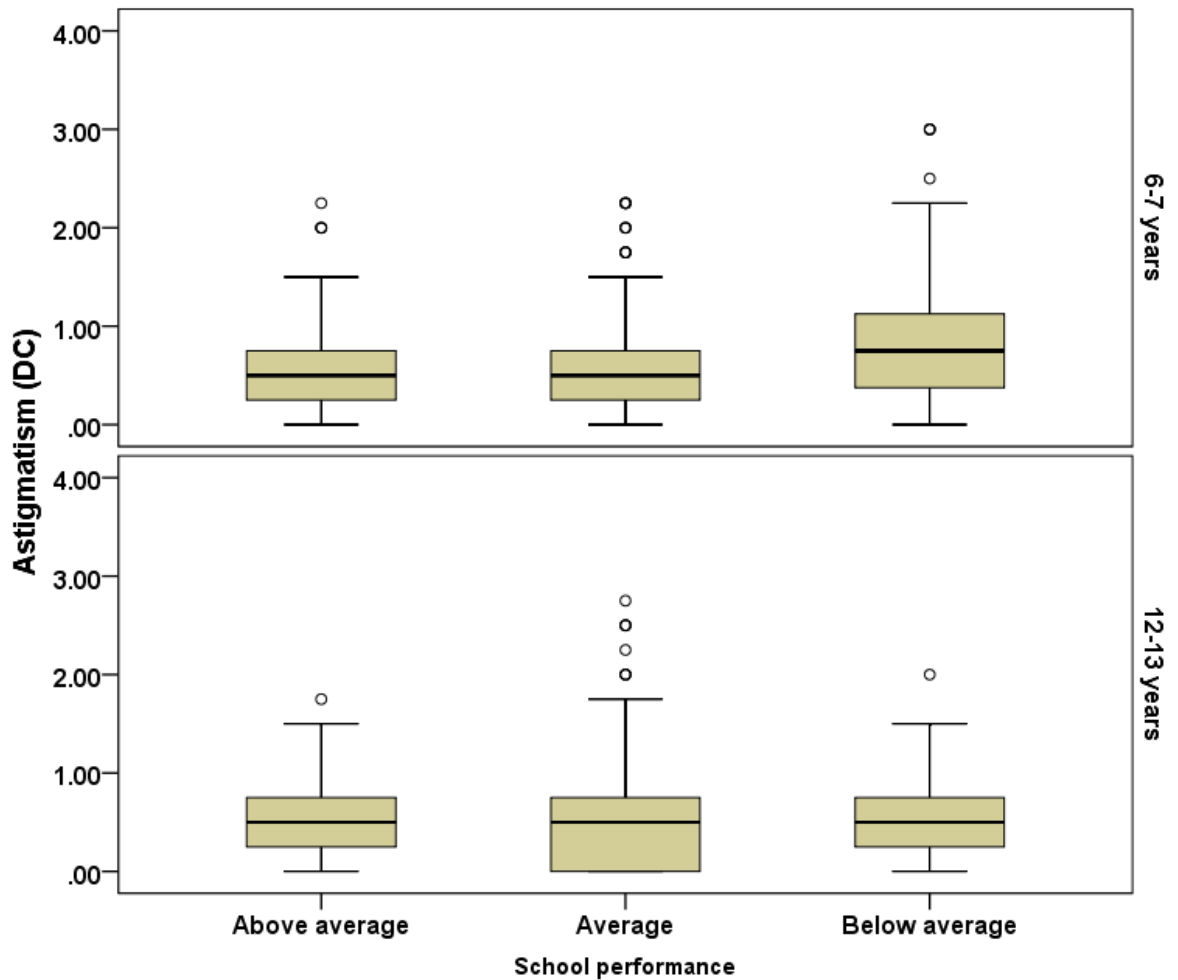
Figure 11.5 The distribution of astigmatism (DC) in 722 6-7-year-olds (top image) and 890 12-13 year-olds (bottom image) by school performance category

From top to bottom the five horizontal bars represent the maximum, 75th percentile, median, 25th percentile the whiskers mark the range of the data with the outliers (<5th percentile or >95th percentile) shown as grey dots. The numbers of participants in each school performance category were as follows in 6-7-year-olds: 120 above average, 535 average and 67 below average. The corresponding numbers in the 12-13-year-olds were: 240 above average, 595 average and 55 below average.

11.4.4 Clinically significant refractive error, spectacle wear and school performance

Emmetropia was associated with performing above average academically (OR=1.4, 95% CI: 1.1 to 1.8, p<0.001). Myopia (SER≤-0.50 D) was significantly associated with

performing above average academically (OR: 2.4, 95% CIs: 1.6 to 4.6, p=0.003). Amongst 6-7-year-olds performing below average academically, there was an association with astigmatism ≥1.00 DC (p=0.003); 17.8% of 6-7-year-olds who performed below average academically had astigmatism, whereas only 6.3% of those without astigmatism performed below average academically.

11.4.5   School performance and spectacle wear

Of the participants who reported below average academically four 6-7 year-olds and eight 12-13-year-olds did not have their prescribed spectacles in school. Amongst 6-7-year-olds who reported below-average academic performance, 14 had PVI (seven bilateral PVI) and never wore spectacles; two were wearing spectacles which required updating and two did not have their spectacles in school. Amongst the 12-13-year-olds who reported not doing as well as their peers in school, two had PVI in both eyes and no history of spectacle wear; three had spectacles which required updating and four did not have their spectacles in school.

11.4.6   Distance presenting vision and school performance

Figure 11.6 displays the distribution of distance presenting vision categorised by age-group and school performance status. Amongst 6-7-year-olds, presenting vision in the distance varied across the school performance categories (p<0.001). The mean ±SD presenting vision was significantly better (-0.01 ± 0.15logMAR) amongst participants who reported above-average school performance when compared to participants with average school performance (-0.0 ± 0.15logMAR), and those who reported below average academically (0.15 ± 0.25logMAR). Post-hoc analysis revealed no significant difference between those who reported above average academic performance and those who reported average academic performance (p=0.84). Amongst 12-13-year-olds distance presenting vision did not vary significantly across the school performance

categories (p=0.20) possibly due to the association between myopia and above average school performance in the 12-13-year-old participants (refer section 11.4.4).
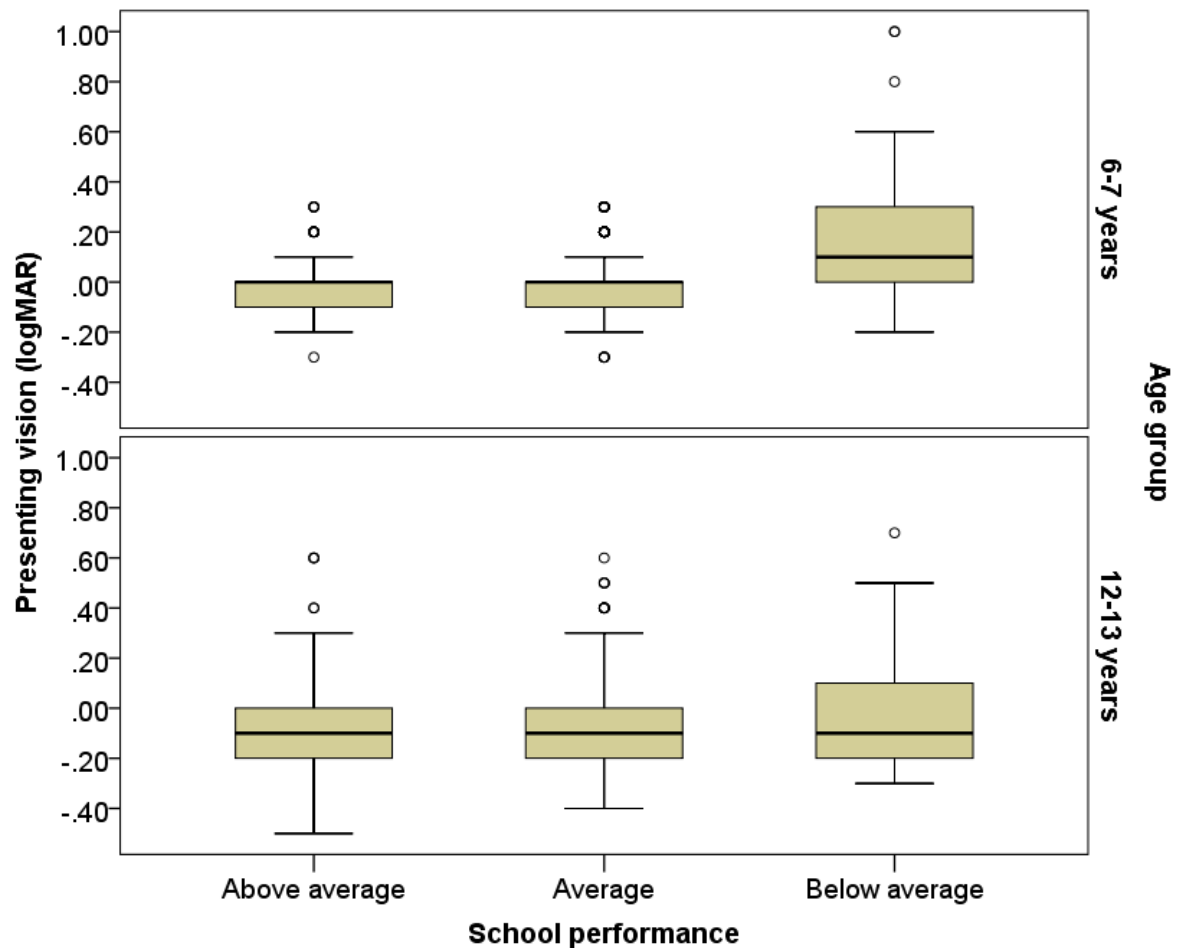
Figure 11.6 The distribution of distance presenting vision in 722 6-7-year-olds (top image) and 890 12-13 year-olds (bottom image) by school performance category

From top to bottom the five horizontal bars represent the maximum, 75th percentile, median, 25th percentile the whiskers mark the range of the data with the outliers (<5th percentile or >95th percentile) shown as grey dots The numbers of participants in each school performance category were as follows in 6-7-year-olds: 120 above average, 535 average and 67 below average. The corresponding numbers in the 12-13-year-olds were: 240 above average, 595 average and 55 below average.

11.4.7 Presenting vision at near and school performance

Presenting vision at near also varied across the school performance categories (p<0.001). Participants aged 6-7 years who reported below average academically had significantly poorer vision at near (0.23 ± 0.35logMAR) than those who performed above average academically (0.08 ± 0.22logMAR) (p<0.001, post-hoc comparison), and those who performed as well as their peers (0.07 ± 0.18logMAR) (p<0.001, post-hoc comparison). There was no significant difference in mean near vision between participants who performed as well as their peers and those who performed above average academically (p=0.81, post-hoc comparison).

Presenting vision at near was significantly associated with school performance in the 12-13-year-old cohort (p=0.02). Participants who struggled academically had poorer presenting vision at near (0.07 ± 0.18logMAR) (p=0.007), when compared to those who performed above average academically (0.03 ± 0.12logMAR). However, there was no significant difference in presenting vision at near between 12-13-year-old participants who reported above average academic performance and those who reported average academic performance (p=0.42).

11.4.8 Stereo-acuity and school performance

Stereo-acuity was significantly poorer amongst 6-7-year-olds (p<0.001) who reported below average academic performance (271.7 ± 315.8 arc seconds) compared to those who performed in line with their peers (135.9 ± 202.6 arc seconds) and those who performed above average (150.4 ± 217.7 arc seconds). Post-hoc analysis did not reveal any difference between those in the average and above average cohort (p=0.49). Stereo-acuity also varied across the school performance categories in the 12-13-year-old cohort (p=0.004). Participants who performed above average had finer stereo-acuity (87.6 ± 163.9 arc seconds) than those reporting below average school performance (149.4 ±

252.3 arc seconds) (p=0.001) and those reporting average school performance (p=0.003). There was no significant difference in mean stereo-acuity between average and above average cohorts (p=0.73) (refer Figure 11.7).
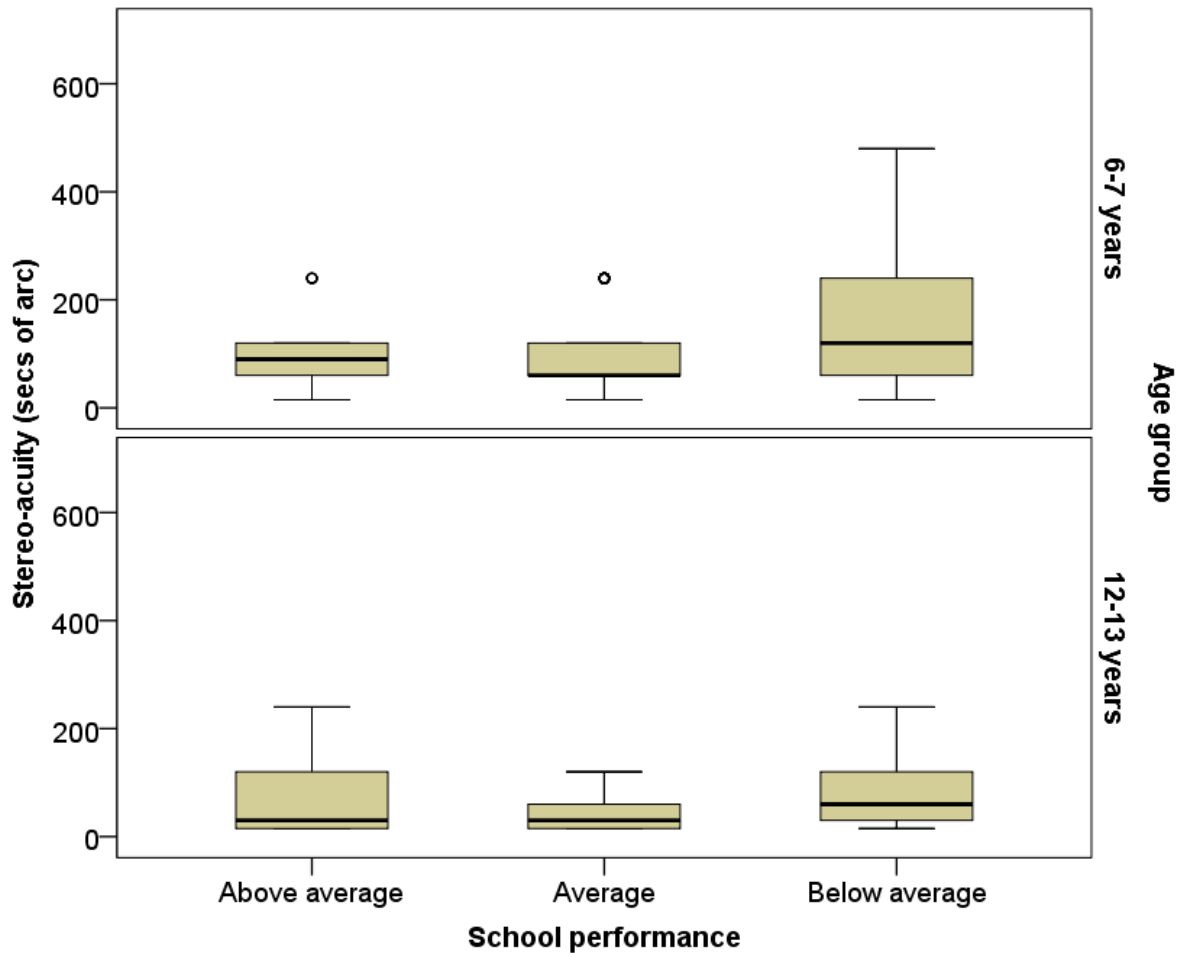
Figure 11.7 The distribution of stereo-acuity (arc seconds) in 722 6-7-year-olds (top image) and 890 12-13 year-olds (bottom image) by school performance category

From top to bottom the five horizontal bars represent the maximum, 75th percentile, median, 25th percentile the whiskers mark the range of the data with the outliers (<5th percentile or >95th percentile) shown as grey dots. The numbers of participants in each school performance category were as follows in 6-7-year-olds: 120 above average, 535 average and 67 below average. The corresponding numbers in the 12-13-year-olds were: 240 above average, 595 average and 55 below average.

11.4.9 Amplitude of accommodation and school performance

The amplitude of accommodation was significantly different across the school performance categories (p<0.001) in the 6-7-year-old age cohort, but not amongst the 12-13-year-olds (p=0.15). Participants aged 6-7-years-old who reported below average academically had significantly poorer accommodation than participants in the average (p<0.001), and the below average academic groups (p<0.001). There was no significant difference in the mean amplitude of accommodation between the average and above average academic performance categories (p=0.07).

11.4.10 Amblyopia and school performance

Amblyopia was significantly associated with performing below average academically (p<0.001). Fifty per cent of the bilaterally amblyopic, 39% with unilateral amblyopia and 6.9% of non-amblyopic 6-7-year-olds reported not doing as well as their peers in school. This pattern was repeated in the older age cohort where 51.7% with bilateral amblyopia, 15.2% with unilateral amblyopia and 5.7% without amblyopia reported struggling in school (refer Figure 11.8).
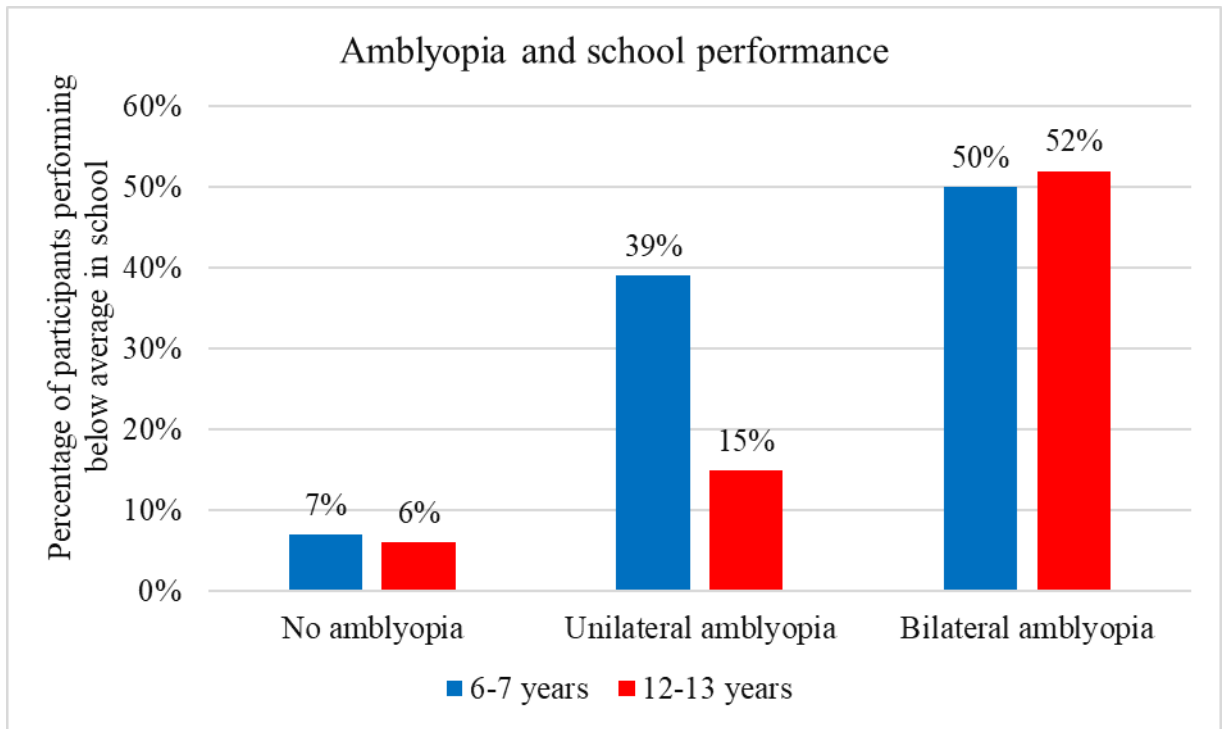
Figure 11.8 The relationship between amblyopia prevalence and performing below average in school in 722 6-7-year-olds (blue bars) and 890 12-13-year-olds (red bars)

The effect of amblyopia treatment on school performance was also examined. Amongst participants without amblyopia and with no history of amblyopia treatment 6.3% (92 of 1453 participants) reported below average school performance. Amongst participants successfully treated for amblyopia the percentage who reported below average school performance was 7.6% (six of 79 participants). The corresponding percentages of below average school performance amongst participants who were treated but remained amblyopic or who were amblyopic and never treated were 19.5% (six of 31 participants) and 37.5% (15 of 40 participants) respectively. This difference in prevalence of below average school performance across the amblyopia treatment categories was significant (p<0.001, Pearson Chi-Square).
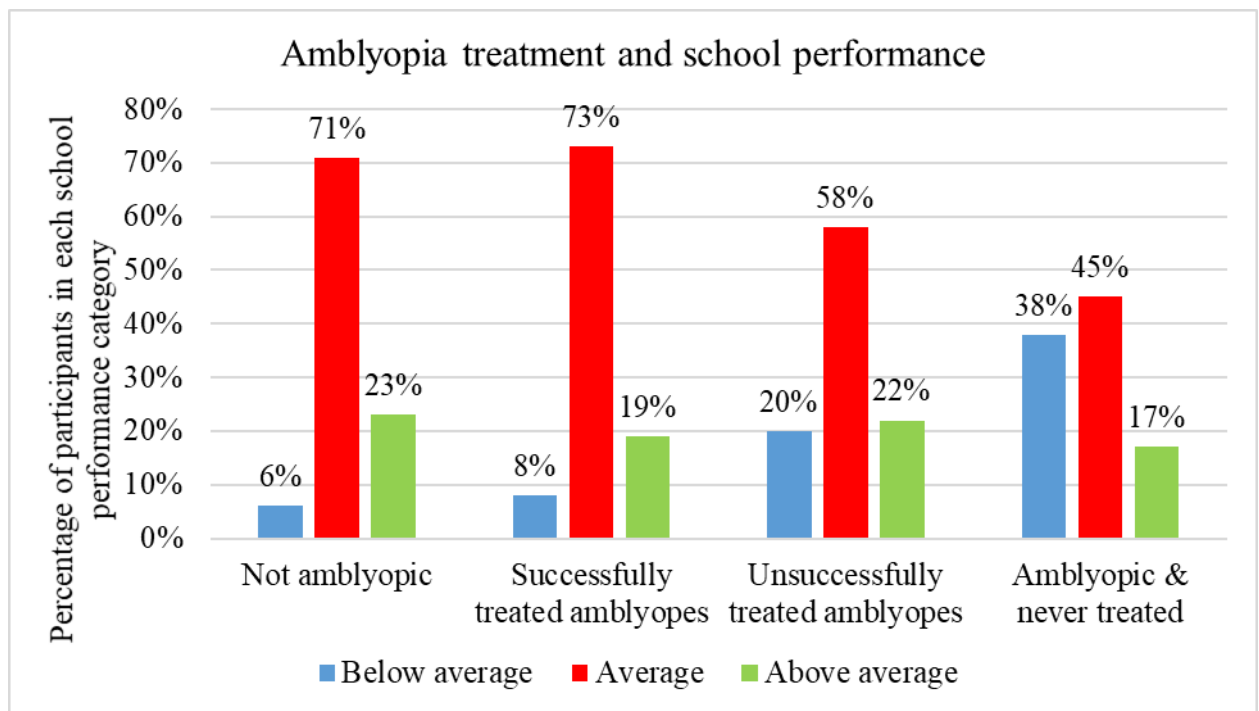
Figure 11.5 Percentage of participants who reported performing below average, average and above average school performance in each of the following categories: not amblyopic with no history of amblyopia treatment (1,453 participants), successfully treated amblyopes (79 participants), unsuccessfully treated amblyopes (31 participants), and amblyopic and no previous history of amblyopia treatment (40 participants)

Table 11.1 presents the relationship between academic performance and selected ocular outcomes in the IES.

11.5 Discussion

The current study is the first to explore the relationship between vision and children's school academic performance in Ireland. Study findings demonstrate a significant association between presenting vision (in the distance and at near) and how children were performing in school. While many previous studies addressed the relationship between specific aspects of academic or educational achievement and vision, such as literacy and numeracy scores (Bruce *et al.*, 2016; Wood *et al.*, 2018), or intelligence and refractive error (Williams *et al.*, 2008b; Akrami *et al.*, 2012), qualitative assessment has

received less interest (Carlton and Kaltenthaler, 2011). The current study addressed the association between how parents/guardians perceived their child's performance at school (qualitative analysis) and various aspects of vision (quantitative analysis). Qualitative analysis procedures rely on subjective judgements (in this case those of the parents/legal guardians) which may limit generalisability (Polit and Hungler, 1995). This is a potential limitation of the present study, however, there does appear to be good agreement between participating schools as to the proportion of schoolchildren performing in line with their peers (refer to Appendix 6, Appendix 7, and Appendix 8 which display the distribution of school performance in the participating schools). Also, quantitative analysis provides the empirical evidence necessary for practice whereas qualitative analysis supports the personal and experimental "knowing" which is critical to the interpretation of study findings and their application to clinical practice (Malterud, 2001). As patient-recorded outcome measures (Tadić *et al.*, 2013) are now routinely used in health settings and essential when updating health policy, generic feedback from parents regarding how their child is performing at school provides invaluable information that may be more context-specific than test scores of mathematical ability or reading speed. In line with previous studies, the present study found performing below average in school was associated with several other factors such as male gender (Weaver-Hightower, 2003), socioeconomic disadvantage (Bruce *et al.*, 2016), and ethnicity (Hoff, 2013). Likewise, Maples (2003) found that "struggling in school" was associated with age, ethnicity and socioeconomic status.

However, the results regarding the association between vision and school performance in the literature have been inconsistent; some studies have found an association (Bruce *et al.*, 2016; Wood *et al.*, 2018), while others have not (Helveston *et al.*, 1985; Dirani, Shekar and Baird, 2008).

11.5.1 Distance and near vision

After adjusting for associated factors such as age-group, gender, socioeconomic status and Traveller ethnicity, presenting distance vision for 6-7-year-olds, and near for both age cohorts was significantly associated with school performance. Furthermore, PVI in the better eye was associated with below average school performance in both age groups. Indeed, Maple's (2003) longitudinal study which involved 2,659 examinations of 540 participants (initial age 6-7-years-old over three years) demonstrated that vision provides a better measure of future academic performance (Iowa Test of Basic skills) than ethnicity or socioeconomic status. Likewise, Goldstand, Koslowe and Parush (2005) reported that Israeli participants (12 years-old) who passed vision screening were more proficient readers and had better visual information processing than participants who failed vision screening.

11.5.2 Refractive error

The association found in the present study between myopia and performing above average academically aligns with previous studies (Saw *et al.*, 2001; Williams, Miller, *et al.*, 2008). Furthermore, the association demonstrated in previous studies between hyperopia and poorer educational attainment was mirrored in the IES (Rosner and Rosner, 1997; Williams *et al.*, 2005). What is more, the association established in the present study between a more hyperopic SER and performing below average academically amongst the 6-7-year-old age cohort agrees with previous studies (Stewart-Brown, Haslum and Butler, 2008; Kulp *et al.*, 2016). The association between a more hyperopic SER and performing below average academically in the 6-7-year-old age cohort is significant albeit somewhat counter-intuitive as the amplitude of accommodation is highest in early childhood. Hence, traditionally, hyperopia ≤+3.00 D is rarely corrected as children aged 6-7-years are considered to have adequate accommodation to compensate for near visual tasks (Arnold, 2004). However, the

present study demonstrated that children performing below average in school had significantly lower mean amplitude of accommodation, specifically in the 6-7-year-old cohort. This may be due to less accurate accommodation in the younger age-cohort when compared to the older children, which align with a previous study (Anderson *et al.*, 2009). Indeed, objectively measured accommodation may be lower than the subjectively measured push-up test in the present study (Anderson *et al.*, 2008). Therefore, further studies examining the association between accommodation and educational performance are crucial, particularly in younger children (younger than eight years old) during the "learning to read" stage when accurate accommodation is essential.

Astigmatism was also significantly associated with poorer academic performance in the IES, and, in line with MEPEDS, coexisted with hyperopia in the younger age-cohort (Kulp *et al.*, 2014). Likewise, astigmatism was associated with reduced educational achievement in Iran (Akrami *et al.*, 2012). Indeed, both the presence and magnitude of astigmatism were significantly associated with performing below average academically in the present study. This has important implications for children in Ireland, where significant amounts of astigmatism exist (Harrington *et al.*, 2018), refer to chapter 7 for more detail on astigmatism prevalence in the IES.

Of further concern was the substantial number of children at school without their prescribed spectacles, many of whom were socioeconomically disadvantaged (Harrington *et al.*, 2018). Compliance with spectacle wear in school is a public health issue in Ireland and research has shown that prescribing spectacles to children who need them can improve academic performance (Ma *et al.*, 2014; Yi *et al.*, 2015; Slavin *et al.*, 2018).

11.5.3   Amblyopia and binocular vision

The current study findings of lower levels of below-average school performance amongst participants successfully treated for amblyopia reinforce the importance early detection, and compliance with amblyopia treatment. The association found in the IES between amblyopia and below average academic performance was also reported in Iranian children aged 9-15 years, where amblyopia was associated with, not only a reduced quality of life but also reduced educational attainment (Khalaj *et al.*, 2011). In contrast, in the 1958 findings from the British birth cohort, quality of life issues and amblyopia were attributed to amblyopia treatment and not the visual disruption (Rahi, Cumberland and Peckham, 2006). However, conversely, previous studies demonstrated a relationship between amblyopia and reading speed (Kelly *et al.*, 2015) and transcribing (Kelly *et al.*, 2018), and that amblyopia and strabismus disrupt reading ability and accuracy (Kugathasan *et al.*, 2019). As amblyopia was significantly associated with not doing as well as classmates in school in the present study, addressing amblyopia early in childhood is essential.

The association between reduced/abnormal presenting stereoacuity and poor school performance concurs with Kulp *et al.* (1999) where stereo-acuity of 240 arc seconds or worse was associated with poor academic attainment. Stereo-acuity at near is a measure of binocular vision, which is affected by reduced VA, inaccurate accommodation and ocular alignment (Li *et al.*, 2016). Studies involving adults demonstrated the functional importance of accurate stereo-acuity in a clinical setting (Al-Saud *et al.*, 2017). Providing support to children with positive orthoptic interventions to improve stereopsis also improved literacy in children to a greater extent than providing just parental literacy support alone in children aged 8-13 years (Ponsonby *et al.*, 2013). The IES findings reinforce the importance of good stereo-acuity and the impact of poor stereo-acuity on how children are performing in school

11.5.4   Public health

The majority of children reported by their parents/guardians as underperforming in school compared to their peers did not have an eye examination within the 12 months before data collection. A significant number of those children presented with VI (presenting VA worse than 0.3logMAR, 6/12 Snellen) in both eyes, which demonstrates a lack of public awareness as to the importance of vision in children's development. For instance, of the parents who reported their child was doing less well than their peers in school, two thirds (67%) said that their child had not had an eye examination within the 12 months before data collection. Hence, it may be postulated that (a) parents were unaware of the association between below average school performance and vision, (b) parents were unaware of how to go about accessing an eye examination for their child, (c) parents may have other commitments such as work or dependants in the home which mean they are unable to bring their child for an eye examination, or possibly (d) parents were unable to afford private eye-care for their child and with the waiting lists for publically funded eye tests currently running at over two years in Ireland (Power *et al.*, 2017), the consequence is that children are not accessing an eye examination in time.

Further research is imperative to accurately understand the barriers to accessing eye-care for children in Ireland. Whilst those parents/guardians who were aware that their child was below average academically when compared to their classmates, most had not brought their child for an eye examination. Hence, public awareness of refractive error is most likely poor in Ireland as evidenced in Sharma's review which addressed school-based approaches to the correction of refractive error in children (Sharma *et al.*, 2012). The current study findings highlight the need for public education programmes addressing the importance of comprehensive eye examinations for all children, ideally in advance of starting school. Early childhood interventions enhance children's wellbeing, and as the Chicago longitudinal study demonstrated every $1 invested

returned $7.5 to society (Reynolds, Temple and Ou, 2003). Thus, the relationship found in other studies between poor vision and unsatisfactory academic performance has again been supported in the IES.

Qualitative assessments of how parents/guardians perceived their child was doing in school were used in the IES, in contrast to quantitative testing such as used in Wood *et al.*'s (2018) paper where the relationship between visual status and reading, writing, spelling, grammar/punctuation and numeracy was examined (Wood *et al.*, 2018). However, qualitative assessment methods are crucial to understanding community needs and issues, as qualitative findings can provide researchers with a better understanding of the meaning and implications of quantitative study findings (Malterud, 2001).

While IES findings of an association between more unsatisfactory school performance and VI in schoolchildren in Ireland are novel, due to the cross-sectional nature of the data, it is not possible to conclude that VI is responsible for performing below average academically. Hence, further studies, including longitudinal studies, are recommended to assess the extent and magnitude of the relationship between vision and how well children perform academically in school.

The IES data, together with the supporting data from previous studies in other countries would suggest strongly that a considerable proportion of schoolchildren in Ireland may benefit from wearing spectacles. Parental/guardian lack of awareness of child vision healthcare and financial barriers are possible factors impeding increased spectacle wear amongst Irish schoolchildren (Aldebasi, 2013; McCrann *et al.,* 2018). Economic and other societal factors may also be reducing spectacle wear compliance by children. All of these are factors in below average educational achievement by children with poor vision.

The strengths of this study include the large sample size, random school selection and the high questionnaire completion rate. School performance data was as per participant parents or legal guardians, who assessed how they believed their child was performing academically at school when compared to their peers. Socioeconomically disadvantaged participants in the IES were significantly more likely to present with VI than socioeconomically advantaged children (refer Chapter three). Therefore, children in socioeconomically disadvantaged schools were compared to children in the same environment and children attending private schools were compared to their peers. There are gaps remaining concerning specific aspects of vision (accommodation, convergence, and stereo-acuity) and their relationship with academic achievement; hence, further research is required to examine what level of VI is likely to interfere with learning.

Longitudinal findings will be beneficial to see if the provision of spectacles improves how children are performing in school.

Chapter 12 presents a summary of the IES findings and future work planned.

12 IRELAND EYE STUDY CONCLUSIONS AND FUTURE WORK

12.1 Summary and discussion

Following an initial survey of the results, the main objectives of the investigation have been attained, which were as follows:

(a)   To provide a comprehensive database on refractive error, VI, amblyopia, together with population norms for ocular biometric measures for school children in Ireland;

(b)   To investigate any relationships between vision, lifestyle and demographic factors; and

(c)   Examine possible connections between vision and school performance.

12.2 Myopia prevalence

The prevalence of myopia found (6-7 years 3.3%, 12-13 years 19.9%) was higher than South Africa (5 years 3.2%, 13 years 3.4%) (Naidoo *et al.*, 2003), Australia (6 years 2%, 12 years 18.6%) (Robaei *et al.*, 2005b; Robaei *et al.*, 2006d), Poland (6-18 years 13%) (Czepita, Zejmo and Mojsa, 2007). Furthermore, myopia prevalence in the current study was broadly in line with Northern Ireland (6-7 years 2.8%, 12-13 years 17.7%) (O'Donoghue *et al.*, 2010), Chile (5 years 3.4%, 15 years 19.4%) (Maul *et al.*, 2000), and lower than China (48%) (Zhao *et al.*, 2000), Sweden (45%) (Ohlsson *et al.*, 2001) and Taiwan (7 years 20%, 12 years 61%, 15 years 84%) (Lin *et al.*, 2004).

12.2.1 Risk factors for myopia

Ireland Eye Study data showed an association between myopia and: age; ethnicity; a paternal history of myopia; daylight exposure during summer; obesity and screen-time. Hence, changing lifestyles may impact on children's vision, increasing the likelihood of VI in later life in susceptible children (Bourne *et al.*, 2017).

12.2.2 Myopia and time spent outdoors during daylight

Participants who reported spending less than one hour outdoors during daylight in summer were five times more likely to be myopic when compared to participants who spent more than four hours outdoors per day during daylight in summer. Furthermore, participants in the lowest time outdoors category had significantly longer ALs and higher AL/CR ratios than participants who spent more than two hours outdoors daily. As myopia and increased AL are associated with ocular pathology in later life (Flitcroft *et al.,* 2019), school intervention programmes promoting time outdoors during daylight of greater than two hours per day during winter ought to be considered. Extending the study to be longitudinal will be informative regarding the effect that time outdoors during daylight plays on myopia progression and axial elongation in children in a Northern European location.

12.2.3 Myopia and technology

Myopia prevalence results supported the conjecture that more time spent on screens and less time spent engaged in physical activities increased the risk of myopia prevalence. Due to the "Digital Strategy for Schools" (discussed in section 2.3), all schoolchildren in Ireland have daily access to screen-based technologies in schools.

"The Investing Effectively in information communication technologies in Schools" report in 2008 established a framework for information communication technologies investment decisions in schools in Ireland. The advisory group prioritised classroom

and student infrastructure, technical support and the virtual learning environment. The framework for delivering these recommendations ran from 2009-2012. Longitudinal studies examining the consequent impact on children's lives and visual development is essential.

12.3 Hyperopia prevalence

The prevalence of hyperopia (6-7 years 25.0%, 12-13 years 8.9%) found was broadly in line with Northern Ireland (6-7 years 26.0%, 12-13 years 14.7%), Poland (7 years 19.2%, 13 years 11.8%) (Czepita, Zejmo and Mojsa, 2007) and Chile (5-7 years 21.6%, 14-15 years 7.5%) (Maul *et al.*, 2000), but higher than RESC studies in South Africa (5 years 2.7%, 13 years 2.9%) (Naidoo *et al.*, 2003), China (5 years 8.5%, 15 years 1.1%) (Zhao *et al.*, 2000) and also higher than in Sydney (6 years 13.2%, 12 years 5.0%) (Robaei *et al.,* 2005b, 2006).

12.3.1   Risk factors associated with hyperopia

Hyperopia was associated with: age-group; amblyopia; strabismus; and VI.

12.4 Astigmatism prevalence

The prevalence of astigmatism (6-7 years 19.2%, 12-13 years 15.9%) was found to be higher than the SMS study (6 years 4.8%, 12 years 6.7%) (Huynh *et al.,* 2007) and was broadly in line with the NICER study (6-7 years 24.3%, 12-13 years 19.7%) (O'Donoghue *et al.,* 2011). The predominant axes of orientation were WTR (80.3%). The RESC studies defined astigmatism as ≥0.75DC (Negrel *et al.*, 2000); hence, direct comparisons of astigmatism prevalence with the RESC were difficult.

12.4.1   Risk factors associated with astigmatism

The current study found astigmatism was primarily associated with: myopia; hyperopia; amblyopia; and VI. The relatively high astigmatism prevalence in Ireland, compared to

the SMS, was a concern, as similar to Dobson *et al.*'s (2003) study involving Native American children, astigmatism was significantly associated with VI and amblyopia in the IES.

12.5 Amblyopia prevalence

The prevalence of amblyopia found was high (6-7 years 5.5%, 12-13 years 3.7%), and was similar to the non-Hispanic White VIP study (5.4%). Using equivalent study protocols and methodology, amblyopia prevalence in Ireland was significantly higher than Northern Ireland (0.8%) despite similar refractive error prevalence (Harrington *et al.*, 2019) and genetic profiles in both jurisdictions, but different health care systems.

12.5.1 Risk factors associated with amblyopia

Study findings established a relationship between amblyopia and: anisometropia; strabismus; VI; socioeconomic disadvantage and low income and parental education and sedentary lifestyle. Furthermore, amblyopia resulted in significant academic underperformance. Amblyopia is, therefore, a public health issue. The absence of a widely accepted operational definition of amblyopia (Ohlsson, 2005), means there is a continued lack of clarity about the characteristics of amblyopia and outcomes associated.

12.6 Presenting visual impairment prevalence

The IES PVI prevalence in the "better eye" (6-7 years 3.7%, 12-13 years 3.4%) was higher than the NICER study (1.5%) (O'Donoghue *et al.*, 2010), Australia (12 years 1.1%) (Robaei *et al.*, 2006b) and South Africa (1.2%) (Naidoo *et al.*, 2003), but lower than China (5-15 years 10.9%) (Zhao *et al.*, 2000).

12.6.1 Risk factors associated with presenting visual impairment

Presenting VI was associated with uncorrected refractive error (6-7 years hyperopia and astigmatism and 12-13 years myopia and astigmatism), amblyopia, and strabismus. Participants with good vision performed better in school than those with poor vision. Presenting VI resulted in poor academic performance and was associated with minority ethnic groups (Traveller and non-White) and socioeconomic disadvantage, as evidenced by the significantly higher of PVI in the Traveller and non-White participants in the IES. Closing the health gap for people and children in particular in these ethnic minority groups is a public health priority (Szczepura, 2005). However, to date, there is a lack of routinely collected ethnicity health data and in particular, a paucity of primary health care data relating to minority ethnic groups. The recently published protocol by the Irish Council for General Practitioners for participatory health research, along with secondary analysis of the Growing Up in Ireland study (Hannigan *et al.*, 2018), in tandem with the IES ought to assist public health initiatives to redress ethnic-specific barriers to assessing health care including eye health care in Ireland. While the primary aim of the Growing up in Ireland study was to inform public health policy in relation to children including various aspects of health and development including hearing, children's vision was not directly addressed in the study (Thornton *et al.,* 2011). Quigley *et al.'*s (2019) recent publication enquired if 9-year-old participants had "vision problems which needed correction", but further analysis of the degree of VA and type of refractive correction needed was not addressed. The authors recommended further research in this regard.

12.7 Uncorrected refractive error prevalence

The estimation of the extent and magnitude of uncorrected refractive error, and documenting the resulting VI in schoolchildren in Ireland is key to informing policy

decisions regarding ophthalmic interventions and treatments. This report provides information to cost future paediatric vision healthcare interventions better.

The prevalence of correctable VI is something that, in theory, can be immediately redressed with spectacle provision. However, spectacle compliance was poor amongst IES participants. The reasons underpinning a failure to wear prescribed spectacles merits further investigation to inform the development of an eye health awareness programme addressing spectacle wear and strategies to reduce vulnerability amongst children who require spectacles to see clearly or maintain ocular alignment (Harrington *et al.*, 2018).

12.8 Strategies to reduce amblyopia prevalence rates in Ireland

Establishing public health priorities requires parents, teachers and the wider primary care community to understand better the health-related choices they and their societies make. This community needs to understand the risks and the benefits associated with alternative courses of action in detecting and treating amblyopia (Fischhoff, 1995). For example, the IES results show that compliance with amblyopia treatment is a contributing factor, hence, it is inevitable that the trade-off made by parents between current (the perceived inconvenience of occlusion treatment) and future quality of life (possible untreatable impaired vision) may significantly impact their children (Fischhoff, 1995, 2013).

In line with the US federally funded National Expert Panel to the National Centre of Children's Vision and Eye Health recommendations, children aged 36 months to 72 months ought to be screened annually (best practice) or at least once (accepted minimum standard) (Cotter *et al.*, 2015).

Given the lack of awareness amongst parents, irrespective of educational background or socioeconomic status, and the importance of significantly improving early intervention, a study recommendation is a mandatory eye examination before commencing primary school for all school children to access free pre-school services or access into primary school. Moreover, children in Ireland are now likely to be older, starting primary school than participants in the present study. For instance, in 2010 the Irish government initiated a free pre-school year for all children in Ireland with a 96% take-up of this preschool year reported by the "Growing up in Ireland Study" in their recently published study of 5-year-olds with a consequently older mean age of children commencing primary school (Murray *et al.,* 2019). In September 2018 a second preschool year was introduced in Ireland; hence children starting primary are more likely to be older than five-years-old with many aged six-years-old starting primary school. As amblyopia treatment is time sensitive conducting vision screening in preschool as practised in Denmark (Hansen *et al.,* 2019), ought to be considered in Ireland in order ensure successful treatment outcomes in susceptible children.

In addition, school vision screening in Ireland ought to include all children in the appropriate age category (whether attending public or private schools), and adequate resources will be required to ensure prompt follow-up clinical assessment for those who fail vision screening using the broader group of community and high street optometrists, orthoptists and ophthalmologists.

Vision screening programmes should be evaluated annually to review vision screening results with comparisons to eye examination results informing screening protocols and tools, to indicate any necessary additional training for staff and to reduce over referral rates (Hartmann *et al.*, 2015).

A vision care electronic data system to link vision information with other health information is the best way to obtain and maintain data and audit outcomes to identify health disparities in regions throughout the country (Hartmann *et al.*, 2015). Population-based data systems recording receipt of services, measuring screening performance and follow-up examinations, tracking the progress of services to ensure alignment with public health goals ought to result in improved outcomes for children (Hartmann *et al.*, 2015).

With limited resources, strabismic children are being treated within the present system in Ireland. However, anisometropic children should also be reviewed regularly, and their parents/guardians should be made fully aware of amblyopia risks through sufficient explanation. While it is important not to cause undue anxiety in parents about their children's eyes, it is prudent to educate parents on the possibility of partial if not total sight loss in one eye in the absence of strabismus (Wellesley-Cole, 1959).

Furthermore, the reintroduction of school vision screening prior to commencing post-primary school is recommended due to the prevalence of PVI (8.4%) in the 12-13-year-old participants, which was significantly associated with uncorrected myopia. Vision screening for reduced vision was stopped in 2015 due to a lack of evidence to support it (Cullen, 2016). However, the results from the present study suggest that almost one in ten 12-13-year-olds would benefit from spectacle correction.

12.9 School performance and vision

The relationship between poor vision and unsatisfactory academic performance found in other studies has again been supported in the IES.

12.10 Public health implications of study findings

This research study demonstrates stark differences in the visual outcomes for schoolchildren in Ireland when compared to schoolchildren in Northern Ireland (the closest comparator). Participants in the NICER study were five times less likely than IES participants to have persistent amblyopia post traditional treatment age (before the age of 8 years) (Harrington *et al.,* 2019). Furthermore, the IES provides evidence of health inequalities in Ireland as participants with PVI and amblyopia were significantly more likely to be socioeconomically disadvantaged. What is more, the present study shows that 6-7-year-old children with unilateral amblyopia, and 6-7-year-olds and 12-13-year-olds with bilateral amblyopia, are likely to struggle in school, reaffirming Kelly *et al.'*s (2015, 2018) findings, and highlighting the negative consequences of delayed access to treatment in Ireland.

The lifelong consequences of untreated preventable visual impairment due to unaddressed amblyopia are well documented in the literature (Chua *et al.,* 2004; Rahi *et al.,* 2002). Not only will amblyopia affect an individual's quality of life, self-esteem, educational attainment and career choice (Carlton *et al.,* 2011), but also, amblyopia significantly increases the risk of bilateral visual impairment in later life, which has financial implications for the community due to lost earnings (Membreno *et al.,* 2002), plus the cost of careers (Carlton *et al.,* 2011), and a range of associated mental health difficulties including anxiety and depression and psychosis (Hayes *et al.,* 2019; De Leo *et al.,* 1999).

The National Council for the Blind in Ireland commissioned De Loitte Access Economics to produce a report, which was published in 2011, entitled "The Impact of Vision Impairment and Blindness to the Irish Economy". The overall cost associated with VI and blindness to the Irish economy for 2010 was estimated at €2.1 billion. The

annual cost to the Irish Healthcare system alone due to visual impairment was €118 million (projected to rise to 137 million in 2020), whilst the total cost to society, due to lost production/employment, informal care provided to visually impaired persons, and deadweight welfare losses from government-funded health care costs, welfare payments to the blind and lost taxation revenue, was €386.1 million. Moreover, the burden of VI and blindness on individuals, measured using disability adjusted life years, which includes healthy years of life lost due to disability, and life lost due to premature death associated with VI, brought the total burden of VI and blindness to €2.1 billion (Deloitte Access Economics, 2011). This report highlighted the importance of screening for eye conditions in Ireland at a time when treatment is likely to be successful.

A more recent report by the National Council for the Blind in Ireland reported only one in five visually impaired adults is employed in Ireland and only two in five visually impaired adults ever leave their house without organized assistance (https://www.ncbi.ie/facts-about-sightloss/). Average life expectancy in 2014 had increased by over 26 years since 1950 (United Nations Population Division 2019), thus, individuals are likely to live longer lives with their VI further increasing costs to the economy.

Of further concern, the majority of IES participants (77%) had not had an eye examination within the 12 months prior to the study. It is imperative that children access appropriate eye care where and when they need it to improve their quality of life, future educational attainment with consequent benefits to the community that addressing health inequalities provides (Marmot, 2010). Finally, data from the IES provides the prevalence estimates required to better cost the provision of paediatric eye care services in Ireland.

12.11 Future work

Due to the considerable amount of data collected in the IES, analysis of all the available data was beyond the scope of the current thesis, for instance, the IES involved examination of colour vision deficiency prevalence and ocular dominance, which has not been presented in this report, however, analysis of these data is ongoing. Also, analysis of the sensitivity and specificity of the various tests carried out in the IES with regard to the detection of amblyogenic factors and refractive errors will be investigated. While myopia prevalence and associated risk factors have been addressed in the current study, as VI related to myopia and amblyopia were the primary focus of the current study the sociodemographic and lifestyle factors related to these conditions have been presented in this report. Further analysis of risk factors associated with hyperopia, astigmatism and also sociodemographic and lifestyle factors related to emmetropia is planned. Furthermore, the high prevalence of astigmatism found in the IES requires detailed analysis due to the association between astigmatism and amblyopia, and also the association between myopia progression and WTR astigmatism (Sienkiewicz *et al.,* 2016; Tong *et al.*, 2004) which was the prominent cylindrical axis of orientation found in the IES. The correlation between corneal and refractive astigmatism will be addressed in future publications as will the relationship between anisometropia and aniso-astigmatism and amblyopia prevalence in Ireland.

Extending the work presented in this report with a longitudinal evaluation of participants in the current study is planned, which will provide valuable insight into the changing prevalence of refractive status with age and the relationship between the refractive state and ocular biometric measures in school children in Ireland. Longitudinal evaluation of the effects of time outdoors and time engaged in near vision

activities, including screen based technologies, on the refractive status and ocular biometry will also be evaluated. The very strong relationship found in the IES between time spent outdoors in daylight and myopia prevalence requires further investigation using objective measures of daylight exposure to confirm study findings. The influence of daylight on the growing eye is critical, and while there are many studies in Asia examining the relationship between light exposure and intensity, there are few in Northern Europe where seasonal differences in day length and light intensity may influence children's development. Further work analysing the relationship between daylight exposure and refractive and biometric analysis would benefit from the use of objectively measured light exposure.

The relationship between school performance and vision is another area which will be of interest in the longitudinal study. For instance, many participants presented with VI due to uncorrected refractive error, many of which reported below average academic performance compared to their peers in school, with 67% not having had eye examination within 12 months of data collection. Longitudinal research will be revealing concerning spectacle compliance and whether the provision of spectacles influenced how participants performed in school.

Areas of concern following the IES included the high prevalence of amblyopia in schoolchildren in Ireland compared to Northern Ireland and Australia, suggesting that school vision screening in Ireland is not sensitive enough or that follow on treatment is taking place too late to affect the treatments necessary to prevent conditions such as amblyopia. Poor compliance with amblyopia treatment, including spectacle compliance in cases of orthotropic/refractive amblyopia, was also a key issue. Moreover, many participants were unaware they had an issue with their vision and parents were also unaware that their child had a visual defect. Also, parents of 12-13-year-old participants

mentioned that their child had had an 'eye test' in school (referring to the vision screening at school entry) and reported that no problems had been reported at that time. Thus, it appears many parents were unaware that eyesight can change quickly as the child grows and their eyes grow. Hence public health education programmes targeting parents, teachers and health care professionals as to the importance of vision and spectacle compliance for children's social and educational development is essential. Also, further research is necessary to understand the barriers (social, personal, financial, educational) to accessing eye health care that exist in Ireland: social (peer pressure, embarrassment regarding wearing spectacles); individual (time poor parents/guardians, unable to leave work to attend appointments); financial (access to free eye tests and spectacles in high street optometrists for children in Ireland) and educational (public health education programmes).

Novel study findings of concern included the strong relationship between myopia prevalence and sedentary lifestyles and obesity in Ireland. With one in five 6-7-year-olds and one in three 12-13-year-olds overweight or obese in the current study, public health education programmes directed particularly at first time parents are crucial to prevent spiralling future public health care costs due to pathological myopia, diabetes and obesity.

12.12 Dissemination

Dissemination of results following completion of the IES in both peer-reviewed journals and the media are essential aspects of creating public awareness about preventable VI and blindness in Ireland. To date, there have been four publications from the IES; two papers addressing IES findings have been published in the British Journal of Ophthalmology, one paper addressing ocular biometry in Clinical and Experimental

Optometry and one paper comparing amblyopia prevalence in Ireland and Northern Ireland in the British Medical Journal Open.

Feedback provided by parents, on completing the study questionnaires, suggested that significant gaps remain in the public's awareness of eye health in Ireland. For instance, some parents reported being concerned that wearing spectacles would make their children's vision poorer, and others were worried that their children would become dependent on their glasses. Several parents reported that their children had 'grown out of' a turn in their eyes. Efforts to increase awareness of the importance of vision and eye care in children's development and educational progression and research are vital.

12.12.1 Papers published

- 'Refractive error and visual impairment in Ireland schoolchildren' (Harrington *et al.,* 2018).

- 'Risk factors associated with myopia in schoolchildren in Ireland' (Harrington, Stack and O'Dwyer, 2019).

- 'Ocular biometry, refraction and time spent outdoors during daylight in Irish schoolchildren' (Harrington and O'Dwyer, 2019).

- Comparison of amblyopia in schoolchildren in Ireland and Northern Ireland: a population-based observational cross-sectional analysis of a treatable childhood visual deficit. (Harrington *et al*., 2019) (Refer to page 430 for the list of publications).

12.12.2 Papers under review

- 'Visual factors associated with school performance in schoolchildren in Ireland.' (Harrington, Davison & O'Dwyer 2019).

- 'Prevalence of colour vision deficiency in schoolchildren in Ireland: demographic, socioeconomic and birth factors.' (Harrington, Davison & O'Dwyer 2019).

12.12.3 Poster presentations

- Poster presentation detailing preliminary findings on myopia prevalence was presented at the Child Vision Research Society conference in Ulster University June 2017.

- Poster presentation at the colour vision and employment symposium at London City University in June 2018.

- Poster presentation reporting amblyopia prevalence in Ireland and NI at the 45th Hospital Optometrists Annual Conference in Belfast (UK) in November 2019.

12.12.4 Presentations

- Presentation of early findings at the Association of Optometrists Ireland annual general meeting, November 6th 2016.

- Preliminary study findings were presented at the European Council of Optometry and Optics (ECOO) conference in Barcelona on May 5th 2017.

- Ireland Eye Study findings were presented at the Association of Optometrists Ireland annual general meeting on November 3rd, 2018.

- Presentation of study findings at the myopia roadshow event in Dublin on January 1st, 2019.

- Presenting study findings at the Schoolvision conference in Oxford UK on 9th June 2019.

- An oral presentation addressing vision and school performance at the Child Vision Research conference in Pisa in Italy on 15th June 2019.

12.12.5 Public dissemination

- An opinion piece was published in the Irish Times newspaper on 13th October 2016 to primarily create public awareness around the importance of checking children's vision, and also to promote the current study, emphasising the importance of randomly selected schools to participate in the study.

- An opinion piece was published in the Irish Times on 25th February 2019 reporting on risk factors associated with myopia in schoolchildren in Ireland

- An opinion piece was published in The Sunday Times new section on June 16th 2019 reporting the association between time spent outdoors and refraction in schoolchildren in Ireland.

- An opinion piece was published in the Irish Times on 12th August 2019 reporting amblyopia prevalence in schoolchildren in Ireland and Northern Ireland.

- Radio interview on RTE news at one on 25th February 2019 outlining IES study findings regarding risk factors for myopia in schoolchildren in Ireland.

- Radio interview on RTE news at one on 12th August 2019 outlining the comparison of amblyopia prevalence in Ireland and Northern Ireland.

- Radio interview on Kildare FM on 13th August 2019 outlining amblyopia prevalence in Ireland and Northern Ireland.

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APPENDIX 1: PARENTAL INFORMATION

Ireland Eye Health Study 2015-2018

Dear Parent,

We want to invite your child's class, to take part in an important study examining the health of children's eyes. Seeing well in childhood affects the ability to learn, contribute in class and success in later life. The World Health Organisation identified untreated eye/vision conditions (short sightedness, long sightedness, astigmatism and lazy eye) as one of the leading causes of blindness and visual impairment. Research carried out in China has found that the incidence of short-sightedness in teenagers has increased from 26% in the 1980s to 80% in 2010. Factors associated with this rapid increase in short-sightedness include reduced time spent outdoors; more people living in large towns/cities; time spent at a very young age on phones/computers; diet etc.

Your child's school is one of 75 schools randomly selected as part of this study.

For a successful study, it is very important that students, who have been selected, participate fully to ensure that this study provides an accurate picture of eye health in today's children - and your co-operation is very important and much appreciated in this respect.

What would taking part in the study involve?

For your child: Your child will have their eyes examined at school, this will include checking distance vision, near vision, 3D vision and colour-vision. We will measure the shape and length of your child's eyes very accurately; these tests are very quick and painless and do not touch the eye. To measure the eyes accurately, best practice requires we put some drops into each eye, which will make the pupils larger (the black part in the middle of the eye). The drops can irritate a little for a few seconds when they are first put into the eyes. Your child may find lights brighter than usual during this time. Vision may be slightly

blurred for up to 12 hours after we put the drops in, hence your child may find school work a little blurred, and we advise that your child does not take part in physical activities or sports during this time. The drops can cause a reaction, but this is very rare (less than 1 in 10,000 people). When it occurs, a rash may appear on the face, and the child may feel a little hot and light-headed. These reactions go away naturally on the same day without treatment. We will also measure your child's height and weight. The detailed eye examination will take half an hour or so.

For you: We need your help with some answers to questions about your child. Your responses will help us understand your child's test results. All questions are relevant to general health and the health of your child's eyes.

To answer the questions, please tick the appropriate box ☑ or write in the space provided. All your answers will be treated in the **strictest confidence.** If you are uncomfortable with any question, please leave it blank. The answers will **only** be seen by the Research Team. If you have any difficulties in completing this questionnaire, please phone or text us on 086-3827440. You can leave your telephone number, and we will call you back to answer your queries. Return the consent form and completed questionnaire to the school with your child.

What will happen after the study?

We will look at the results carefully. We will send you a report on your child's eyes. Where we identify any eye health concerns, we will contact you directly and your child can then either attend the National Optometry Centre (NOC) for a full eye examination or attend an optometrist of your choice.

We hope very much that your child will be able to take part in the survey – many other children have now taken part and have found it both enjoyable and interesting. All information from the study will be treated in complete confidence. Please discuss the study with your child (details of the measurements are shown on the information sheet for children that accompanies this letter).

Thank you very much for your help.

Yours faithfully,

Síofra Harrington (FAOI)

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APPENDIX 2: CHILD INFORMATION SHEET

We want to ask you and other children in your school to help us with an important study, looking at the health of children's eyes. The study will help us to find out more about children's eyes and to understand why some children do not see clearly.

What will the study involve?

On the day of the study, we will ask you to come and have your eyes examined by an optometrist. He or she will measure:-

- **How well you can see-** by reading some letters on a chart (or by recognising some shapes), and whether you might need glasses to help you see well.
- **Your height and weight-** using scales and tape measures.
- **3D and colour vision**
- **The shape and length of your eye** - to do this we will need to use an eye measuring computer, and we will need to put drops in your eyes. The drops can irritate when they are first put into your eyes, but this only lasts for a few seconds. The drops will make your vision blurry, and your pupils (the black part in the middle of the eye) larger for a few hours. You may have difficulty reading, and you will not be able to play sports on the day that we test your eyes. You may also find lights are brighter than usual. These effects do not last long, and your eyes will soon be back to normal.
- We will also look at your eyes with a special torch to make sure they are healthy

What happens when I have finished the tests?

- **Certificate –** To show that you have played an essential part in this research, we will give you a special certificate to say `thank you'.

Thank you for reading this letter. We hope you will be able to take part in this study. If you have any questions, you can contact us by telephone, email or by writing to us at Ireland Eye Health Study, Dublin Institute of Technology, Kevin Street, Dublin 8. Email: siofra.harrington@dit.ie

STORYBOARD: THE EYE TEST

Created with Storyboard That for Siofra Harrington

APPENDIX 3: PARENT/GUARDIAN CONSENT

FORM

TAKING PART IN THE Ireland Eye Health Study

Please discuss the study with your child, TICK ONE BOX AND SIGN BELOW.

☐ *Yes, I give permission for my son/daughter to take part in the Ireland Eye Health Study.*

☐ *No, I do not wish my son/daughter to take part in the Ireland Eye Health Study*

Name of Child: *Child's Class:*

Child's Date of Birth:

Signature of Parent or Legal Guardian _____   *Date* _____

Name of Parent or Legal Guardian (please print) _____

YOUR CHILD'S HEALTH: If your child has any specific health problem which you think might be important, please give details here. If your child suffers from an allergy to eye drops, they should not take part in the study. If you have any doubts or queries, we will be happy to talk these over with you.

ADDRESS Please write your address here, so that we can keep in touch with you about the results of the study.

If you are not sure about any part of this consent form or wish to discuss it with us, please telephone 01 4024697or email us at Siofra.harrington@dit.ie Please put 'Eye Study' in the subject heading of the e-mail.

Please return this form to school in the envelope provided as soon as possible. Thank you for your help

Parental Questionnaire

Ireland Eye Health Study

Child's full name:

QUESTIONS 1 TO 3 Child's Details

1.1   Date of birth?   --/--/---- (dd/mm/yyyy)

1.2   Male ☐   Female ☐

1.3   Birth weight? (If you don't know, please do not guess, but tick 'Not known')

          ☐☐ lb ☐☐ oz **OR**   ☐☐ kg **OR** Not known ☐

1.4   Was this child born:

On time, (i.e. within three weeks of the due date)   ☐

Early by more than three weeks   ☐

Not known   ☐

1.5   Was this a multiple birth? (i.e. a twin, triplet, etc.)   Yes ☐   No ☐

1.6   Did the child sleep at night with a bedroom light or night light on in early life (under the age of 2 years)?

                             Yes ☐   No ☐

If YES, was the light a   Bedroom Light?   ☐

                         Night light (or low illumination light)   ☐

MEDICAL HISTORY AND EYE HEALTH

2.1   How often has this child **visited their local General Practitioner** in the **last 12 months?**

More than four times   ☐

Two to four times   ☐

Once   ☐

Not at all   ☐

2.2   Has this child been **admitted to hospital or eye hospital** for any reason in the **last four years**?

           Yes ☐   No ☐

If YES, please give details:_____

2.3(a)   Has this child **ever** had **eye surgery**?   Yes ☐   No ☐
If YES, please give details (including which eye): _____

2.3(b)   Has this child **ever** been told to wear an **eye patch**? Yes ☐   No ☐
If YES, please give details (including which eye): _____

2.4   Has this child ever worn spectacles?   Yes ☐   No ☐ (If No, go to 2.5)

If YES, are they   Tick one box only

           Worn all / most of the time?   ☐

           Worn for certain activities but not full time?   ☐

           Advised to wear them but does not   ☐

           Stopped wearing them because no longer needed   ☐

_____

2.5   Has this child's eyes been examined (by an optician or ophthalmologist) during the **last 12 months**?

           Yes   ☐

           No   ☐

           Not Known   ☐

EXERCISE, OTHER ACTIVITIES AND DIET

3.1   Which of the following best describes your child's **level of physical activity** outside school?

                                     Tick one box only

Spends all or most leisure time on phone/computer/TV,   ☐

Spends time occasionally in light physical activities (e.g. cycling, walking)   ☐

Participates in regular sporting activities for up to 3 hours a week   ☐

(e.g. football, swimming, gymnastics, basketball, etc.)
Participates in regular sporting activities for more than 3 hours a week   ☐

(e.g. football, swimming, gymnastics, basketball, etc.)

3.2   How many **hours each day** does this child spend **doing school homework**?

None   ☐

An hour or less   ☐

1-2 hours   ☐

More than 2 hours   ☐

3.3   Compared to other children of the same age, how well (in your opinion) is this child doing at school?

Much better than others   ☐

About the same as others ☐

Not as well as others   ☐

3.4   Please tick one box below (**child's leisure time spent reading/writing**)

Child spends **all** or most of leisure time reading books, writing   ☐

Child spends leisure time **frequently** reading books, writing   ☐

Child spends leisure time **occasionally** reading books, writing   ☐

Child **seldom/never** spends leisure time reading books, writing   ☐

3.5 How many hours per day does this child spend **using a screen** (this includes: computer screens, Nintendo screens, iPad, smartphones, Television,)

Tick one box only

Less than one hour per day ☐

Between one and two hours per day ☐

Between two and four hours per day ☐

Over four hours per day ☐

3.6 How many hours does this child spend **outdoors** on average during **daylight hours**?

In winter:

Tick one box only

Less than one hour per day ☐

Between one and two hours per day ☐

Between two and four hours per day ☐

More than four hours   per day ☐

In summer:

Tick one box only

Less than one hour per day ☐

Between one and two hours per day ☐

Between two and four hours per day ☐

Over four hours per day ☐

3.7   Does the child usually sleep with a bedroom light or night light on?

Yes ☐   No ☐

If YES, is the light a   Bedroom Light?   ☐

Night light (or low illumination light)   ☐

3.8   How was this child fed in the first 3 months of life?

Tick one box only

Breast fed   ☐

Fed on formula milk   only   ☐ Go to 3.10

Fed on **both** breast and formula milk   ☐

3.9   If the child was breastfed for how long was this continued from birth?   Enter the number of months in the box

3.10   How often does this child eat the following foods?   (Please tick the appropriate box for each food item)

	More than once a day	Once a day	Most days	One or two days a week	Less than once a week	Never
Fresh fruit	☐	☐	☐	☐	☐	☐
Green vegetables	☐	☐	☐	☐	☐	☐
Fish (all kinds)	☐	☐	☐	☐	☐	☐

THE FOLLOWING QUESTIONS ARE ABOUT THE CHILD'S BIOLOGICAL PARENTS.

PLEASE ANSWER THESE QUESTIONS FOR BOTH MOTHER AND FATHER

		Mother	**Father**
5.1	Do the parents live with the child?	Yes ☐ No ☐	Yes ☐ No ☐
5.2	What is the ethnic group of each parent? (tick all that apply)		
	White / Caucasian	☐	☐
	Chinese/ Filipino/ Malay/Japanese	☐	☐
	Pakistani/ Bangladeshi/ Indian	☐	☐
	Black – African/ Caribbean	☐	☐
	Arab	☐	☐
	Irish / UK Traveller	☐	☐
	Other – please give details	_____	_____
5.3	How tall is each parent?		
	Metres and centimetres	____ metres____ cms	____ metres____ cms
5.4	How much does each parent weigh?		
	Stones and pounds **OR**	____ st ____ lbs	____ st ____ lbs
5.5	Do the parents wear spectacles?	Yes ☐ No ☐	Yes ☐ No ☐

	Mother / Female Guardian	Father / Male Guardian
If YES, are they… (tick all boxes that apply)		
Short-sighted (needs spectacles to see far away)	☐	☐
Longsighted (needs spectacles more for close up work)	☐	☐
Astigmatic (i.e. has astigmatism)	☐	☐
Not known	☐	☐

THE NEXT QUESTIONS ARE ABOUT THE PARENTS / GUARDIANS WHO LIVE WITH THE CHILD NOW – WHETHER OR NOT THEY ARE THE BIOLOGICAL PARENTS

If there is only one parent or guardian living with the child, question for the other parent can be left blank

		Mother / Female Guardian	Father / Male Guardian
6.1	Which of these options best describes the **work situation** of each parent?		
	in full-time paid work	☐	☐
	in part-time paid work	☐	☐
	unemployed	☐	☐
	looks after family full-time	☐	☐
	in full-time education	☐	☐
	other (please give details)	_____	_____
6.2	What was the highest level (First, Second or Third Level) the parent attained in full-time **education**?	_____	_____
6.3	Has the parent ever **smoked** cigarettes regularly?	Yes ☐ No ☐	Yes ☐ No ☐
6.4	How many cigarettes does the parent usually smoke each day at present?	_____	_____

THANK YOU VERY MUCH FOR YOUR HELP IN COMPLETING AND RETURNING THIS QUESTIONNAIRE.

This study will examine any possible link between short-sightedness, height, weight and ethnicity in Ireland. **All the information you have provided will be treated confidentially and will only be seen by our research team.** Please seal the questionnaire in the attached envelope provided and return to the school with your child.

For comments

Ireland Eye Health Study; Dublin Institute of Technology, Kevin Street, Dublin 8

APPENDIX 4: **Odds ratio of myopia, controlling for age group, for socio-demographic and lifestyle risk factors in the Ireland Eye Study**

Risk Factor (response rate %)	Myopic n/total N	(%)	Odds Ratio (95% CI)	*P* value
Demographics				
Age group (100%)				
6-7 years	27/728	(3.7)	Ref	
12-13 years	205/898	(22.8)	7.68 (5.07 – 11.63)	**<0.001**
Gender (100%)				
Male (881)	124/881	(14.1)	Ref	0.83
Female (745)	108/745	(14.5)	1.035 (0.78 -1.37)	
Ethnicity (100%)				
White	155/1290	(12.0)	0.27 (0.19 - 0.40)	**<0.001**
Traveller	20/151	(13.2)	0.30 (0.16, 0.54)	**<0.001**
Non-White	57/185	(30.8)	Ref	
Socioeconomic status (100%)				
Disadvantaged	37/353	(10.5)	1.15 (0.77 – 1.72)	0.49
Advantaged	195/1273	(15.3)	Ref	
Living environment (100%)				
Urban	182/1119	(16.3)	0.90 (0.62 – 1.29)	0.56

Rural	50/507	(9.9)	Ref	
Afterschool activities (98.3%)				
Mainly on phone/screens (sedentary)	50/194	(25.8)	2.90 (1.90 – 4.44)	**<0.001**
Infrequent activity	41/345	(11.9)	1.67 (1.08 – 2.57)	**0.02**
Sporting activities up to 3 hours/per week	60/463	(13.0)	1.43 (0.98 – 2.09)	0.06
Sporting activities >3 hours per week	74/596	(12.4)	Ref	
Near work time close work (98.2%)				
Most time close work	7/36	(19.4)	3.00 (1.13 – 8.00)	**0.02**
Frequent close work	87/551	(15.8)	2.20 (1.37 – 3.50)	**0.001**
Occasional close work	102/766	(13.3)	1.60 (0.98 – 2.50)	0.06
Little close work	28/243	(11.5)	Ref	
Homework time (per day) (98.1%)				
None	3/19	(15.8)	0.80 (0.21 – 3.07)	0.74
An hour or less	76/894	(8.5)	0.72 (0.43 – 1.23)	0.23
1-2 hours	114/575	(19.8)	0.76 (0.47 – 1.23)	0.27
>2 hours	28/104	(26.9)	Ref	
Screen-time (hours per day) (98.5%)				
Less than 1 hour	26/313	(8.3)	0.27 (0.16 - 0.47)	**<0.001**
1-3 hours	83/707	(11.7)	0.51 (0.34 – 0.77)	**0.001**

More than 3 hours	118/582	(20.3)	Ref	
Daylight exposure winter (hours per day) (98.0%)				
Less than 1 hour	62/376	(16.5)	1.48 (0.55 – 4.01)	0.44
1-2 hours	119/873	(13.6)	1.30 (0.49 – 3.45)	0.60
2-4 hours	34/295	(11.5)	1.12 (0.40 – 3.12)	0.83
More than 4 hours	5/49	(10.2)	Ref	
Daylight exposure summer (hours per day) (98.1%)				
Less than 1 hour	17/43	(39.5)	5.00 (2.42 – 10.32)	**<0.001**
1-2 hours	47/185	(25.4)	2.70 (1.78 – 4.10)	**<0.001**
2-4 hours	97/640	(15.2)	1.56 (1.12 – 2.25)	**0.01**
More than 4 hours	65/735	(10)	Ref	
Birth season (100%)				
Spring	62/400	(15.5)	1.92 (1.14 – 3.23)	**0.015**
Summer	64/434	(14.7)	1.52 (0.90 – 2.58)	0.12
Autumn	67/442	(15.2)	1.63 (0.97 – 2.76)	0.07
Winter	39/350	(11.1)	Ref	
Use of nightlight (under the age of 2 years) (97.0%)				
Sleep with night light	42/356	(11.8)	1.42 (0.96 – 2.10)	0.08
Sleep without a night light	177/1237	(14.3)	Ref	

Child factors

When born (97.0%)

On time	190/1428	(13.3)	0.83 (0.48 – 1.44)	0.52
Early by more than three weeks	18/121	(13.3)	Ref	
Birthweight myopic (mean±SD) = 3.45±0.66Kg (84%)	165/1364	(12.4)	0.95 (0.74 – 1.24)	0.72
Breast fed only for first 3 months (98.0%)	98/620	(15.8)	0.90 (0.63 – 1.30)	0.59
Bottle fed only for first 3 months	66/651	(10.1)	0.54 (0.37 – 0.80)	**0.002**
Combined breast and bottle fed for the first three months	54/314	(17.2)	Ref	
BMI (mean±SD) = 20.60±4.17Kg/m² **(99.9%)**			1.14 (1.10 – 1.18)	**<0.001**

BMI group (99.9%)

Healthy weight	139/1193	(11.6)	0.37 (0.26 – 0.54)	**<0.001**
Overweight	45/249	(18.1)	0.63 (0.39 – 0.99)	**0.04**
Obese	48/136	(35.3)	Ref	

Height (99.9%)

6-7 years height (mean±SD) =126.06±6.86mm	27/728	(3.7)	1.02 (1.01 – 1.04)	**0.01**
12-13 years height (mean±SD) =159.84±9.21mm	204/897	(22.7)	1.02 (1.01 – 1.03)	**0.004**

Diet (98%)

Fresh fruit

>1/day	101/722	(14.0)	0.93 (0.46 – 1.90)	0.84

1/day	54/426	(12.7%)	0.77 (0.37 – 1.62)	0.48
Most days	25/209	(12.0)	0.60 (0.27 – 1.35)	0.22
1/week	18/113	(15.9)	0.75 (0.32 – 1.77)	0.51
Never	18/106	(16.9)	Ref	
Green vegetables				
>1/day	36/206	(17.5)	1.62 (0.83 – 3.16)	0.16
1/day	62/452	(13.7)	1.27 (0.68 – 2.36)	0.45
Most days	61/412	(14.8)	1.39 (0.75 – 2.59)	0.30
1/week	30/261	(11.5)	0.90 (0.39 – 2.06)	0.80
Never	27/255	(10.6)	Ref	
Fish				
>1/day	3/19	(15.8)	1.71 (0.43 – 6.68)	0.44
1/day	2/18	(11.1)	1.16 (0.24 – 5.68)	0.24
Most days	17/82	(20.7)	2.06 (1.05 – 4.03)	**0.04**
1/week	102/737	(13.8)	1.25 (0.83 – 1.89)	0.29
Never	92/730	(12.6)	Ref	
Parental factors				
Parental myopia				
Father myopic (93%)	84/382	(22.0)	2.4 (1.80 – 3.30)	**<0.001**

Father not myopic	117/1130	(10.4)	Ref	
Mother myopic (95.3%)	76/493	(15.4)	1.23 (0.91 – 1.62)	0.22
Mother not myopic	136/1056	(12.9)	Ref	
Parental education				
Mothers educational level (91%)				
Primary	4/42	(9.5)	0.81 (0.27 – 2.420	0.71
Secondary	51/442	(11.5)	0.82 (0.58 – 1.17)	0.28
Third level	143/987	(14.5)	Ref	
Fathers educational level (88.5%)				
Primary	3/44	(6.8)	0.61 (0.18 – 2.09)	0.43
Secondary	56/466	(12.0)	0.97 (0.68 – 1.38)	0.87
Third-level	121/839	(14.4)	Ref	

N: number of participants; n: frequency, CI: confidence intervals, SD: standard deviation, BMI: body mass index, Ref: reference category, Significant P values highlighted in bold.
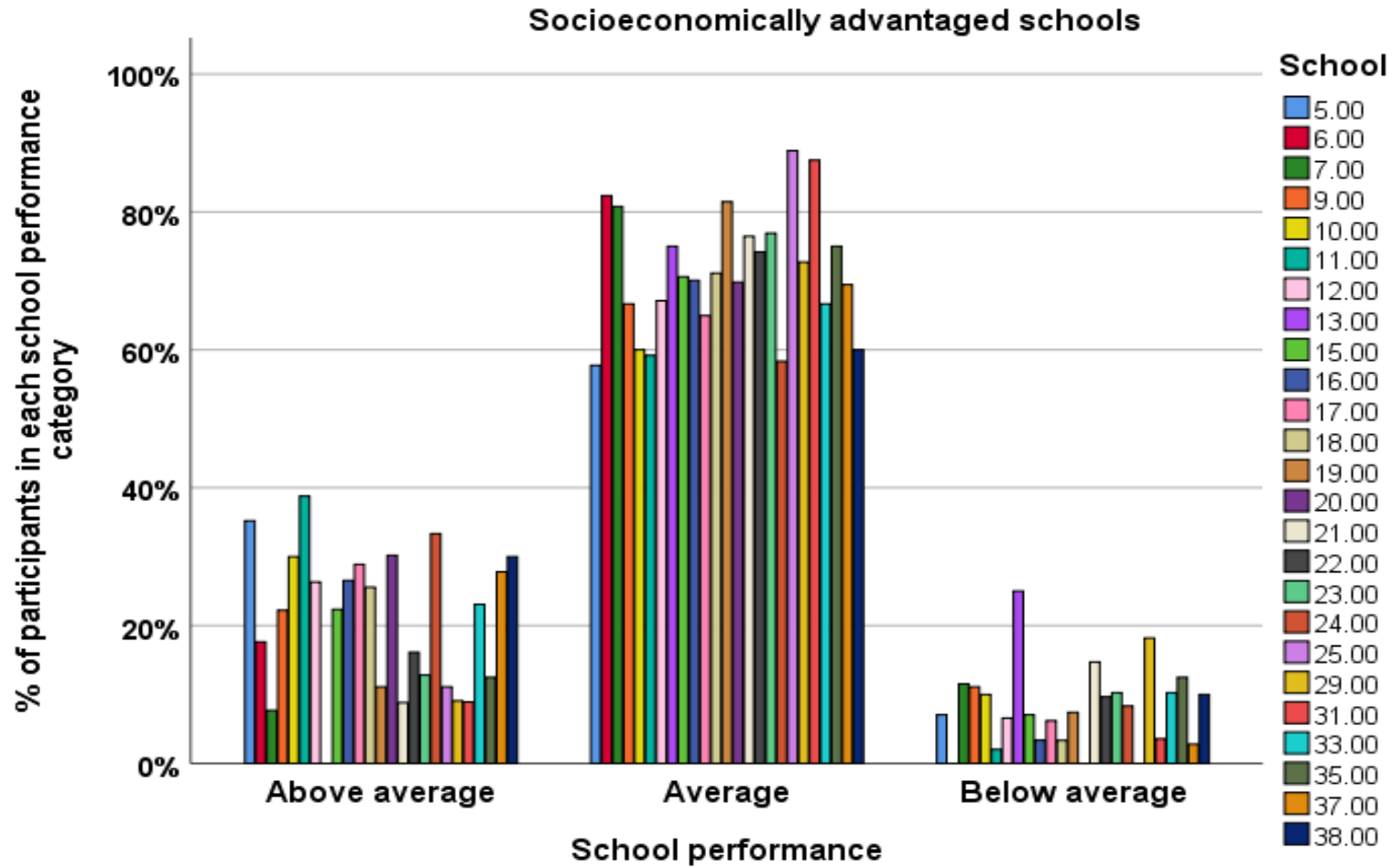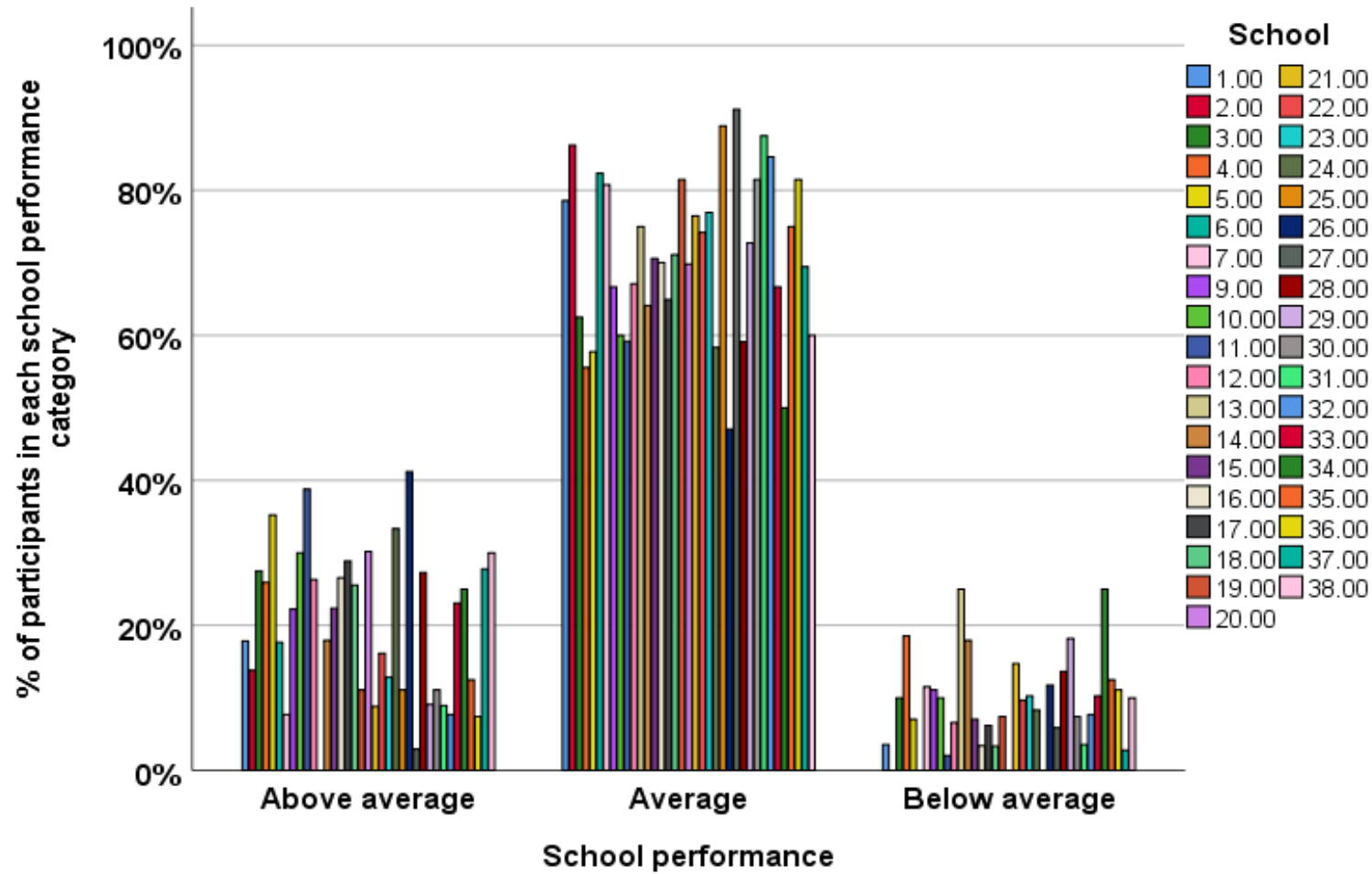
APPENDIX 5: PARTICIPANT FEEDBACK
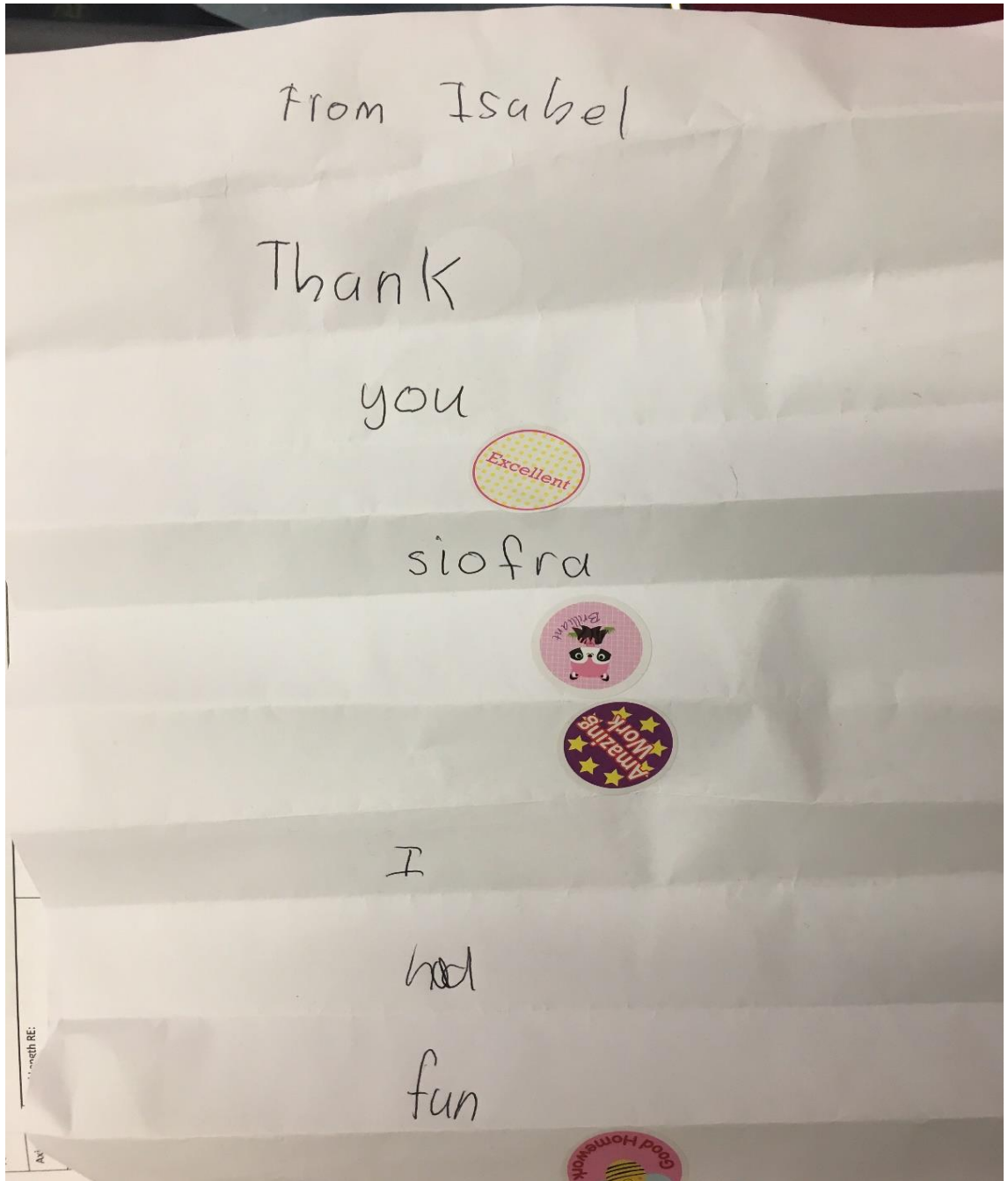
APPENDIX 6: SCHOOL PERFORMANCE IN DISADVANTAGED SCHOOLS
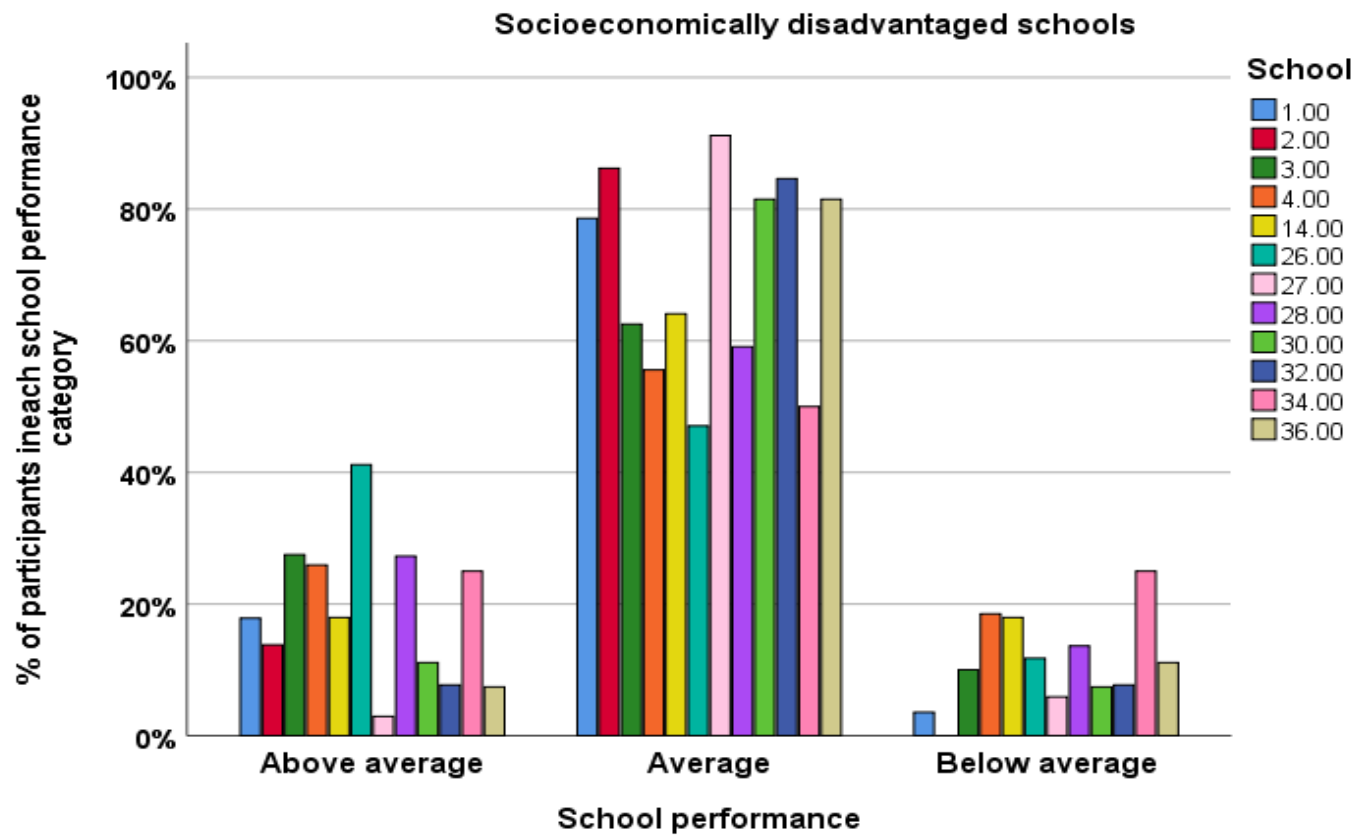
APPENDIX SEVEN: SCHOOL PERFORMANCE IN ADVANTAGED SCHOOLS

Socioeconomically advantaged schools

APPENDIX 8: SCHOOL PERFORMANCE IN ALL PARTICIPATING SCHOOLS

LIST OF PUBLICATIONS

1. Harrington, S., Stack, J., Saunders, K. & O'Dwyer, V. (2018) 'Refractive error and visual impairment in Ireland schoolchildren.', *British Journal of Ophthalmology*, Published Online First: 12 October 2018. doi: 10.1136/bjophthalmol-2018-312573.

2. Harrington, S., Stack, J. & O'Dwyer, V. (2019) 'Risk factors associated with myopia in schoolchildren in Ireland.', *British Journal of Ophthalmology*, Published Online First: 11 February 2019. doi: 10.1136/bjophthalmol-2018-313325.

3. Harrington, S. & O'Dwyer, V. (2019)'Ocular biometry, refraction, and time spent outdoors during daylight in schoolchildren in Ireland', *Clinical and Experimental Optometry*. doi: 10.1111/cxo.12929. Published online first 1st of June 2019.

4. Harrington, S., O'Dwyer, V., Breslin, K. & Saunders, K. (2019) 'A comparison of amblyopia in schoolchildren in Ireland and Northern Ireland: a population-based observational cross-sectional analysis of a treatable childhood visual deficit' *BMJ open,* doi: 10.1136/bmjopen-2019-031066.

LIST OF EMPLOYABILITY SKILLS AND

DISCIPLINE SPECIFIC SKILLS TRAINING

Structured PhD programme modules completed

It is a requirement by TU Dublin to undertake a number of post-graduate modules (employability skills 20 ECTS, and discipline-specific skills 20 ECTS).

Modules completed as part of the Structured PhD programme:

- **Discipline-specific postgraduate modules**

  ➢ Paediatric Optometry – Cardiff University, Wales (10 ECTS).

  ➢ Improving Healthcare through Clinical Research – University of Leeds, England (3 ECTS).

  ➢ EHealth – the University of Twente, Netherlands (4 ECTS).

  ➢ Geo-health – the University of Twente, Netherlands (3 ECTS).

  ➢ Global Blindness – London School of Hygiene and Tropical Medicine, England (2 ECTS).

  ➢ Medical Imaging – TU Dublin (5 ECTS)

  Total discipline-specific skills: 27 ECTS

- **Employability specific postgraduate modules**

  ➢ Logical and Critical Thinking – The University of Auckland, New Zealand (5ECTS).

  ➢ Pedagogy – TU Dublin (5ECTS).

  ➢ Man and Machine – TU Dublin (5ECTS)

- Blended Learning Essentials and Blended Learning getting started – The University of Sheffield, England (5ECTS).

- Clinical Supervision with Confidence – The University of East Anglia, England (2.5ECTS).

- Academic integrity – The University of Auckland, New Zealand (2.5ECTS).

- Quality Improvement in Healthcare – The University of Bath, England (3ECTS).

- Social Determinants of Health – British Medical Journal, BMA House, Tavistock Square, London, UK (2ECTS).

- Man and Machine – TU Dublin (5ECTS).

- Statistical methods – TU Dublin (5ECTS).

  Total employability specific skills: 40 ECTS

- **Additional postgraduate modules completed**

  - Emergency and Urgent Care for Children – University of Birmingham.

  - "Data tells a story" - Loughborough University.

  - The Right to Education – University of Glasgow.

  - Measuring and Valuing Health – The University of Sheffield, England.