Healthy bodies, healthy eyes? Quantifying the impact of modern lifestyles on children's eye health

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I confirm that the word count of this thesis is less than 100,000 words

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Abstract

Background

Myopia prevalence is rising around the world at a rate that cannot be explained by genetics alone therefore, environmental risk factors must have an influence. Accurate measurements of refractive error and potential risk factors are required to better understand the relationship between environment and refractive development such that evidence-based advice can be provided to patients and parents by eye care professionals. This thesis was designed to investigate some potentially modifiable risk factors for myopia in young UK children.

Methods

One hundred children (aged 6-9) participated in cross-sectional evaluation of previously proposed environmental risk factors for myopia. Spherical equivalent refraction (SER) and axial length (AL) were determined by cycloplegic autorefraction and ocular biometry. Potential risk factors for myopia were measured using Actiwatch 2 and Clouclip devices. Screen time, sleep, physical activity, and parental myopia data were collected using questionnaires. 42 children were followed up 12-months after baseline and change in SER and AL measures examined. Correlations were explored between change in SER and AL and baseline environmental exposure profiles.

Results and Conclusions

The data demonstrated that:

- Compared with children classed as non-myopic (≥+0.75 D), pre-myopes/myopes (<+0.75) go to bed later and fall asleep faster (increasing their sleep efficiency), are exposed to higher illumination during sleep, and have poorer subjective sleep quality. Over 12-months, higher sleep efficiency and less wake after sleep onset were associated with faster axial elongation, whereas less time spent in mesopic light was associated with faster myopic progression.
- Compared with children classed as non-myopic, pre-myopes/myopes spent significantly more time undertaking moderate-vigorous physical activity later in the day, potentially disrupting circadian rhythms.
- More myopic SER's were significantly associated with increased time spent viewing at near on weekday mornings and increased time spent on intermediate viewing was significantly related to greater myopic shift over 12-months.

- Using a phone/tablet for 1-2 hours/day, watching TV/video games 1-3 hours/day and a higher duration of near work all increased the likelihood of children demonstrating accelerated eye growth over a 12-month period.
- Parents wishing to mitigate against myopia-promoting eye growth should encourage; less near work, less time on phones/tablets or watching TV/video games, less bright light and less physical activity in the evenings, earlier bedtimes and sleeping in darkness.

List of Abbreviations

7-MX	7-Methylxanthine
ACD	Anterior chamber depth
AL	Axial length
ALSPAC	Avon Longitudinal Study of Parents and Children
ANOVA	Analysis of Variance
ATOM	Atropine for the Treatment of Myopia
AW	Actiwatch
CC	Clouclip
CLEERE	Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error
cm	Centimetres
COMET	Correction of Myopia Evaluation Trial
cpm	Counts per minute
CREAM	Consortium for Refractive Error and Myopia
CSHQ	Children's Sleep Habits Questionnaire
D	Dioptres
DC	Dioptres Cylinder
DLMO	Dim light melatonin onset
DS	Dioptres Sphere
GEM	Genes in Myopia
GMT	Greenwich Mean Time
GPS	Global Positioning System
ICC	Intraclass correlation coefficients
IES	Ireland Eye Study
IMI	International Myopia Institute
KNHANE	Korea National Health and Nutrition Examination
LE	Left Eye
LED	Light-emitting diode
LOAs	Limits of Agreement
LT	Lens thickness
MF	Multifocal
mins	Minutes
mm	Millimetres
NHANES	National Health and Nutrition Examination Survey

NHS	National Health Service
NI	Northern Ireland
NICER	Northern Ireland Childhood Errors of Refraction
NREM	Non-rapid eye movement sleep
OECD	Organisation for Economic Co-operation and Development
Ofcom	Office of Communications
OK	Orthokeratology
PA	Physical Activity
PALs	Progressive Addition Spectacles
PAQ-C	Physical Activity Questionnaire for Children
PISA	Programme for International Student Assessment
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomised Control Trial
RE	Right Eye
REM	Rapid eye movement
ROAM	Role of Outdoor Activity in Myopia
ROC	Recess Outside the Classroom
s	Seconds
SCN	Suprachiasmatic nuclei
SD	Standard Deviation
SER	Spherical equivalent refraction
SMS	Sydney Myopia Study
SVLs	Single Vision Lenses
UK	United Kingdom
USA	United States of America
W/D	Weekdays
W/E	Weekends
WHO	World Health Organisation

Chapter 1:
Literature Review of Childhood Myopia and Risk Factors for Myopia

Chapter 1: Literature Review of Childhood Myopia and Risk Factors for Myopia

This chapter will highlight myopia prevalence and its increase worldwide and then go on to highlight some of the previously reported modifiable and non-modifiable risk factors for childhood myopia. This chapter will also emphasise gaps in the current field of research where further research is still required.

1.1. Background to Myopia

1.1.1. Childhood Myopia

Myopia, which also known as short-sightedness, is the most common refractive error of the eye and arises from a disparity between the axial length of the eye and the focal power of its refractive elements, the cornea and crystalline lens. This thesis concentrates on childhood onset myopia caused by excessive axial elongation. In myopic eyes the parallel light rays coming from an object in the distance are refracted in front of the retina creating a blur circle on the retina and hence a blurred distance image. However short-sighted people can normally see near objects such as a book or a computer screen with ease. This blurred distance image can be easily corrected with the use of concave (minus) lenses in the form of glasses and/or contact lenses. The concave lens refocuses the parallel light rays onto the retina. Myopia can however lead to irreversible vision loss due to an increased risk of sight threatening diseases such as glaucoma, cataract, maculopathy and rhegmatogenous retinal detachments. The risk of these conditions increase with higher levels of myopia, high myopia has been defined as spherical equivalent refractive error of ≥-6.00D in either eye (Flitcroft *et al.*, 2019). The earlier the onset of myopia in childhood the larger the eventual magnitude of this condition due to its progressive nature, and thus imposing a higher risk of these visual impairing conditions.

1.1.2. Emmetropization

Emmetropization is the natural process in which infants and young children's axial elongation resulted in normal eye growth to produce emmetropia (no refractive error). Any disruption to the normal visual feedback may result in continued axial growth beyond the point of emmetropia leading to myopia. Myopic development and progression are primarily due to increasing vitreous chamber depth as rates of progression of myopia

were not significantly correlated with the rates of change in corneal curvature, anterior chamber depth, or lens thickness (Saw *et al.*, 2005).

Many animal models have been used in the past to study emmetropization, the visual regulation of eye growth and myopia development including macaque and marmoset monkeys, tree shrews, guinea pigs, mice, and chickens. All of these animals have proven to develop myopia in response to visual form deprivation, compensate for optically imposed defocus (whether it be myopic or hyperopic) by regulating axial length, and recover from the induced refractive error when the form deprivation or optical defocus is removed (Schaeffel *et al.,* 1988; Troilo *et al.*, 2019).

Form deprivation myopia in animals is achieved either by suturing the eyelid shut or attaching a translucent diffuser over the treated eye, with both methods disrupting normal visual feedback causing the eye to elongate in an unregulated manner. When sutures or diffusers are removed the treated eye exhibits myopic defocus and therefore dramatically reduces the axial elongation rate in that eye, while the untreated eye continues growing at a normal rate. Once the vitreous chamber depth of the untreated eye catches up with that of the previously treated eye, the two eyes then grow at a similar rates (Schaeffel and Howland, 1991). Rearing of different animals in constant darkness also deprives the eye of form vision but the outcome is different depending on the animal. Chicks reared in constant darkness experience eye enlargement alongside significant corneal flattening leaving them more hyperopic than those not raised in darkness (+3.11 vs +0.65 D) (Yinon and Koslowe, 1986). Rhesus monkeys in constant darkness fail to emmetropize, leaving them more hyperopic than normal rhesus monkeys at the same age (+5.30 vs +2.80 D) (Guiton *et al.*, 1989). Tree shrews on the other hand, became significantly more myopic under constant dark conditions (Norton *et al.*, 2006). These findings, albeit differing, support the important of visual feedback for normal emmetropization (Troilo *et al.*, 2019).

Schaeffel *et al.* (1988) first demonstrated the ability of young chicks eye to compensate for the imposed defocus of a positive or negative spectacle lenses, essentially emmetropizing through the defocus imposed by the lens treatment. A negative lens in front of an emmetropic eye optically simulated hyperopia and to compensate for the lens the chick eye grew until it developed a degree of myopia equivalent to the power of the lens. A positive lens produced myopic defocus on the retina, which led to inhibition of eye growth, resulting in the eye becoming more hyperopic to re-establish an emmetropic

refractive state through the lens. These findings demonstrated that the eye could detect the sign of defocus and alter its growth in the appropriate direction to eliminate both myopic and hyperopic defocus. Many other animals tested have shown the same abilities but all have a different range of spectacle powers for complete compensation (Troilo *et al.*, 2019). Recent human studies have also documented small, short-term bidirectional changes in axial length and choroidal thickness in response to 1-2 hours of myopic and hyperopic defocus in young adult subjects (Read, Collins and Sander, 2010; Wang *et al.*, 2016), indicating that the human eye can also detect the sign of imposed optical defocus and compensate appropriately.

Mutti *et al.* (2005) examined cycloplegic refractive error and ocular biometry on babies aged 3 months and again at 9 months and found a statistically significant decrease in hyperopic refractive error in that time period. There were also decreases in lens and corneal power but, change in axial length was the only variable linked with decreasing hyperopic refractive error between the two age points. Mayer *et al.* (2001) also found a significant decline in hyperopic refractive error between one month to 48 months old. The authors also found that full emmetropia has yet to be reached by four years old but the rate of change of refractive error was most rapid in the first year of life.

Morgan *et al.* (2010) found that emmetropia (>−0.50 D but ≤+0.50 D) does not appear to be the endpoint for children's refractive development and by 15 years old, the populations were either predominantly mildly hyperopic or the population quite rapidly shifted to predominant myopia. Movement into the emmetropic category from the mildly hyperopic category with increasing age, appears to be counter-balanced by movement from the emmetropic category into the myopic category, therefore maintaining the low proportion of the population in the optically emmetropic range. Those mildly hyperopic children maintain good visual acuity (VA) due to their high accommodative abilities. The findings of this multi-site study reinforce that there is no indication of great precision in the endpoint of emmetropization providing good VA can be achieved with accommodative effort.

1.1.3. Pre-Myopia

The International Myopia Institutes white papers define pre-myopia as "a non-myopic refraction in which a combination of risk factors and the observed pattern of eye growth indicate a high risk of progression to myopia" with a refractive state of an eye of ≤+0.75

D and >-0.50 D (Flitcroft *et al.*, 2019). The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study identified cycloplegic spherical equivalent refractive error as the single best predictor of future myopia, defining cut off points for certain age groups for which eye care professionals should be considering providing advice regarding the onset of myopia. These cut offs are <+0.75 D for 6- year olds, ≤+0.50 D for 7- and 8- year olds, ≤+0.25 D for 9- and 10- year olds, and ≤0.00 D for 11-year olds (Zadnik *et al.*, 2015). The Northern Ireland Childhood Errors of Refraction (NICER) Study found that from their original 2006-2008 cohort of 6-7-year-old children, followed over a 9-year period, those with a SER <+0.75 is relatively sensitive (75.56%) and specific (82.96%) for predicting the development of future myopia in a Northern Irish population (McCullough *et al.*, 2020).

1.1.4. Increase in Childhood Myopia Worldwide

Previous research had determined that childhood refractive error was largely regulated by genetics; (Sorsby, Leary and Fraser, 1966) but due to extensive studies on animal models, it is widely accepted that both genetic and environmental factors are involved in refractive development (Troilo *et al.*, 2019). Recent meta-analysis from the Brien Holden Vision Institute identified that, based on current trends, by 2050 half the world's population will be myopic with as many as 10% of individuals being highly myopic (Holden *et al.*, 2016). In East Asia 80-90% of students finishing high school are myopic (Lin *et al.*, 2014). Ulster University's Northern Ireland Childhood Errors of Refraction (NICER) study has demonstrated that prevalence of myopia amongst white UK teenagers has more than doubled in the last 50 years and is becoming more prevalent in younger children than in previous decades (McCullough, O'Donoghue and Saunders, 2016). Early onset of myopia results in an increased risk of progression to high myopia, inflating the risk of secondary sight threatening ocular pathologies (Flitcroft, 2012). Rising levels of myopia will impose a significant burden on both the individuals and the already strained NHS in the UK. Up to date information on prevalence and age of onset of myopia is required as these metrics will have bearing on the scale, scope and targeting of future optometric services.

The worldwide rise in myopia prevalence has occurred at a rate that cannot be explained solely by genetic factors (Wu *et al.*, 2016) and the influence of environment and lifestyle must be acknowledged (Morgan *et al.*, 2018). The non-modifiable risk factors for childhood myopia include parental myopia and ethnicity. The potentially modifiable risk factors for childhood myopia include less time spent outdoors, being under more

educational pressure, spending more time on near activities, leading less active lifestyles, having poor sleep quality and increased screen time (Saw, Chua, *et al.*, 2002; O'Donoghue *et al.*, 2015; Zhou *et al.*, 2015; Ayaki *et al.*, 2016; Jee, Morgan and Kim, 2016).

To date, key environmental risk factors such as such as time spent outdoors, time spent on near vision activities, and physical activity have been primarily assessed using a self-report rather than objective measurements. There is currently minimal robust quantitative data including cycloplegic measures of refraction in the UK or Ireland which describe the relationship between myopia and time spent outdoors, physical activity, reading and other near vision tasks including smartphone/tablet use.

1.2. Myopia Prevalence

A recent literature review details how those studies assessing myopia prevalence with non-cycloplegic measurements report much higher prevalence rates than those with the use of cycloplegia, hence reinforcing the need for a standardised protocol for an epidemiological study of myopia (Grzybowski *et al.*, 2020). The review also notes another critical parameter is age, as prevalence rates of myopia are known to increase significantly with age. The recently published International Myopia Institute report classified myopia as spherical equivalent refractive error (SER) ≤ -0.50 dioptres (D) and high myopia as SER ≤ -6.00 D (Flitcroft *et al.*, 2019).

1.2.1. Asia

A systematic review and meta-analysis of global myopia prevalence over time reports a non-linear increase in myopia prevalence with age with the highest prevalence of myopia stemming from East Asia where about 80% of children are myopic before 18 years of age with over 90% of East Asians living in Singapore being myopic and 72% of East Asians living in China. The report states a 2.6 times increased risk of myopia in children living in urban vs. rural environments. The systematic review and meta-analysis concluded that there is the possibility that the younger the child is exposed to formal education, the higher the risk of childhood myopia (Rudnicka *et al.*, 2016). There is an increasing prevalence of myopia worldwide but myopia is an epidemic in a lot of Asian and East Asian countries (Pan, Ramamurthy and Saw, 2012). In Japan, 65.6% of 17-year olds have myopia (Matsumura and Hirai, 1999), whilst in Beijing, China there is a prevalence of 80.7%

myopia between 16-18-year olds. (Wu *et al.*, 2015). South Korean male conscripts had a prevalence of 96.54% myopia at 19-years old (Jung *et al.*, 2012). Taiwan reported significant rises in the rate of myopia in different age groups from 64.2% in 1983 to 81% in 2000 (in 15-year-olds) and from 74% in 1983 to 84% in 2000 (in 18-year-olds) as well a drop in the average age of onset of myopia from 11 years old to 8 years old (Lin *et al.*, 2004). However, in rural Taiwan on Chimei Island there was a much lower myopia prevalence of 31% and the authors reported that the increased outdoor activity was associated with a decreased risk of myopia (Wu *et al.*, 2010).

Lesser developed Asian countries still demonstrate very low levels of myopia, for example Mongolia reports a total prevalence of myopia of 5.8% between the ages of 7-17 (Morgan *et al.*, 2006). In rural Mongolia children go to school for half a day (3 hours) and only start formal schooling at 7-years old. These figures support the theory that the rise in myopia worldwide is due to environmental risk factors.

1.2.2. USA and Canada

In the USA National Health and Nutrition Examination Survey (NHANES) of 12-54-year-olds, the myopia prevalence increased from 25% in 1971-72 to 41.6% in 1999-04. The largest increase in myopia over the 28-year period was amongst those of African American ethnicity and this was proposed to be due to increased access to education for this cohort (Vitale, Sperduto and Ferris, 2009). However, the NHANES study was limited by non-cycloplegic autorefraction, and could have therefore overestimated the levels of myopia due to insufficient control of the participants' accommodation. Chiang *et al.* (2019) examined the changing prevalence of myopia based on ethnicity in the USA between 1999-2007. The authors found that the prevalence of myopia among the white population was stable at around 30%, whereas there was an increase in prevalence in the Mexican American, Black, and Hispanic populations. In Canada a cross-sectional myopia prevalence study was carried out, reporting myopia prevalence's of 6% in 6-8-year olds and 28.9% in 11-13-year olds (Yang *et al.*, 2018).

1.2.3. Europe

Although there is an epidemic among Asian populations there is also an increasing prevalence among white populations, however this varies with the severity depending on geographic location. Particular lifestyle habits in different populations may provide some explanation for the variance in myopia prevalence across geographic locations and also

recommendations to implement preventative strategies such as outdoors programs and changes to near activities in pre-school aged children (Grzybowski *et al.*, 2020). Given that such recommendations are fairly recent, this would not explain the more modest increases in prevalence in Europe compared to Asia but may be effective at stemming future increases. In Europe there has been an increase in myopia prevalence in recent years, yet not to the same extent as Asian populations. Williams *et al.* (2015) found an overall prevalence of myopia of 24.3% across all age groups but highest at 47.2% in 25-29-year olds. The prevalence of myopia was higher with more recent birth decade and increasing education levels (Williams *et al.*, 2015).

In Sweden there was a myopia prevalence of 49.7% in 12-13-year olds (Villarreal *et al.*, 2000). Vannas *et al.* (2003) reported an overall prevalence of 22.2% among Finnish army conscripts via questionnaire-reported glasses wear for short-sightedness. This could be unrepresentative of the true prevalence, particularly for low levels of myopia which may not corrected. In Poland 13.3% of students in the age group from 6-18-years old were reported to be myopic (Czepita, Zejmo and Mojsa, 2007) and in Denmark the prevalence of myopia among Danish conscripts in 2004 was 12.8% (Jacobsen, Jensen and Goldschmidt, 2007), both of which are lower than the European average. However, in Denmark a study of medical students in Copenhagen found that 50% had myopia-again indicating a link between education and myopia and this figure remained stable over time (Fledelius, 2000). In Norway the prevalence of myopia appears stable with 13.4% of young adults with myopia in 2018 being nearly identical to a prevalence of 13.7% which was measured in 1971 (Hagen *et al.*, 2018).

A non-population-based study in France found myopia prevalence values of 19.1% and 42.7% in the 0-9 and 10-19 age groups, respectively (Matamoros *et al.*, 2015) and a cross sectional study in Spain used non-cycloplegic retinoscopy to find 19.1% prevalence of myopia among 5-7-year olds in 2017, which was increased from 16.8% in 2016 (Alvarez-Peregrina *et al.*, 2019).

The Northern Ireland Childhood Errors of Refractions (NICER) study found that between 2006-2008 there was a myopic prevalence of 2.8% in 6-7-year olds and 17.7% in 12-13-years olds (L. O'Donoghue *et al.*, 2010). The Ireland Eye Study used an identical sampling framework to that utilised by the NICER study and reported a myopic prevalence of 3.3% in 6-7-year olds and 19.9% in 12-13-year olds between 2016-2018

(Harrington, Stack and O'Dwyer, 2019). These results are very comparable between the ethnically and culturally identical Northern Irish and Irish cohorts. The Northern Ireland Childhood Errors of Refraction (NICER) Study also demonstrated that the prevalence of myopia among UK teenagers has more than doubled over the last 50 years and is appearing in children at a younger age than in previous decades (McCullough, O'Donoghue and Saunders, 2016).

1.2.4. Australia

The Sydney Myopia Study (SMS) found a myopia prevalence of 0.7% in white 6-7-year olds and 5.1% in white 12-13-year olds (Rose *et al.*, 2008). There are higher levels of myopia in Northern Irish school children in comparison to ethnically similar (European Caucasian) school children in Australia (French *et al.*, 2012). In the six-year follow up of the SMS the prevalence of myopia in the older cohort (17-18-year-olds) increased to 17.7% and 8.6% in the 12-13-year-olds. This older cohort is more comparable to the ethnically similar Northern Irish children in the six-year follow up with 18.6% prevalence in 18-19-year olds (McCullough, O'Donoghue and Saunders, 2016), but there still remains a significant difference in myopia prevalence in the younger group (12-13-year-olds) with 8.6% in Australia compared to 14.6% in NI (French *et al.*, 2013).

1.2.5. Africa

A systematic review and meta-analysis of global myopia prevalence reports that in Africa the black adolescent population have the lowest worldwide myopia prevalence with only 5.5% of 15-year olds being myopic (Rudnicka *et al.*, 2016).

1.3. The Non-Modifiable Risk Factors for Myopia

1.3.1. Parental Myopia

The NICER study found that children with one or both myopic parents were 2.91 and 7.79 times more likely to have myopia, respectively (O'Donoghue *et al.*, 2015). The Ireland Eye Study found that those participants with myopic fathers were twice as likely to be myopic (22.0% vs 10.4%), however, the relationship between maternal myopia and myopia in the child was not statistically significant (Harrington, Stack and O'Dwyer, 2019). Mutti *et al.* (2002) in Orinda, California found that hereditary factors were significantly associated with childhood myopia. They found a 32.9% incidence of myopia in children with two myopic parents, compared with 18.2% of the children with only one

myopic parent and 6.3% of the children with no myopic parents. In Spain among children aged 5-7 years the prevalence of myopia in those with no myopic parents is 9.7%, increasing to 28.3% if both are myopic (Alvarez-Peregrina *et al.*, 2019).

Lim *et al.* (2014) found that in China the prevalence rate of myopia increased with the number of myopia parents, and that those children with two myopic parents were also at higher risk of developing a higher level of myopia. In North India the odds ratios for myopia is 5.1 for two myopic parents compared to no myopic parents (Singh *et al.*, 2019). In Taiwan a study found that having one parent with myopia increased the odds by 2.1 times and having two myopic parents increased the odds to 2.4 times (Holton *et al.*, 2019). A study in Jordan found the prevalence of myopia was 8.7% for those who had no family history, of myopia, and was highest (43.2%) for those with 2 myopic parents and with at least 1 myopic sibling (Khader *et al.*, 2006). A study on high myopia in families found that those with highly myopic parents were more likely to be myopic and to have an earlier onset of myopia. The odds increased with more than one highly myopic parent/highly myopic sibling (Liang *et al.*, 2004).

A number of studies found a significant correlation between the refractive error and axial length of children and their parents (Guggenheim, Hill and Yam, 2003; Liang *et al.*, 2004; Kurtz *et al.*, 2007; Lee *et al.*, 2015; Terasaki *et al.*, 2017). Saw *et al.* (2003) also found a strong correlation between the amount of myopic progression in children and the number of myopic relatives with the progression increasing with the number of relatives.

Parental myopia provides evidence for not only an increased genetic risk of myopia, but also an increased environmental risk. It has been suggested that myopic parents not only pass on their myopia-risk genes, but also bring their children up in a myopiagenic environment (Morgan, French and Rose, 2020).

1.3.2. Genes Related to Myopia

Previous literature reviews have concluded that refractive error is a complex phenotype with influence from both environmental factors and genetic predisposition. Genetic association investigations have identified variants in at least 25 genes involved in refractive error. This implies that most genetic variants involved in human myopia and refractive control are yet to be discovered. It is also probable that variants in several genes interact with one another, as well as with environmental factors, to mediate ocular growth

and produce the distributions of refractive error. This highlights the need for environmental and genetic risk factors be accounted for in future genetic epidemiological studies (Wojciechowski, 2011; Tjoa and Putra, 2019).

The International Myopia Institute's report on myopia genetics by Tedja *et al.* (2019) reiterates that up to 50 loci and genes have been linked with myopia but accepts that as most of the phenotypic variance of refractive errors is still unexplained, larger sample sizes are required with deeper coverage of the genome. The report acknowledges that due to the recent global rise of myopia; prevalence is unlikely to be due to genetic factors alone, but the degree of myopia may still be under genetic control. There is evidence for gene- environment interaction also for example those at profound genetic risk with higher education appeared particularly susceptible to developing myopia and polygenic risk scores based indicate that persons at high genetic risk have an up to 40 times increased risk of myopia compared with persons at low genetic risk (Tedja *et al.*, 2019).

The Consortium for Refractive Error and Myopia (CREAM) presented results from the largest international genome-wide meta-analysis on refractive error with almost 38,000 individual participants. The CREAM study identified 24 new loci associated with refractive error from international ancestry studies. The findings were clinically significant, with a tenfold increased risk of myopia in those individuals carrying the most alleles (Verhoeven *et al.*, 2013). Some studies reported a significant association between Type ll collagen and high myopia in Caucasians through the gene COL2A1 but no association with and mild/moderate myopia, which supports the idea of involvement of multiple genes in the development of myopia (Mutti *et al.*, 2007; Metlapally *et al.*, 2009).

A literature review notes that twin studies provide the strongest conclusive evidence that myopia is inherited, and the authors define the several new loci related to myopia and high myopia especially those collagen type genes. However, the literature review agrees on the importance of assessing the role of environmental factors alongside genotype (Hornbeak and Young, 2009). The Genes in Myopia (GEM) Twin study reports a significantly higher correlation in refractive error and ocular biometry measures in monozygotic twins than dizygotic twins. Both additive and dominant genetic effect involvement suggests the involvement of multiple genes in the aetiology of refractive error (Dirani *et al.*, 2006). The Finnish and Danish Twin cohorts also found that the mean

difference in refractive error between the monozygotic pair was significantly lower than that of the dizygotic twins (Teikari *et al.*, 1991; Lyhne *et al.*, 2001).

The Avon Longitudinal Study of Parents and Children (ALSPAC) Study in the UK calculated genetic risk scores for each participant using genetic variants that showed genome-wide significant association with refractive error in a genome-wide association study. This study found that both the number of myopic parents, and the genetic risk score alone were weakly predictive of children's refractive error at ages 7 and 15. However, a combined model of both predictors improved the predictive performance at each age category. The combined predictive performance was still low, with limitations of non-cycloplegic refraction and oldest measurement of SER as 15 years old, as the predictive models are more accurate for assessing adults SER (Ghorbani Mojarrad, Williams and Guggenheim, 2018).

Generation R studies in Rotterdam, Netherlands found that children with a high genetic risk scores in combination with high environmental risk score had a greater risk of myopia compared to children with only one of these factors, and this gene-environment interaction was statistically significant. Parental myopia was associated with both environmental and genetic risk scores, indicating that parental myopia comprises shared genetic and environmental factors. The prevalence of myopia was 8.3% in children with no myopic parents, 13.7% in children with 1 myopic parent, and 18.4% in children with both parents being myopic. The environmental risk factors noted in this study were short reading distances, reading >1 book per week, and spending <7 h outdoors per week (Enthoven *et al.*, 2019).

1.3.3. Body Stature

There is some evidence for an association between body stature and myopic status. Some have found a link between increased weight and increased myopia (Dirani, Islam and Baird, 2008), or increased axial length (Terasaki *et al.*, 2017), but others have found no such association (Northstone *et al.*, 2013). Higher body mass index (BMI) were linked with increased odds for myopia in Ireland (Harrington, Stack and O'Dwyer, 2019) and longer axial lengths in Japan (Terasaki *et al.*, 2017). A number of studies have reported a linear correlation between height and axial length with increasing age (Northstone *et al.*, 2013). Taller children were found to have increased odds for myopia in the Ireland Eye Study (IES) (Harrington, Stack and O'Dwyer, 2019), yet in Japan height was not

significantly correlated with longer axial lengths (as a surrogate for myopia) (Terasaki *et al.*, 2017). Yip *et al.* (2012) reported that Singaporean children with earlier onset and peak progression of myopia were found to achieve peak height velocity at an earlier age than their peers with later onset myopia. The authors postulated that this earlier onset of myopia could be a result of the surge in growth hormones during the time when children achieve peak height velocity.

1.3.4. Birth Order

There is some evidence for a relationship between birth order and increased risk of myopia. A multi-study comparison of cohorts from UK, Singapore, Israel and Australia found a small increased risk of both myopia and high myopia in first-born children compared to non-first born children (Guggenheim *et al.*, 2013). In the UK, first-born participants were approximately 10% more likely to be myopic than non-first-born participants and equated to first-born individuals having a refractive error < −0.25 D more negative, therefore a small association. The association was larger before adjustment for educational exposure. This suggests that reduced parental investment in the education of children of later birth order could play a part in the association between birth order and myopia (Guggenheim and Williams, 2015).

1.3.5. Ethnicity

Kleinstein *et al.* (2003) reported myopia prevalence from the four main ethnic groups in the USA from the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study, which was a large, multicentre, longitudinal and observational study of refractive error and ocular development. Ethnicity was determined by both parental report and investigator observation. The Asian population in this study had the highest prevalence of myopia, followed by Hispanics. African Americans and Caucasians had the lowest prevalence of myopia. The prevalence of myopia among the different ethnic groups in the study population (aged 5-17 years) ranged from 4.4% to 18.5%.

The Correction of Myopia Evaluation Trial (COMET) was a randomized, double-masked, multicentre clinical trial in the USA that evaluated whether progressive addition lenses (PALs) vs single vision lenses (SVLs) slowed the rate of myopia progression in children (aged 6-11 years) with juvenile-onset myopia over the course of three years. This trial found that Asian children progressed the most over the period and African American children the least.

1.3.6. Gender

A number of studies have reported a higher incidence of childhood myopia among girls than boys (Kleinstein *et al.*, 2003), in addition to experiencing greater progression of myopia and axial elongation (Hyman *et al.*, 2005). However Yip *et al.* (2012) reported that in Singapore, girls had significantly earlier peak height velocity than boys (mean ages of 11 and 12 years, respectively) and they also had earlier peak axial length velocity earlier than boys 10.6 vs 10.7 years. This difference between sexes could be a result of the surge in growth hormones during the time when children achieve peak height velocity with girls having this peak at an earlier age than boys.

1.4. The Potentially Modifiable Risk Factors for Myopia

1.4.1. Light Exposure and Time Spent Outdoors

Animal studies have demonstrated that higher light intensities (either outdoors in direct sunlight or intense laboratory lights) prevent the development of form deprivation myopia in chicks (Ashby, Ohlendorf and Schaeffel, 2009), and in in rhesus monkeys (Smith, Hung and Huang, 2012), with evidence that early life sunlight exposure promotes normal emmetropization later in life (Wang *et al.*, 2015). Light exposure and time spent outdoors have been widely reported to have a protective effect on the development and/or progression of myopia in children (Lisa A Jones *et al.*, 2007; Rose *et al.*, 2008; Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018).

The exact mechanism by which this works is still unknown but there are a number of theories: release of retinal dopamine in response to sunlight (inhibits axial elongation in experimental myopia) (Ashby and Schaeffel, 2010; Feldkaemper and Schaeffel, 2013), increased light intensity outdoors (leading to pupil constriction, increasing depth of focus, decreasing blur, and slowing eye growth) (Chakraborty, Read and Vincent, 2020), more uniform dioptric space therefore reducing the myopiagenic hyperopic defocus (García *et al.*, 2018; Flitcroft, Harb and Wildsoet, 2019; Chakraborty, Read and Vincent, 2020; Lingham *et al.*, 2020), exposure to UV light (Jiang *et al.*, 2018; Strickland, Landis and Pardue, 2020) and changes in the spectral composition of visible light (Chakraborty, Read and Vincent, 2020) could also be factors in the reduced risk of myopia development and progression.

A study in Xichang, China where the researchers failed to find an association between outdoor activity and myopia (Lu *et al.*, 2009). However, this study had many myopes (83.1%) and therefore it could have been difficult to detect myopic risk factors from this sample. Rose *et al.* (2008) reported myopia prevalence's of 29.1% and 3.3% in East Asian 6-7-year olds living in Singapore and Sydney, respectively. The study showed that East Asian children in Singapore spent just over three hours per week outdoors whereas in Sydney they spend 14 hours per week outdoors. This evidence suggests that as the genetics were similar between the two populations, environmental factors must be the cause for such a significant difference in prevalence between the two cohorts. Interestingly the authors discovered that more total near-work activity was being performed by the children in Sydney. A major factor that contributes to the high levels of myopia in Singapore may be Singapore's competitive, academically oriented schooling. This study indicates a protective effect of time spent outdoors even in the presence of increased near work activity.

The CLEERE study in multiple sites in the USA found that those children who became myopic spent less time on outdoor activity/sports than the emmetropes, and the difference between the groups was identified as many as four years prior to the onset of myopia. The study also reported that differences in time spent reading for pleasure and time spent studying/gaming between the emmetropes and those who became myopic were only found after the onset of the myopia (Jones-Jordan *et al.*, 2011). These findings indicate that near working habits might be an effect of myopia whereas time spent on outdoor activity/sports is more likely to be a cause of myopia due to the differences between the groups prior to the onset of myopia. The study however, is limited by the failure to distinguish between time spent outdoors and time spent on physical activity. In Beijing, Lin *et al.* (2014) findings support those above as children with a high level of outdoor time exhibited significantly less myopic refraction than children with moderate and lower levels of outdoor time but only at primary school level. Some studies also reported than indoor sports time was not associated with the children's refraction hence supporting that time outdoors is the important environmental risk factor for myopia (Rose *et al.*, 2008; Lin *et al.*, 2014).

A meta-analysis of how outdoor activities affect myopia control by Deng and Pang (2019) found a reduced risk of myopia development with more hours of outdoor activities/week

(relative risk 0.66). They also reported a slower overall rate of myopic progress (0.13 D/year) and slower axial elongation (-0.03 mm/year). Slowing myopic shift in refractive error was demonstrated in all initially non-myopic cohorts and two out of three myopic cohorts. These slowing of myopic progression and axial elongation were clinically insignificant. A literature review by Weiss and Park (2019) agrees that there is strong evidence that increased time spent outdoors prevents the onset of myopia, but argues evidence for slowing the progression of myopia is not so strong. However, seasonal variation in myopia progression has been translated as evidence for time spent outdoor in higher light intensities effecting the progression of myopia (Fulk, Cyert and Parker, 2002; Donovan *et al.*, 2012; Gwiazda *et al.*, 2014; Ulaganathan *et al.*, 2019).

There are also a few RCTs examining the impact of increased time spent outdoors on myopia control. In Guangzhou, China researchers added one additional 40-minute class of outdoor activities to each school day in six intervention primary schools and encouraged the participation in outdoor activities in after-school hours. There were also six control schools who continued their normal patterns of activity over the three-year period. After the three years there was a significantly reduced cumulative incidence rate of myopia between the intervention and control group (30.4% vs 39.5%, $p<0.001$). There was also a significant difference in the three-year change in SER between the intervention and control groups (-1.42 vs -1.59 D, $p=0.04$), but there was no significant difference between the groups axial elongation (0.95 vs 0.98 mm, $p=0.07$) (He *et al.*, 2015).

In Northwest China, the Sujiatun Eye Care Study introduced two additional 20-minutes of recess outside the classroom for the intervention group, with no changes to the control group for one school year. The incidence of new myopia was 3.7% and 8.5% for the intervention and control group, respectively ($p=0.048$). The mean myopic progression of SER was significantly less in the intervention group (-0.10 vs -0.27 D, $p=0.005$) as was the axial length change (0.16 mm vs 0.21 mm, $p=0.034$) (Jin *et al.*, 2015).

In Taiwan, a Recess Outside the Classroom (ROC) intervention school were introduced to 80 minutes of outdoor recess, while the control school had no change to their recess for a year. The incidence of new myopia was significantly lower in the intervention than the control group (8.41% vs 17.65%, $p<0.001$), and there was less myopic shift in the intervention group (-0.25 vs -0.38 D, $p=0.029$). The findings of myopic progression of SER were only significantly lower in the intervention group in the non-myopic subjects

(-0.26 vs -0.44 D, p=0.02), whereas among the myopic subjects (without atropine treatment) there was no significant difference in the progression of myopia (-0.20 vs -0.37, p=0.125), for the intervention and controls, respectively. Such findings could indicate that increased time spent outdoors is protective against the onset of myopia and myopic shift in non-myopes but not protective against the progression of myopia in those already myopic subjects (Wu *et al.*, 2013). Following on from this study, Wu *et al.* (2018) developed the school-based Recess Outside Classroom Trial 711 (ROCT711) to increase time spent outdoors, alongside objective measures of light intensity. The in-school intervention involved 40 minutes/day outdoors and they were recommended to have 11 hours of time outdoors every week. After one year the myopic progression was significantly less in the intervention group compared to the control (-0.35 vs -0.47 D, p=0.002), as was the axial elongation (0.28 vs 0.33 mm, p=0.003). The incidence of new myopia was also lower in the intervention group (14.47% vs 17.40%). However, contrary to the research groups previous findings (Wu *et al.*, 2013), this study revealed that the myopic shift was significantly different between intervention and control groups for both the non-myopes (-0.32 vs -0.43 D, p=0.02) and the myopes (-0.57 vs -0.79 D, p=0.007) (Wu *et al.*, 2018). This provides evidence that increased time outdoors could also have a protective effect over the progression of myopia as well as the onset.

An interesting intervention study in Shenyang, China introduced the rebuilding of school lighting systems to increase the light intensity in the intervention classrooms, whereas the control group had no changes to their current lighting system. The light intensities were increased from 74 lux to 558 lux. After the year the intervention group had less myopic progression (-0.25 vs -0.47 D, p<0.001), and less axial elongation (0.13 vs 0.18 mm, p=0.023) than the control group for the non-myopes. For the myopes there was no significant different in myopic progression between groups (-0.25 vs -0.31 D, p=0.39), but there was significantly less axial elongation in the intervention group compared to the control (0.20 vs 0.27 mm, p=0.0001). The prevalence of new onset myopia was also significantly lower in the intervention group than the control (4% vs 10%, p=0.029). This study concluded that an increase in ambient light levels in classrooms appear protective over the onset of myopia and also slowed axial growth in those already myopic (Hua *et al.*, 2015). A systematic review and meta-analysis by Sherwin *et al.* (2012) found a 2% reduced odds of myopia per additional hour increase in time spent outdoors per week, equivalent to and odds ratio of 0.87 for an additional hour of time outdoors per day.

1.4.2. Near Work

A number of studies have reported a positive association with close working distances and more myopic refractive error in childhood (Haro, Poulain and Drobe, 2000; Ip *et al.*, 2008; Lu *et al.*, 2009; Lee *et al.*, 2015; Li *et al.*, 2015; Guo *et al.*, 2016; Hsu *et al.*, 2016; Huang *et al.*, 2019) with one study finding that that after six-months those with near work distance <30cm had significantly more myopia progression than those with near work distance >30cm (Huang *et al.*, 2019).

Bao *et al.* (2015) examined myopes near working distances using an electromagnetic motion-tracking system in Wenzhou, China. The findings were average near working distances of 27.2 cm and 24.9 cm for reading and writing respectively, but that these distances decreased further on playing video games, indicating that the working distance decreased while attentional and haptic workload and concentration increased. This study indicates that myopes typically have a closer working distance than the traditional near point distance (33 cm) used for ophthalmic examinations such as near visual acuity and Amsler grid (Bao *et al.*, 2015). However, this study was limited by not including non-myopic subjects to enable comparison between refractive groups.

To date it is not known whether the link between myopia and close working distances is causal, or whether myopic children reduce their working distance alongside the development of myopia. Increased near work may be result of myopia development rather than causal, because myopia might make extended periods of near work more comfortable in comparison to distance work. A literature review by Morgan *et al.* (2020) concluded that longitudinal studies were necessary in order to verify whether the close working distances were adopted prior to, or in conjunction with the development of the myopia, as well as assessing the efficacy of controlling reading distance for myopia progression. Lingham *et al.'s* (2020) review states the importance of wearable devices in future studies to measure distance between the eyes and objects in order to understand the defocus patterns of the visual environment.

There are many studies that have reported increased near work activity such as reading for pleasure, and time spent on homework presents an increased risk of myopia among children (Mutti *et al.*, 2002; Saw *et al.*, 2002; Ip *et al.*, 2008; Deng, Gwiazda and Thorn, 2010; French *et al.*, 2013; Saxena *et al.*, 2015; Li *et al.*, 2015; Guo *et al.*, 2016; Hsu *et al.*, 2016; Williams *et al.*, 2018; Singh *et al.*, 2019; Han *et al.*, 2019; Harrington, Stack

and O'Dwyer, 2019). Children who spent longer periods of continuous reading tended to be myopic, (Ip *et al.*, 2008; Li *et al.*, 2015; Hsu *et al.*, 2016; Huang *et al.*, 2019) and have more myopia progression per year (Jones-Jordan *et al.*, 2012; Öner *et al.*, 2016).

In Israel, male Orthodox Jews aged 14-18 years old were found to have a significantly higher prevalence of myopia (81.2%) than males attending general schools (27.4%) with the females in both types of schooling having similar myopia prevalence's of 31.7% and 36.2% in general and Orthodox schools, respectively. These findings rule out genetics as being the main source of variability as the male Orthodox Jews female sibling's prevalence of myopia was still much lower than the males. A potential reason for this significant difference in prevalence is the uncommon study habits characterized adopted by Orthodox males including; sustained near vision, frequent changes in accommodation due to the swaying habit during study, the variety of print size, and the need for accurate accommodation when reading tiny print (Zylbermann, Landau and Berson, 1993). A more recent study of adolescents in Israel agreed with these findings. They reported that in 17-18-year-old male transcripts, there was a myopia prevalence of 82.2% in those attended ultra-Orthodox schools, 50.3% in those in Orthodox schools and 29.7% in those in the secular educational system. This backs up the evidence that intensive reading and other near-work activities at a short working distance may have a role to play in the development and progression of myopia (Bez *et al.*, 2019).

A systematic review and meta-analysis by Huang *et al.* (2015) suggested that the association between near work and myopia indicated a 2% increased odds of myopia per additional dioptre-hour of time spent on near work per week. It was found that myopic children spend more time reading for pleasure than non-myopes and the authors recommended that more longitudinal and randomized controlled trials should be performed to confirm whether near work is a risk factor for the development of myopia (Huang, Chang and Wu, 2015).

A study of Norwegian engineering students by Kinge *et al.* (2000) found that the amount of time spent at lectures, reading scientific literature, and on practical near-work activities during holidays were all significantly related to myopic progression. This study shows that the type of near-work performed does influence the development of myopia as the authors found that reading scientific literature had a significant dose-response relation. This could be due to the intensive and longer periods of near focus involved compared

with other near tasks such as reading magazines/newspapers/fiction or performing calculation tasks. Another novel finding of this study was the relationship between time spent at lectures and myopic refractive change as this is predominantly distance-based viewing but, some students take notes during lectures and lecture attendance may be associated with more intense study behaviour.

There is evidence for a role of defocus in the progression of myopia in humans. The Correction of Myopia Evaluation Trial (COMET) found that the children with larger accommodative lags had significantly more myopia than children with smaller lags. Gwaizda *et al.* (2004) found that COMET children most at risk for increased progression of myopia over 3 years had, at baseline, a larger accommodative lag in combination with near esophoria and wore the conventional treatment for myopia (single vision lenses). Multifocal lenses slowed progression in these children and in those with larger accommodative lags in combination with a shorter reading distance, more hours of near work, or lower baseline myopia. The COMET study also found that reading distance emerged as a risk factor for progression among children with close reading distances and larger accommodative lags wearing single vision lenses. For the COMET children wearing single vision lenses, the level of baseline myopia was not a significant risk factor, but a large accommodative lag (assessed objectively) was. Children with larger accommodative lags wearing single vision lenses showed the most progression, and children with larger lags wearing multifocals showed reduced progression (Gwiazda *et al.*, 2004).

A recent literature review by Chakraborty *et al.* (2020) discusses multifocals ability to slow the progression of myopia and how they would improve accommodation accuracy and limit a lag, therefore adding weight to a potential role of accommodation in the development and progression of myopia. The authors did note however that the underlying mechanism of myopic control with these lenses could be due to the imposed peripheral retinal defocus, or a reduction in the near vergence demand. The review also points to the inconsistencies in findings regarding the link between near work and myopia development suggesting a potential role for other factors, such as a lack of outdoor light exposure. Alternatively, it could be a combination of both risk factors as the typical pattern of retinal focus experienced in outdoor environments (less near focusing and less exposure to hyperopic blur), may also play a protective role over the progression of myopia (Chakraborty, Read and Vincent, 2020).

1.4.3. Education

Level of education is often determined via questionnaire in adulthood, whereby participants are classified as having completed primary, secondary or higher education (Mirshahi *et al.*, 2014; Williams and Hammond, 2014; Nickels *et al.*, 2019). Such studies have provided evidence that while the proportion of individuals progressing to higher education has increased over recent decades in Europe, this cannot entirely explain the increased levels of myopia seen in European cohorts, signalling that others factors must be at play (Williams and Hammond, 2014). However, these subjective measures are more suitable to adults who have completed education, it is difficult to apply these metrics to children who are still undergoing education. Other potential measures of education and educational pressures would be age of starting school (Hsu *et al.*, 2016), parents level of education (Han *et al.*, 2019), type of schooling (O'Donoghue *et al.*, 2015) and use of extra tutorial classes outside of school (Saw *et al.*, 2002).

In the UK and Ireland, all children are mandated to receive full-time education until at least 16 years of age, after which individuals can choose to remain in full-time school-based education for a further two years or choose to leave school-based education to pursue employment, apprenticeships, or vocational training within a further education college. In the 2020/2021 academic year 63% of 16-17 year olds were enrolled school-based education (Department of Education, 2021). In Northern Ireland, historically there is stratification within the post-primary sector with secondary level schools being academically selective (grammar) or non-selective (non-grammar). This academic selection used the results of an Educational Authority's regulated '11+' examination which was removed in 2008. While it was still in force, NICER 1.0 found that the odds of myopia prevalence were more than 2.5 times higher among children attending grammar schools than non-grammar schools in Northern Ireland (O'Donoghue *et al.*, 2015). This '11+' examination has largely been replaced by entrance assessments held by the grammar schools themselves since 2008, which are not regulated by the Education Authority. The annual enrolment statistical bulletin (2021) for the academic year 2020/2021 determined that 66 post-primary schools in Northern Ireland are academically selective (grammar schools) and the remaining 127 post-primary schools are non-grammars and do not require and entrance assessment and 42.9% of all children attended the grammar schools (Department of Education, 2021).

In the case of educational pressures, evidence of causality comes from the high prevalence of myopia and high myopia in Jewish boys attending Orthodox schools in Israel as previously mentioned. The Orthodox boys schooling entails intense near work along with frequent changes in accommodation due to the swaying habit during study and the varying print size along about 16 hours a day of studying for boys aged 13 years and older. Orthodox girls are subjected to 8 hours a day of studying and sewing/drawing while in general mixed schooling the school day is 6 hours, which is comparable to Western countries (Zylbermann, Landau and Berson, 1993).

Some studies have found an association between academic performance and myopia risk, particularly in language and reading based subjects rather than mathematics (Mutti *et al.*, 2002; Saw *et al.*, 2002; Saw *et al.*, 2007). In addition, there is strong evidence for more time spent in education increasing the risk of myopia (Mirshahi *et al.*, 2014; Lee *et al.*, 2015; Williams *et al.*, 2015; Mountjoy *et al.*, 2018; Han *et al.*, 2019). One such study discovered a linear relationship between time spent in education and the level of myopia with mendelian randomisation analysis showing that every additional year spent in education resulted in a more myopic refractive error of −0.27D (Mountjoy *et al.*, 2018).

A systematic review and meta-analysis of myopia prevalence in Europe found the overall myopia prevalence from 13 population-based studies was 23.8% and high myopia was 2.1%. Myopia was more common in the younger cohorts with 42.3% in those aged 20-30 years. A cohort effect for rising myopia prevalence was apparent. Education level was strongly associated with myopia, and education levels have risen. However, the length of time in education does not fully explain the cohort effect, therefore birth year must also have an effect (Williams *et al.*, 2015). Williams and Hammond (2014) reported the European age-standardized myopia prevalence for those completing primary, secondary, and higher education as 25.4%, 29.1%, and 36.6% respectively.

Mirshahi *et al.* (2014) reported a significant association between professional education with 53% of university graduates being myopic vs 34.8% of secondary school graduates in Germany. In the United Kingdom (UK) researchers reported a myopia prevalence of 64% among university students, which is much higher than the national average, hence reinforcing the idea that education is a risk factor for myopia (Guggenheim, Hill and Yam, 2003). The UK Biobank study report that increasing educational achievements in the UK were significantly associated with a higher frequency of myopia (Cumberland *et*

al., 2015). The National Health and Nutrition Examination Survey (NHANES) in the USA found that mean spherical equivalent refraction was inversely proportional to level of education and that myopia prevalence increased with increasing levels of education. Myopia was present in 16.8% of those with less than 9th grade education (aged 14-15 years old) and in 45.0% of those graduated from college or other higher education (Nickels *et al.*, 2019).

In the East (e.g., Asia), the educational system is very different from in the West (e.g., Europe and USA). Eastern parents pay a lot of attention to the academic performance of children and encourage more time spent on near work. In contrast, Western parents pay more attention to children's physical wellbeing and encourage more outdoor activities (Jerrim, 2015). This difference might partly contribute to the particularly high prevalence of myopia in the East. There are parts of East Asia where after-schools tutorial classes for children are commonplace and attendance at these after school "cram schools" is strongly associated with myopic refractive error and increased myopia prevalence in these populations (Hsu *et al.*, 2016; Guan *et al.*, 2019; Ku *et al.*, 2019). One such study found that children attending extra tuition classes were twice as likely to have high myopia (Saw *et al.*, 2002). The underlying mechanism linking cram schooling and myopia remains unclear, but it is possible it is a combination of increased the amount of near visual activity, as well of depriving the children of time to spend outdoors (Ku *et al.*, 2019). In East Asia, a study comparing myopia rates in Singapore to Xiamen, China found the myopia prevalence was 2 times higher in Singapore (36.7% vs 18.5%) ($p<0.001$), and the prevalence of high myopia was 3 times higher (9.8% vs 2.5%). In both countries identical study protocol was followed, and the children have similar hereditary predispositions, therefore environmental factors are likely to contribute to the differences in the prevalence rates. The researchers concluded that the higher prevalence rates in Singapore were due to it being a more urbanized and rapidly developing country with a highly competitive education system, whereas Xiamen is less urbanized and the schooling system is not so demanding (Saw *et al.*, 2002).

There is evidence for differences in myopia prevalence's within populations, related to differing levels of schooling. In Singapore the prevalence of high myopia in one of the highest ranked schools in the country was 17.2% vs 4.0% in one of the lowest ranked schools (Saw *et al.*, 2002). In Delhi, India the prevalence of myopia was significantly higher among children attending private schools (17%) compared to government schools

(7.9%) and children in these private schools were found to spend a significantly greater number of hours in reading and writing at home and greater likelihood of attending extra classes and private tuitions (Saxena *et al.*, 2015).

A systematic review and meta-analysis by Morgan and Rose (2013) accessed data from 2009 Organisation for Economic Co-operation and Development (OECD) Programme for International Student Assessment (PISA) survey on educational achievements of 15-year olds internationally and compared this to myopia prevalence data from countries around the world. Their findings were that all the jurisdictions identified as locations with a high prevalence of myopia are in the top quartile of performers in PISA. However, several other jurisdictions also achieve high educational outcomes, without any evidence of a high prevalence of myopia, for example, Australia and Finland. A possibility for this contrast is that populations of certain ancestry are more susceptible to environmental risk factors associated with education. Other evidence suggests that tutorial use is high in the high prevalence of myopia/high performance locations and this extra education outside of school hours could be preventing time being spent outdoors for protective effects (Morgan and Rose, 2013).

In the British Twins Early Development Study Williams *et al.* (2018) found a significant association between higher grades at 16-years old and myopia but only in univariate analysis. They also reported a higher odds ratio of myopia in children born in the summer and postulated that this is likely due to early exposure to the education system. Another twin study, on discordant twin refractive errors found that the more myopic/less hyperopic twins self-reported higher occupational status and more close work than their twin. Both near work and educational attainment were shown to be independent risk factors in multivariate analysis. A novel finding from this study was the strongest effects were seen comparing the twin pairs where one was myopic and the other emmetropic or hyperopic-highlighting that comparing affected myopic subjects against 'unaffected' may be more powerful than comparing within a group of subjects with differing degrees of myopia (Ramessur, Williams and Hammond, 2015).

There are some subjective metrics that can be used to determine education as a potential risk factor. The number of years spent in education and the highest level of qualification are some (Mirshahi *et al.*, 2014; Williams *et al.*, 2015; Mountjoy *et al.*, 2018). However, these subjective measures are more suitable to adults who have completed education, it

is difficult to apply these metrics to children who are still undergoing education. Other potential measures of education and educational pressures would be age of starting school (Hsu *et al.*, 2016), parents level of education (Han *et al.*, 2019), type of schooling (O'Donoghue *et al.*, 2015) and use of extra tutorial classes outside of school (Saw *et al.*, 2002).

1.4.4. Urbanization

There is evidence for differences in myopia prevalence between urban vs. rural environments which is suggestive of the environmental effect, given genetic backgrounds are similar in those living in urban and rural areas of the same country (He, Zheng and Xiang, 2009). However, the urban vs rural difference may be a surrogate for other "myopiagenic" environmental risk factors such as reduced time spent outdoors, increased time spent sedentary and increased near work/educational pressures (Saw *et al.*, 2001). There is also some suggestion that the reason for increased myopia prevalence in urban environments is due to peripheral hyperopic defocus. An indoor environment is much more dioptrically varied than outdoors as objects tend to be nearby, whereas outdoors the vast majority of objects are far enough away to make the visual scene more uniform (Flitcroft, 2012). A systematic review and meta-analysis of global myopia prevalence over time reports a 2.6 times increased risk of myopia in children living in urban vs. rural environments (Rudnicka *et al.*, 2016).

Ip *et al.* (2008) examined risk factors for childhood myopia (aged 12-13-years old) in Sydney via child and parent questionnaires including the type of housing and proximity of their home to other homes, shops, or high-rise buildings along with other environmental risk factors. This study found that the prevalence of childhood myopia was lowest in the outer suburban region and highest in the inner-city region (6.9% vs 17.8%) and the mean SER was increasingly myopic from outer suburban to inner city region. Myopia was significantly more frequent in children who lived in smaller, confined housing types such as terrace houses (21.4%) and apartments (26.3%) than those living in stand-alone or separate houses (11.3%). Housing density was not significantly related to myopia in this study sample, but it was determined by asking about number of houses seen from the participants house which might be an unreliable indicator of urbanisation. Housing type and proximity to city was significantly related to myopia in this sample independent of factors such as outdoors activity, near work activity and ethnicity (Ip *et al.*, 2008).

In China a large study across 12 different cities found that the prevalence of myopia was higher in those living in urban areas compared to rural areas. The odds ratio for myopia increased with increasing living floors compared to those living on the ground floor with odds ratios of 1.28, 1.84 and 2.02 for those living on 1-3, 4-6 and 7 floor or more, respectively (Wu *et al.*, 2016), but myopia was self-reported in this study. In Guangdong, China, Zhang *et al.* (2010) found that higher population density was an independent risk factor for myopia, even after adjustment for other factors with 1.00-1.50 D difference in the mean SER of 12-14-year olds in the highest and lowest densely populated areas (Zhang *et al.*, 2010).

In Hong Kong a study using non-cycloplegic autorefraction on children aged 7-12-years old found longer axial lengths and more negative SER as the population density of the residential districts increased, with a significant difference observed in districts with low population density when compared with high population density. As home size increased, the participants SER was less negative and axial length was shorter (Choi *et al.*, 2017). The Avon Longitudinal Study of Parents and Children (ALSPAC) found evidence for associations between myopia and population density in the UK with those children living in more population dense areas had a higher risk of incident myopia compared to those in less population dense areas. The ALSPAC concluded that it is possible that population density is merely a reflection of other lifestyle traits which are risk factors for myopia (Morris *et al.*, 2019).

In contrary to these findings, a study in Northern Ireland (NI) found no significant effect from urbanization on the odds of myopia in Northern Irish 12-13-year-olds. However, the authors concluded that the likely reason for the lack of findings could be that the most urban parts of Northern Ireland are still significantly less urban than Sydney or East Asian cities. Additionally, population densities might not be accurate in areas in close proximity to large bodies of water which is common in NI (O'Donoghue *et al.*, 2015).

1.4.5. Screen Time

Phase 1 of the NICER Study was undertaken over 13 years ago in Northern Ireland, this period has seen huge advances in technology. For example, the first iPhone was only released in 2007. Ofcom's Children and Parent Media Use and Attitudes Report (2021) found that 14% of children aged 5-7-years owned a smartphone and 57% had their own

tablet, and 91% of children aged 12-15-years owned a smartphone and 59% had their own tablet. Whereas in 2010 Ofcom reported that 3% of children aged 5-7 years old, and 35% of children aged 12-15 years old owned a smartphone and they estimated that only 5% of UK children aged 5-15 years had access to a tablet (Ofcom, 2011). This increasing demand for digital devices has encouraged the media to 'blame' handheld electronic devices such as tablets and smartphones when rising levels of myopia are reported (Boots Opticians, 2016). It is important to note that previous studies have found no association between the use of computer screens and childhood myopia (Kinge *et al.*, 2000; Deng, Gwiazda and Thorn, 2010), however this typically applies to the use of a desktop computer/laptop screen, whereas in recent times most screen time is performed on phones and tablets. There is a lack of research into handheld electronic devices and specifically teasing out their impact on refractive status, as opposed to time spent in other near vision activities and refractive error. The concern with these devices is that the viewing distance is much closer and extensive near work is known to be linked with myopia. These devices have become an inescapable as well as inevitable part of childhood in the 21st Century and it is important that we know whether they actually constitute a modifiable risk factor for myopia.

A recent report from the World Health Organization (WHO) provides guidelines to restrict sedentary screen time for children under five years old as evidence suggests that screen time may increase sedentary behaviour with negative impact for children's health (WHO, 2019), but is it also possible that sedentary screen time could have a negative impact on children's eye health? Alarming data from Singapore's GUSTO cohort stated that children aged two were spending an average of 2.4 hours a day on screens (both TV and handheld electronic devices). By age three this time increased on average by 0.33 hours per day mainly through increased use of handheld devices (Bernard *et al.*, 2017). The American Academy of Pediatrics (AAP) guidelines for children aged 2-5 years old is to limit the screen time to 1 hour per day and for children under 18 months to avoid the use of screens entirely (American Academy of Pediatrics, 2020) therefore, 75% of Singapore's GUSTO cohort were exceeding the AAP guidelines (Bernard *et al.*, 2017).

There is the possibility that handheld electronic devices could potentially provide increased risk of myopia but only because they fall under the blanket of "near work" rather than being an independent risk factor. A published viewpoint by Dirani *et al.* (2019) highlights this by stating that using books read as a proxy for near work activity is

inaccurate and outdated in the current digital age. The authors also attribute the increased screen time to a rise in sedentary behaviour and lack of outdoor activity which we already know are risk factors for the development and progression of myopia. Therefore, it could be possible that the increased screen time is simply a surrogate for less time outdoors/less time exercising. Zadnik and Mutti (2019) also express that it may not be the use of digital devices, but instead, the societal shift to indoor activities while using handheld electronic devices, leading to a worldwide, projected increase in the prevalence of myopia. Morgan *et al.* (2020) also concluded that there is no current evidence that use of digital devices are more detrimental for the development or progression of myopia than reading for the same amount of time. However, they did agree that digital devices do increase the appeal of near work activities and indoor lifestyles.

The Ireland Eye Study (IES) reported an increased risk of myopia with increased time spent on screens from questionnaire data. They found that with children aged 6-7-years old, the prevalence of myopia increased fivefold from 3.0% in the <1 hour screen time group to 15.5% in the >3 hours screen time group. Within the 12-13-year old group the difference was smaller but still significant with myopia prevalence increasing from 21.0% among participants who spent <1 hour per day on screens to 27.0% among those who spent >3 hours per day on screens (Harrington, Stack and O'Dwyer, 2019). The Copenhagen Child Cohort 2000 Eye Study found that compared with <2 hours of screen time per day the odds ratios for myopia increased to 1.85 for 2-4 hours of screen time per day, and 1.95 for >6 hours per day even following adjustment for other factors (Hansen *et al.*, 2019).

Bababekova *et al.* (2011) study of font sizes and viewing distances of smartphones found that both were significantly smaller when viewing a webpage as opposed to typing a text message. The mean working distance was 36.2 cm. Yoshimura *et al.* (2017) also examined viewing distances during smartphone use in both seated and lying positions. The authors found the seated viewing range was 13.3-32.9 cm and the lying range was 9.9-21.3 cm. Both these studies report shorter viewing distances for smartphone use than typical near working distances for hardcopy text of 40 cm (Bababekova *et al.*, 2011). The close viewing distances and smaller text are placing increased demands on the accommodation and vergence of the user, especially if used for extended periods. Bao *et al.* (2015) postulated that viewing distance decreased while attentional and haptic workload and concentration increased. Thus, the visual hazard of handheld electronic

device could be worse than traditional near-vision tasks (reading and writing on paper) by inducing higher levels of accommodative lag.

A study of lifestyle associations and baseline axial length in Japan found a significant correlation between duration of computer and smartphone use and the AL in the univariate analysis, but the correlation did not remain significant in the multivariate analysis. However, this study did not have any measurement of refractive error (Terasaki *et al.*, 2017). Several Asian studies examined the relationship between questionnaire-derived risk factors and refractive error in different settings. Liu *et al.* (2019) found a myopia prevalence of 59.2% in Tianjin, China. They found no association between the use of electronic devices and the prevalence of myopia but, they found a more negative SER and longer AL in those children spending more time on smartphones and computers, but not with those spending more time on tablets or watching TV. Guan *et al.* (2019) a significant association between time spent on computers and smartphones and more myopic refractive errors. Singh *et al.* (2019) found a positive association of myopia prevalence with children playing computer/video/mobile games for >2 hours per day. Hsu *et al.* (2016) found that use of phone/tablets/computer >2 hours per day increased the risk of myopia in this age group by 41% compared to those spending <2 hours per day on the devices.

An interesting pilot study in Pakistan assessed 100 adult's refractive status using an autorefractor before and after one hour of smartphone use in ambient lighting and found a statistically significant myopic shift of 0.25-0.50 D. The myopic shift was apparent for both myopes and non-myopes and was transient, disappearing after a few minutes (Afzal and Chaudhry, 2017). One major limitation to this study were that there was no control group (either traditional reading or not reading at all for the one hour), therefore this myopic shift could be a normal change in the eyes following any near work and might not be specifically linked to smartphone use.

A systematic review and meta-analysis by Lanca and Saw (2020) found inconsistency between the use of computers and myopia, with some studies finding an association between the prevalence and magnitude of myopia but some found no consistent results. The meta-analysis found a pooled OR of 1.02 indicating no association between screen use and myopia, however the review concluded that further investigation was necessary as it was based on studies which all used non-validated self-reported measures of screen

time and there remains the need for objective measures of screen time via apps. Additionally, assessment of time spent outdoors is required to examine if the increased screen time is just a proxy for increased time spent indoors.

A large-scale study in Longhua, China found that those children with parental-reported screen exposure during the first and second year of life had a statistically significant higher risk of myopia than those without screen exposure with prevalence ratios of 4.02 and 1.82, respectively. Those with both myopic parents and screen exposure demonstrated higher risk of myopia irrespective of the initial exposure age, with prevalence ratio decreasing from 9.20 to 2.82 as the initial exposure age rose from 0–1 year to after 3 years. Children initially exposed to electronic screens during the first year of life all had significantly higher risk of myopia, irrespective of the average daily screen time, while those initially exposed between 1-2 years old demonstrated a higher risk of myopia with more than 60 minutes of screen time per day, after which there was a dose dependent risk of myopia with increasing exposure durations. The findings of this study led the researchers to the hypothesis that the postnatal first year might be the sensitive period in early life for the association between screen exposure and the development of childhood myopia. This could be due to the fastest rate of eye growth during the first year of life and steady fixation at near at such a young age might contribute to myopia, therefore supporting that outdoor activities would be more beneficial as they encourage more frequent shifts of attention and focus (Yang *et al.*, 2020).

Interestingly, there is a significant difference between app-measured screen time and self-reported screen time, for example Lin *et al.* (2015) found average app-measured screen time of 29.39 hours/week, whereas the self-reported screen time however was significantly lower at 20.11 hours/week. The study also found that the more time spent on smartphones the larger the underestimation in the self-report.

There are also several recent studies regarding the relationship between screen use and sleep and there is evidence for reduced sleep quality and myopia (Ayaki *et al.*, 2016). In France, Leger *et al.* (2019) examined young adults sleep quality and melatonin production with varying degrees of blue blocking filters worn four hours prior to bedtime for seven days. They found that four hours of exposure to screens and domestic lighting with no filters suppressed melatonin by 47% compared to the dark condition, but with the blue blocking filter this suppression was reduced significantly to 12%. Sleep duration was also

extended by 27 minutes, sleep onset was advanced by 25 minutes and sleep quality was improved, which were all significantly different to the non-filtered scenario.

Wood *et al.* (2013) had 13 young adult participants using a tablet under three conditions; tablet only, with orange-tinted glasses and with googles directing blue light towards the participants cornea. Each participant experienced all three conditions each one week apart and kept sleep logs throughout. They also provided saliva samples at hourly intervals throughout each experiment night, and it was found that compared to the orange-tinted glasses (blue-blocking), melatonin suppression was 7% by the tablet only condition, and 48% by the blue light condition. The authors also acknowledged that using electronic devices prior to sleep may results in disrupted sleep even without melatonin suppression as alerting or stressful stimuli can lead to sleep disruption.

In Switzerland healthy volunteers were exposed to both and LED and a non-LED screens on separate occasions to watch a movie on, with regular breaks for saliva collection and to complete sleepiness questionnaires. The LED-backlit screen emitted 3.32 times more light in the blue range between 440 and 470 nm than the non-LED screen. The researchers determined that salivary melatonin levels were suppressed and rose later under exposure to the LED screen compared with the non-LED screen. They also found that the participants sleepiness levels decreased and there was an increase in cognitive performance when watching the LED screen in comparison to the non-LED screen. These findings agree that short-wavelength light before bedtime significantly impacts on an individual's alertness and circadian rhythm (Cajochen *et al.*, 2011).

Another study found that the use of electronic devices in bed before sleep was also related to shorter sleep duration on weekday nights and sleep difficulties. Owners of smartphones specifically, reported later bedtimes and shorter sleep durations. This study also reported spending time online in bed before sleeping was most strongly correlated with sleep disturbance (Lemola *et al.*, 2014). In the USA a study on adults found that increased screen time was statistically significantly associated with reduced sleep efficiency and shorter sleep durations but not associated with mood or levels of physical activity (Christensen *et al.*, 2016). Similarly, Munezawa *et al.* (2011) found that mobile phone use for texting or calling at night were related to all four types of sleep disturbance assessed in the study in Japan (shorter sleep duration, poorer sleep quality, excessive daytime sleepiness and insomnia symptoms). They found a lot of children, particularly

girls and those in senior high school, spent more time on their mobile phones after lights out and therefore could experience symptoms of sleep disturbance. However, both studies noted a casual nature could not be determined by this study as the direction of causality could also be that those students with difficulty falling asleep could be spending time on their phones instead.

Yoshimura *et al.* (2017) found that while lying down, viewing distances were shorter and linked to poorer sleep, lower sleep efficiency and longer sleep latency. By contrast, the seated viewing distances which were longer were not associated to any of the sleep parameters. Hence, this raises the question, could screen time could pose an increased risk of childhood myopia due to disrupting of normal sleep patterns? Or does increased screen time act as a proxy for increased near work, time spent sedentary, and time spent indoors? Is there an increased risk of childhood myopia due to a combination of all these factors?

1.4.6. Physical Activity

The National Health Service (NHS) in the UK recommends that children aged 5-18 years old need to do at least 60 minutes of physical activity (PA) per day to maintain a basic level of health. It is stated that this should range from moderate to vigorous physical activity and that three days per week these activities should involve exercises for strong bones and muscle. Examples of moderate physical activities include walking, cycling on flat, playing in the playground and riding a scooter. Examples of vigorous physical activities are dancing, swimming, running, gymnastics, football, cycling on hills and martial arts. Examples of muscle and bone strengthening exercises that are suitable for children include playground equipment bars, gymnastics, tree climbing, football, rugby, tennis, skipping. The NHS also recommends that children and young people need to reduce the amount of time spent sitting sedentary for extended periods of time (National Health Service, 2011). These recommendations are linked to better general health, stronger bones and muscles, and higher levels of self-esteem, but to date, we do not know how PA affects children and young peoples' eyesight.

There have been conflicting reports in recent years over whether PA influences the development/progression of myopia. Although it is common knowledge that higher levels of PA have benefits for the rest of the body and too much sedentary behaviour can cause several adverse health outcomes, little is currently known about the relationship between

PA and the regulation of the growth structures within the eye. To date there have been a number of different ways that researchers have assessed PA in relation to myopia, the most common methods are via questionnaires/interviews for subjective assessment. Objective measures of PA can be performed with the use of accelerometers, or by a physical fitness test as a biomarker for PA levels.

The Northern Ireland Childhood Errors of Refraction (NICER) study discovered that in 12- 13-year olds regular PA (>3 hr/week) was associated with a lower estimated prevalence of myopia compared to those leading more sedentary lifestyles (O'Donoghue *et al.*, 2015). The Ireland Eye Study used an identical sampling framework to that used by the NICER study and found that within their 6-7-year-old cohort, 8.1% of those with sedentary lifestyles were myopic, dropping to just 3.1% for those more active. The same was demonstrated in the 12-13-years-old cohort, where 35.2% of participants with sedentary lifestyles were myopic, decreasing to 14.4% among more active participants (Harrington, Stack and O'Dwyer, 2019). The Avon Longitudinal Study of Parents and Children (ALSPAC) study in the UK found that non-myopes have significantly higher levels of moderate-vigorous physical activity as measured on accelerometers, when compared to their myopic peers and the myopes spent more time sedentary (Deere *et al.*, 2009). Guggenheim et al. (2012) objectively recorded physical activity with an accelerometer in a non-cycloplegic study of refractive error and identified that greater levels of overall PA and time spent on moderate to vigorous PA were associated with a lower risk of myopia and greater levels of sedentary time were associated with an increased risk of myopia development.

Mutti *et al.* (2002) found that children with myopia spent more time engaged in near activities and less time engaged in sports, but time engaged in sports was not a statistically significant factor in myopia prevalence as were hereditary and near activities in this study. In Rotterdam, Netherlands a population of six-year olds with a low myopia prevalence of 2.4% found that children with myopia had participated less in sports and had a higher BMI than the non-myopes (Tideman *et al.*, 2018). In Australia researchers found that time spent on indoor sport had no significant effect on refractive error and only time spent on outdoor sport was associated with a less myopic refractive error (Rose *et al.*, 2008), while another study in Australia found a significant association between average daily light exposure and the average daily physical activity level, indicating a tendency to perform PA when outdoors. However, the researchers found no significant association between

PA and myopia (Read, Collins and Vincent, 2014). Dirani *et al.* (2009) found that myopic subjects participated in less PA than the emmetropic participants and the participation of outdoor sports was associated with a reduced prevalence of myopia in Singapore but, there was no association between indoor PA and myopia. A systematic review and meta-analysis by Sherwin *et al.* (2012) suggested that increasing time outdoors may be associated with a reduced risk of myopia and myopic progression, but because there is no protective association between indoor sports and myopia unlike outdoor sports, therefore suggesting that physical activity may be a surrogate for outdoor activity. A large questionnaire-based study of children in Taiwan found that moderate-vigorous physical activity of at least one hour per day reduced the odds of myopia by 20%, as did the same amount of outdoor activity time but to a greater degree. However, this found time spent outdoors, rather than the level of physical activity, was linked with the severity of myopia. This study further supports the finding that it is time outdoors rather that is the primary driver of a protective effect on myopia development (Holton *et al.*, 2019).

In the UK, a large study sample (n=1010) by Cooper *et al.* (2010) used GPS and Actigraph accelerometer data to determine children's patterns of outdoors time and PA. The findings were that PA levels outdoors were consistently higher than indoors, with counts per minute (cpm) almost three times higher outdoors than indoors (1345.8 vs 508.9 cpm). There was marked seasonal variation in outdoor PA, but it remained consistently higher than indoor PA, as indoor PA remained at a consistent level throughout the year. Time outdoors was a strong predictor of PA in the analysis and the researchers concluded that public health interventions to increase the physical activity of young people may be directed towards enabling more time spent outdoors.

Muhamedagić *et al.* (2014) assessed physical activity with both questionnaires and a fitness test, and discovered that the student participants with greater physical activity and physical competence had smaller differences of cycloplegic autorefraction readings between measurements, leading to the conclusion that greater physical activity did not cause myopia progression. An interesting study by Read and Collins (2011) investigated the influence of moderate intensity exercise on ocular biometrics and intraocular pressure (IOP) on 20 young adults. Measurements were taken immediately after, 5mins, and 10mins after completion of the exercise. Axial length exhibited a significant reduction following exercise but 10 min after the exercise task, it returned to baseline. The short-term changes in axial length are unlikely to be of clinical significance, but they do

demonstrate that a short period of dynamic exercise leads to transient changes in ocular biometrics. The significant reduction in axial length could indicate that exercise induces changes in IOP and blood flow and may have implications for refractive error development.

A study on the relationship between parental and children's PA levels found that girls who have mainly sedentary parents are more likely to be sedentary, but there were no associations between parent and child PA. There was also an association between higher parental TV viewing and an increased risk that children spent >4 hours per day watching TV (Jago *et al.*, 2010). These findings back an overlap between genetics and environmental factors when assessing children lifestyle behaviours that might be risk factors for myopia.

Jones *et al.* (2007) found a significant association between sports/outdoor activities and the development of myopia but did not separate the two variables. And in a follow-up study they found that outdoor/sports activity was significantly different between the subjects who became myopic and those remaining emmetropic, with the difference evident as early as four years before myopia onset. (Jones-Jordan *et al.*, 2011).

A couple of studies in Copenhagen, Denmark reported an inverse association between time spent on PA and myopia, with one suggesting a protective effect of one hour of PA per day is equal in magnitude to the detrimental effect of three hours of study per day (Jacobsen, Jensen and Goldschmidt, 2008) and the other finding that those 16-17-year olds that were physically active >3 hours/week had 40% reduced odds for myopia compared to those active <3 hours/week (Hansen *et al.*, 2019). In Southern California, Theophanous *et al.* (2018) found that at least 60 min of daily exercise was significantly associated with lower prevalence of myopia. In Amman, Jordan a study found that myopic children spent significantly less time playing sports compared to non-myopic children (1.87 vs 4.04 hours per day) (Khader *et al.*, 2006). However, all four studies failed to assess whether the PA in question was performed indoors or outdoors so again, increased PA could just be a surrogate for increased time spent outdoors.

Conversely, a study in Denmark used accelerometer devices for objective measurements of PA and found no significant association between PA and refractive error or axial length (Lundberg *et al.*, 2018). A systematic review by Thykjær *et al.* (2017) concluded that

there was a general connection between PA and myopia but that more studies are needed which include objective measurements of PA alongside robust evaluation of childhood refractive status. The systematic review also encouraged that future studies should clearly distinguish between the PA and outdoor light exposure (Suhr Thykjær, Lundberg and Grauslund, 2017). Such studies are required in order to determine if lower levels of physical activity are a risk factor for myopia or simply a proxy for reduced time spent outdoors.

In the future, it would be important to separate time spent on physical activity and time spent outdoors in order to assess whether or not lower levels PA are a risk factor for the development/progression of myopia or whether lower levels of physical activity are just a surrogate for indoor sedentary behaviour, while higher levels of PA are mainly performed while outdoors. The most accurate way to achieve such result would be via device measured physical activity and time spent outdoors in conjunction with each other.

1.4.7. Sleep Quality

Circadian rhythms have a period of approximately 24-hours. They are generated by circadian clocks, which are autonomous cell-based molecular timing mechanisms. Circadian clocks regulate daily rhythms of sleep and alertness, blood pressure and heart rate, locomotor activity, hormone secretion, body temperature, metabolism, and many other physiological processes. Most of these rhythms are controlled directly or indirectly by the 'master clock' in suprachiasmatic nuclei (SCN) of the hypothalamus which receives direct input from the eyes. (Klein et al., 1992). Weiss and Schaeffel (1993) found that chick eyes grew in a rhythmic manner, elongating more during the day than at night. Increased night-time melatonin promotes sleep, and decreased daytime melatonin promotes alertness. It is known that even brief exposure to bright light during the night-time can disrupt circadian patterns by decreasing melatonin levels. Light is the most important Zeitgeber for regulating circadian activity. A Zeitgeber is an environmental agent that provide the cue for setting or resetting a biological clock into a 24-hr cycle. Normally melatonin undergoes a sharp rise approximately one to three hours before bedtime, which onsets in response to dim light, known as dim light melatonin onset (DLMO). Similarly, there is a sharp fall in melatonin in response to light onset. DLMO is considered to be a reliable, non-invasive circadian phase marker (Pandi-Perumal *et al.*, 2007). Short wavelength light, in the blue portion of the visible spectrum, is most potent for acute suppression of melatonin through activation of melanopsin containing ipRGCs.

Accumulating evidence suggests that LED displays are contributing to night-time melatonin suppression and sleep difficulties (Tähkämö, Partonen and Pesonen, 2019). Further research is still required around the speculation of a link between melatonin, circadian rhythm and eye growth in myopia and whether this is a pathway through which light exposure has a protective effect on the development and progression of myopia (Ostrin, 2019). A literature review by Chakraborty *et al.* (2018) hypothesizes a role for circadian disruption as a mechanism for myopic development and recommended further studies into the timing of light exposure and its relationship with refractive change and in turn, therapeutic interventions.

A few studies have demonstrated how light exposure disrupts circadian rhythm and sleep. In Houston, Texas Ostrin *et al.* (2017) assessed the night time melatonin levels and the Pittsburgh Sleep Quality Index (PSQI) score of young adults before and after two weeks of wearing blue blocking glasses a few hours prior to bedtime. The study found a statistically significant increase in melatonin levels by 58% and improvement or stability of PSQI scores for all participants after wearing the blue blocking lenses. The participants sleep duration significantly increased by 24 minutes and sleep onset was 27 minutes earlier. These findings indicate that the blue blocking glasses seem to prevent the circadian delay that has been shown to occur with exposure to short wavelength light in the evenings (Ostrin, Abbott and Queener, 2017). In France, Leger *et al.* (2019) also assessed young adults with varying degrees of blue blocking filters worn four hours prior to bedtime for seven days, for sleep quality and melatonin production, and their findings were remarkably similar to those in Houston, Texas. They found that four hours of exposure to screens and domestic lighting without the filters suppressed melatonin by 47% compared to the dark condition, but with the filter this suppression was reduced significantly to 12%. Sleep duration was extended by 27 minutes, sleep onset was advanced by 25 minutes and sleep quality was improved, all significantly different to the non-filtered scenario.

Cajochen *et al.* (2011) found that participants sleepiness levels decreased and there was an increase in cognitive performance when watching the LED screen in comparison to the non-LED screen, and it was found that the LED-backlit screen emitted 3.32 times more light in the blue range between 440 and 470 nm than the non-LED screen.

A study in Boston, USA found that in room light (<200 lux), melatonin onset occurred 23 min before scheduled sleep, whereas in dim light (<3 lux), melatonin onset occurred 1 hr 57 min before scheduled bedtime ($p<0.05$). Melatonin onset was earlier in dim light vs. room light which shows that brighter room lighting late in the evening suppresses the onset of melatonin synthesis, shortening melatonin duration by about 90 min in turn reducing the pre-sleep levels of melatonin by 71.4% and total daily levels of melatonin by about 12.5%. When room light exposure continues for the entire night, total daily melatonin is suppressed by more than 50% in most individuals (Gooley *et al.*, 2011). Wood *et al.* (2013) found compared to the orange-tinted glasses (blue-blocking), melatonin suppression was 7% by the tablet only condition, and 48% by the blue light condition. These studies all acknowledge that use of electronic devices and our bright room light exposure prior to sleep may result in disrupted sleep by significantly impacts on an individual's alertness and circadian rhythm.

A systematic review examined the association between time spent on different screens and a number of sleep outcomes including, sleep timing, duration, quality, onset latency and daytime tiredness. 76% of studies found an adverse association between television watching and adverse sleep outcomes, such as delayed bedtime and shorter total sleep time. 94% of studies found an association between computer use and at least one of the sleep outcomes. 86% of studies found an association between video games use and sleep patterns such as delayed bedtime and reduced total sleep time. 83% of studies found an association between mobile phone use and at least one sleep outcome. Adolescents mobile phone use at bedtime reduced sleep time by an average of 21 minutes in one study, and in another sleep was reduced by 45 minutes. TV watching was least likely to have an adverse association with sleep and this is likely due to the passive nature of watching TV in comparison with active screen use such as mobile/computer use. The systematic review however concludes that without a control group it is not possible to confirm if the association is causally linked, and a gold standard method to assess the effect would be via an intervention study using actigraphy to monitor sleep behaviours, rather than self-report (Hale and Guan, 2015).

Now that this literature review has discussed how light exposure impacts on circadian rhythms and sleep quality, it is time to discuss the relationship between sleep (and hence circadian rhythms) and myopia. There have been several recent studies suggesting a

relationship between the two leading researchers to question, could disrupted circadian rhythms impact on eye growth as well?

In Texas, the Pittsburgh Sleep Quality Index (an objective measurement of sleep quality) identified significantly poorer self-reported sleep quality metrics for myopic adults (Abbott, Queener and Ostrin, 2018). Part of the Korea National Health and Nutrition Examination (KNHANE) survey found that the odds of myopia were 41% less in adolescents with >9 hr of sleep compared with those with <5 hr of sleep after adjusting for other factors, and they also found that the risk for myopia was decreased by 10% per hour increase in sleep per night. But they found no association between high myopia and sleep duration after adjustment for other factors. These results indicate that chronic sleep deprivation in adolescents is associated with the extremely high prevalence of myopia in Korea (Jee, Morgan and Kim, 2016). In Tokyo grouped subjects into myopes (−5.75D to −0.50D), high myopes (≤-6.00D) and non-myopes (−0.25D to + 2.75D). The Pittsburgh Sleep Quality Index (PSQI) was used, and it was found that the children with high myopia had the worst PSQI scores. This correlation with sleep was lost among the adults. Poor sleep quality was significantly correlated with myopic refractive error with the high myopes most affected, they had the shortest sleep duration, latest bedtime, as well as the lowest subjective sleep score in PSQI (Ayaki *et al.*, 2016). In Beijing, China, Gong *et al.* (2014) found the prevalence rate of myopia was 68.45% in children who slept <7 hours, and 34.8% in children who slept >9 hours. The researchers found that myopia was associated with near working distance and hours spent studying as well as parental myopia. There was no significant relationship between myopia and time spent on sport, TV, or on computer use. Xu *et al.* (2017) reported that the more sleep a school-aged child got, the lower the prevalence of myopia. The researchers found that every point increase in sleeping time shifted refraction by 0.09 D less myopic ($p<0.001$) and the association with myopia was independent of near work and hours of sport per day. All four studies were limited due to the lack of cycloplegic refraction which may have overestimated the prevalence of myopia, the use of questionnaires which can be subject to recall bias, and perhaps most importantly, the duration of outdoor activity/sunlight exposure and near work which were not evaluated in these studies meaning their relative contribution to the presence or magnitude of myopia could not be assessed. The findings of these studies provide evidence of an association between disrupted circadian rhythm and myopia which warrants further investigation.

The Guangzhou Outdoor Activity Longitudinal Study used the Children's Sleep Habits Questionnaire (CSHQ) to elicit details about 9-year-olds sleep quality and the association between cycloplegicly measured refractive error, alongside assessment of time spent on after-school activities including cram schools and outdoor activities found that both bedtime resistance and parentally reported poor sleep were significantly higher for myopes than non-myopes. However, the mean total score of the CSHQ was not significantly different for myopes vs non-myopes (Zhou *et al.*, 2015). Pan *et al*. (2019) found a myopia prevalence of 29.5% and used a propensity score matching analysis technique to suggest that there may not be any real association between disordered sleep and myopia, however, the prevalence of disordered sleep was 78.3% in this cohort.

An interesting study on parental attitudes towards children's visual care and risk of myopia found, that by ensuring sufficient sleep for their children, parents can reduce the risk of childhood myopia, as those children who had a long enough night's sleep were less likely to be myopic (Zhou *et al.*, 2017). In contrast to these findings, a study found that the duration of sleep per day was significantly associated with the presence of myopia and found that those who slept for >8 hours per day were at a greater risk of developing myopia (Binu *et al.,* 2016*)*. Such findings could imply that longer sleeping hours might not necessarily be indicative of good sleep quality.

A study of medical students in India found that 48.3% had myopia and the prevalence of myopia was significantly higher in those who read at night and slept after 12am, and total sleep time was shorter in myopes than non-myopes (5.9 vs 6.8 hours) (Patel, Desai and Ramavat, 2019). In Shenyang, China, an intervention study with participants aged 6-14-years old found that those with a longer sleeping duration had less myopic refractive change, as well as less axial growth among non-myopic children (Hua *et al.*, 2015). The Anyang Childhood Eye Study by Wei *et al.* (2020) examined 5-6-year olds annually and found that sleep duration was not significantly associated with baseline cycloplegic refractive error, axial length, myopia progression or axial elongation. When the results were split by sex, the girls demonstrated decreasing myopia progression and axial elongation with increased sleep duration, but the boys did not.

The Role of Outdoor Activity in Myopia (ROAM) study objectively measured participants (aged 10-15-years old) sleep using Actiwatch 2 devices on two occasions over a 12-month period for 14-day periods, approximately six months apart. The

participants were classified based on their non-cycloplegic SER at their first study visit as being either myopic (≤–0.50 D), or non-myopic (+1.25 to –0.50 D). Myopes slept 28 minutes more than non-myopes on shorter/cooler days (p=0.01). A significant difference in latency between refractive groups was only observed on weekends, with myopes demonstrating a shorter sleep latency than non-myopes (8.77 vs 17.60 minutes, p=0.005). Sleep efficiency was higher in myopes than non-myopes, but the difference was only approaching statistical significance (p=0.05). The model revealed that time spent outdoors was significantly associated with sleep duration (p= 0.03), and that mean daily physical activity was significantly associated with wake time (p<0.001). Neither refractive error change nor axial elongation over the 12-month period were correlated with any of the sleep parameters tested (all p> 0.05). Sleep latency refers to the duration of time between when the lights are turned off and when the child fell asleep. Shorter sleep latencies have been associated with greater sleep debt and sleep deprivation. Of interest, myopic children in this study showed significantly different sleep duration across days, as well as seasons, whereas non-myopic children showed more consistent sleep durations. Considering the significant effects on sleep duration and wake time, time outdoors and physical activity may be important meditators of sleep for children. Further investigation is warranted to understand the impact and mechanism of associations between myopia and sleep (Ostrin *et al.*, 2020).

Some studies have begun examining the relationship between sleep and myopia by using clinical biomarkers for circadian rhythms including circulating and salivary melatonin/dopamine levels. Ulster University's research group in Northern Ireland assessed circulating serum concentrations of melatonin and dopamine from fasting blood samples and found that adult myopes exhibited significantly higher melatonin concentrations than non-myopes at phase 1 and at phase 2. Although myopes also exhibited significantly lower dopamine concentrations than non-myopes at phase 2 this association was not significant at phase 1. This shows an indication between disrupted circadian rhythms and myopia and warrants further investigation in the context of understanding the role of circadian rhythms and refractive development especially in childhood (Kearney *et al.*, 2017). Abbott *et al.* (2018) assessed myopic and non-myopic adults sleep quality and light exposure subjectively using the PSQI and outdoors questionnaire and, objectively using the Actiwatch Spectrum in Houston, Texas. The researchers also collected morning salivary melatonin samples. Increased time outdoors during the previous week was associated with higher morning melatonin concentration

but the differences between myopes and non-myopes did not reach statistical significance, even though the myopes had a trend towards higher levels of melatonin. PSQI was significantly lower for emmetropic subjects than myopic subjects indicating a tendency towards poorer sleep quality in the myopes. However, sleep times and sleep efficiency were not significantly different between myopes and non-myopes from the Actiwatch. This study was limited by a single melatonin sample at one time point, as melatonin levels are known to undergo a diurnal rhythm in which the systemic levels increase at night-time and decrease in the morning. Therefore, it would be interesting to note if the diurnal rhythm had shifted.

As most research into sleep and its relationship with myopia is recent, there are questions that remain unanswered. For example, is it possible that sleep quality is affected in myopes due to their tendency to have decreased bright light exposure during the day? Is sleep quality poorer in myopes due to their tendency to have more time spent sedentary during the day? Or, is there a possibility that myopes are using more screens before sleep or night-lights during sleep and therefore suppressing their melatonin production? Is the relationship between sleep quality and myopia casual or simply an effect of myopia?

1.5. Conclusion

This literature review has highlighted some gaps in the current field of research regarding childhood myopia. Light exposure/time spent outdoors has been proven to be protective over the development of myopia but a protective effect over the progression of myopia remains inconclusive. This emphasises the need for objective measures of light exposure/time spent outdoors in a longitudinal study design to examine this. Additionally, there is contrasting findings regarding any relationship between physical activity and myopia, whereas device-measured physical activity would help explore this further. Near work and educational pressures have long since been linked to myopia but the direction of causation is unknown. It would prove beneficial to examine young children's near viewing behaviours objectively prior to the onset of myopia, and follow-up in a longitudinal manner to determine if changes to near viewing behaviours occur prior to or after the onset of myopia. Screen time has also been criticised for the increase in myopia worldwide, however there are a lack of studies examining screen time as a separate risk factor rather than falling under the blanket of near viewing behaviours. Sleep quality and its association with myopia appears to be a new and interesting area of research, particularly in Asian countries. There have been notable differences in sleep parameters

been myopic and non-myopic children via questionnaire data, and wearable devices would enable more robust measures to examine this risk factor and the potential disruption of circadian rhythms more closely.

Chapter 2: Literature Review of Methodologies for Assessing Myopic Risk Factors

Chapter 2: Literature Review of Methodologies for Assessing Myopic Risk Factors

This chapter will briefly recap modifiable risk factors for childhood myopia. It will also describe, and critique previous methods used to measure these specified risk factors and consider potential new methods.

To date, key environmental risk factors such as such as time spent outdoors, and time spent on near vision activities have been primarily assessed using a self-report rather than objective measurements. There is currently minimal robust quantitative data including cycloplegic measures of refraction in the UK or Ireland which describe the relationship between myopia and time spent outdoors, physical activity, reading and other near vision tasks including smartphone/tablet use.

There is the need for accurate assessment into the potentially modifiable risk factors for childhood myopia and their relative contribution to the presence and magnitude of myopia. Myopia is growing worldwide, and a robust evaluation of the potential risk factors is needed to support public health advice for parents, children, and eye care professionals.

The following sections (2.1.-2.5.) will describe how the potentially myopiagenic risk factors have been assessed prior to this thesis.

2.1. Light Exposure and Time Spent Outdoors

Bright light exposure has been widely reported to have a protective effect of the development/progression of myopia (Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018). The exact mechanism by which this factor influences eye growth, and its regulation is still unknown. A number of theories have been proposed including; the release of retinal dopamine in response to sunlight inhibiting axial elongation (shown in experimental myopia), increased light intensity outdoors (leading to pupil constriction, increasing depth of focus, decreasing blur, and slowing of eye growth), low accommodative demand for distance vision when outdoors (Ashby and Schaeffel, 2010; Smith, Hung and Huang, 2012), and the optical uniformity of the outdoor environment reducing hyperopic defocus (Flitcroft, 2012).

Some studies have researched the differences in light exposure and/or time spent outdoors between the two refractive groups; myopes and non-myopes and have found that myopes spent significantly less time outdoors and have significantly different light exposure profiles than non-myopes (Read, Collins and Vincent, 2014; Ulaganathan *et al.*, 2019). There is also some evidence for disparity in the progression of myopia between different seasons with studies reporting faster myopia progression in winter than in summer (Fulk, Cyert and Parker, 2002; Donovan *et al.*, 2012; Gwiazda *et al.*, 2014; Ulaganathan *et al.*, 2019). This could be due to increased light exposure and/or time spent outdoors during the summer months, but alternatively, this disparity could be attributed to reduced time spent on near work during the school summer holidays (Donovan *et al.*, 2012; Gwiazda *et al.*, 2014).

2.1.1. Questionnaire Based Data

Questionnaires are the most used method for assessing light exposure and time spent outdoors. The recent Ireland Eye Study by Harrington *et al.* (2019) found that the prevalence of myopia was significantly was higher in those spending fewer than two hours per day outdoors during summertime ($p<0.001$), but winter daylight exposure was not found to be significantly associated with myopia, in agreement with a previous study (Ulaganathan *et al.*, 2019). The researchers hypothesised that a relationship did not exist between myopia prevalence and outdoor activities during the winter due to limited daylight hours (7-8 hours per day in Ireland), and the large overlap between these daylight hours and the 5-7 hour school day (Harrington, Stack and O'Dwyer, 2019). The Ireland Eye Study also reported that child participants (two cohorts 6-7- and 12–13-year-olds) who reported spending fewer than one hour/day outdoors and 1-2 hours/day outdoors were more myopic on average by −1.04 D and −0.41 D respectively, in comparison to children spending the most time outdoors (>4 hours per day). In comparison to participants who report spending the most time outdoors per day (> 4 hours), axial length was 0.31 mm ($p = 0.01$) longer in those with the least time spent outdoors (<1 hour per day), 0.17 mm ($p = 0.02$) longer in those spending 1-2 hours per day outdoors, and 0.12 mm ($p = 0.01$) longer in those spending 2–4 hours outdoors per day (Harrington and O'Dwyer, 2019).

Questionnaire-based assessment of time spent outdoors used in published studies require parent(s) and/or participants estimating time spent outdoors, before, during, after school

and at the weekend. Some studies have required parents and/or participants to keep a diary recording the estimated total time spent outdoors over the course of one week (Jones-Jordan *et al.*, 2012). A limitation of questionnaire-based data and self-reported time spent outdoors is that they cannot be used to estimate the intensity of light to which children are exposed, only how much time was spent outdoors.

It is now widely accepted that questionnaire data is not the most accurate way to assess daily activities as they are subject to recall bias. Alvarez and Wildsoet (2013) report that questionnaires were an unreliable and suboptimal method for estimating time spent outdoors as they generally overestimated both the time spent both outdoors and indoors in comparison to objectively measured data via sensors. In agreement with these findings, a study using adult participants found that 58% of subjects overestimated their time outdoors (by up to 4:29 hours/week) when questionnaire data were compared with objectively measured light exposure using Actiwatch 2 devices (Ostrin, 2017). Parental reports of how much time children spent outdoors was also poorly correlated to objective measures (Ostrin, Sajjadi and Benoit, 2018).

2.1.2. Objective Measures

Light exposure levels greater than 1000 lux are deemed to be outdoors and therefore protective against myopia (Lanca *et al.*, 2019). Objective measures are required to accurately distinguish how often and for how long a participant is exposed to different levels of light intensity. A recent systematic review and meta-analysis concluded that increased time outdoors should be promoted to reduce both the incidence and the progression of myopia, and the authors suggested that 10 hours/week, or 120 minutes/day of outdoors time can reduce the incidence of myopia by 63.7% in Asian populations by 0.16 D/year. However, the review concluded that more studies are required for other ethnicities to determine potential ethnic differences (Ho, Wu and Liou, 2019).

There are several recent studies in which objective light exposure was measured using wearable devices (Read, Collins and Vincent, 2014; Ostrin, Sajjadi and Benoit, 2018). From these light exposure measures, time spent outdoors was extrapolated from the amount of time spent in >1000 lux. These devices utilised for these studies include; the Actiwatch2, Actiwatch Spectrum (both Philips, NV, USA) and the Clouclip (Model F1, Patent NO.2017109797802, by HangZhou Glasson Technology Co), as well as an application (app) called FitSight, (alpha prototype app downloaded to a Sony Smartwatch

3; SonyCorp., Minato, Tokyo, Japan) for recording light levels to determine time spent outdoors (Verkicharla *et al.*, 2017).

Actiwatch devices and the FitSight app on Apple/Android watches are all wristworn light sensor devices with physical activity monitors and the Clouclip is a spectacle-mounted device. The Clouclip measures light exposure at eye level as well as the viewing distance of the wearer for near activities up to 120cm. In the past it was considered that light exposure measured at the wrist would not be correlated with eye level light exposure. However, a recent study found that the estimates of light exposure at eye and wrist level were strongly correlated, r=0.76, therefore wrist measurements were deemed representative of eye level illumination with the exception of night-time measures when wrist worn devices tend to be placed under bedcovers (Okudaira, Kripke and Webster, 2017).

In Brisbane, Australian researchers found significantly higher daily light exposure in emmetropic children compared to myopic children and reported a significant positive correlation between children's average daily light exposure and average daily physical activity level. However, the authors found no significant correlation between mean physical activity and myopia in their population. These results indicate that the main contributor to myopia prevention is light exposure, as opposed to physical activity (Read, Collins and Vincent, 2014). The same group also reported a modest but statistically significant relationship between objectively measured daily light exposure and axial eye growth in children over a 18-month period indicating a role for light exposure in controlling myopic progression (Read, Collins and Vincent, 2015).

Ulaganathan *et al.* (2019) used the Actiwatch 2 to explore light exposure and seasonal differences in axial elongation over a 12-month period and found that daily outdoor light exposure was significantly greater in young adult emmetropes (67 ± 34 min) than their myopic peers (35 ± 36 min) in summer ($p = 0.05$), but there were no significant differences in outdoor light exposure between the groups in winter. Their analyses indicated that axial elongation was slower by 0.002 mm/year for every minute per day spent in bright outdoor (>1000 lux) light levels in these young adults, equating to ~0.06 mm less annual axial elongation (or approximately 0.2 D/year less refractive progression) for each additional 30 minutes of daily outdoor light exposure (Ulaganathan *et al.*, 2019).

Wen *et al.* (2020) recruited 10-11 year old children from both an urban and a rural school in China and carried out cycloplegic autorefraction and assessment of light exposure for one week using the Clouclip. During school hours and on the weekends the rural children were exposed to significantly higher levels of light exposure than the urban children, but there were no significant differences in light exposure between the groups in the after-school period, possibly because there was less opportunity to spend time outdoors during the after-school period. The rural children also experienced longer durations exposed to bright light (>1000 lux) than the urban children. The study however failed to differentiate between refractive groups so could not report on differences in light exposure between groups.

In Singapore an app called FitSight has been developed for both Apple and Android watches and provides the means to monitor both light exposure and physical activity. The app feeds back to the wearer to enforce the attainment of set targets for time spent outdoors. When using the app to set a target of spending at least three hours outdoors per day, most wearers (children aged 6-12 years) agreed that the watch was wearable and that the app worked well in providing messages encouraging the wearer to go outdoors (Verkicharla *et al.*, 2017).

Ulaganathan *et al.* (2017) studied the impact of differing the duration and frequency of light exposure measures on the variability of results obtained on the Actiwatch 2 in children and young adults. The findings suggested that a measurement duration of at least one week and a measurement frequency of every two minutes or less provided the most reliable estimates of personal outdoor light exposure measures when compared against an assumed gold standard duration of 14-days and frequency of 30 seconds.

To date, it has not been determined whether is it the intensity, or the duration and frequency of light exposure that provides the protective effect against the incidence and/or progression of myopia. Another theory is that the visual 'diet' experienced outdoors has a protective effect over the development of myopia due to peripheral defocus (Ngo *et al.*, 2013). When outdoors the visual environment is much more optically uniform, with no significant levels of optical defocus across the visual field. However, indoors there is a wider range of hyperopic and myopic defocus across the visual field, depending on what task is being performed and essentially is never optically uniform. Indoors there is significantly more hyperopic defocus than outdoors regardless of the visual task being

performed, and hyperopic defocus is known to promote myopia development (Flitcroft, 2012). Therefore, additional studies are required in which both the intensity of the light exposure, as well as the duration and frequency of time spent outdoors are assessed in conjunction with reliable measures of refractive error, ocular biometry and refractive change and growth over time.

In summary, there are some questions remaining about the relationship between light exposure and time outdoors and myopia, including:

- **Does light exposure and/or time outdoors slow the progression of myopia, or protect against the onset of myopia alone?**
- **Is the onset and/or progression of myopia affected by seasonal changes in light exposure in different parts of the world?**
- **What is the mechanism behind the protective effect of light exposure/time spent outdoors?**

2.2. Near Activities

Increased near work in the form of reading, writing, and using laptops or handheld devices has long been linked to myopia. A number of studies have used questionnaire-based 'dioptre-hours' to describe the balance of near and distance vision activity undertaken (Mutti *et al.*, 2002). This method involves surveying parents to estimate the number of hours per week (outside of school) a child spends on four activities namely, (1) reading or studying for school assignments, (2) reading for pleasure, (3) watching television, and (4) playing video/computer games or working on the computer at home. These activities are analysed separately and as a composite variable for near work weighted by the dioptric equivalent of an assumed working distance for the four activities reported on. Dioptre-hours are defined as follows:

Dioptre hours = 3 × (hours spent studying + hours spent reading for pleasure) + 2 × (hours spent playing video games or working on the computer at home) + 1 × (hours spent watching television).

The advantage of this method is the ability to estimate near work in terms of time and accommodative effort required for common childhood activities (Zadnik *et al.*, 1994). The main disadvantage, as with all methods which rely on parental report is that they are

subject to recall bias, but another disadvantage is that near work during school time is not quantified by parents in this paradigm.

2.2.1. Near Working Distance

A short near working distance has been linked with myopia (Haro, Poulain and Drobe, 2000; Ip *et al.*, 2008; Lu *et al.*, 2009), but to date it is unknown whether or not this link is causal, or whether myopic children reduce their working distance in response to the development of their myopia. Increased amounts of time spent in near vision activities may be a consequence of myopia development, rather than being causative as uncorrected myopia may make extended periods of near work more visually comfortable than distance tasks and allow myopes to comfortably spend more time in near vision pursuits than their non-myopic peers who require more accommodative effort for such activities. A literature review by Morgan *et al.* (2020) concluded that longitudinal studies were necessary in order to verify whether the close working distances evidenced in association with myopia were adopted prior to, or in conjunction with, the development of myopia. The authors also highlight the need for further assessments evaluating the efficacy of controlling reading distance for as a method of restricting myopia progression.

Many studies use parental report of near working distance in their analysis which, as for all self- or parent-reported data, could be subject to recall bias. Another limitation of parental reported studies is the variability which exist in the study co-ordinators definition of a 'close' working distance, ranging from definitions of less than 20, 25 or 30 to less than 33cm.

To date, two methods of objectively measuring subjects near working distances have been adopted by previous studies. We will describe the mechanics of these devices further in section 2.7. of this chapter. The first method was via a Fastrak electromagnetic motion-tracking system which, when applied to a group of 6-13-year-old myopes (n=120), recorded average near working distances of 27.2 cm and 24.9 cm for reading and writing respectively and identified that working distances decreased further when playing video games (21.3cm). The working distance decreased as attention and concentration increased. This study highlighted that myopes typically have a closer working distance than the traditional near point distance (33 cm) used to assess near vision function (e.g. near visual acuity and Amsler assessment of the macula) in ophthalmic examinations worldwide (Bao *et al.*, 2015).

Another relatively new alternative method for quantifying near viewing distance is the Clouclip, a wearable spectacle mounted device which measures the near working distance by a built-in infrared distance sensor and also records light exposure by using a light intensity sensor (Wen *et al.*, 2016).

2.2.2. Near Work Time

Traditional near work activities include, schoolwork, homework, reading/writing for pleasure, colouring in, crafts etc. More recent additions to near work activity are phone, tablet, or smartwatch use. Traditional near work activity can only realistically be assessed with the use of questionnaire-based data and occasionally via an activity diary, with both methods being subject to recall bias. In relation to monitoring near work activity, the most common questionnaire items include; the number of books read per week (Saw *et al.*, 2002; Konstantopoulos, Yadegarfar and Elgohary, 2008; Williams *et al.*, 2018), the amount of time spent continuously reading (Saw *et al.*, 2007; Ip *et al.*, 2008), and dioptre-hours calculations (Mutti *et al.*, 2002; Jones-Jordan *et al.*, 2012; French *et al.*, 2013; Huang, Chang and Wu, 2015).

The majority of published studies have identified strong links between increased near work activity and myopia (Zylbermann *et al.,* 1993; Mutti *et al.*, 2002; French *et al.*, 2013; Saxena *et al.*, 2015; Bez *et al.*, 2019; Guan *et al.*, 2019; Harrington, Stack and O'Dwyer, 2019) however, a number of studies found that increased near work does not remain an independently associated with myopia after controlling for other variables such as the time spent outdoors (Konstantopoulos, Yadegarfar and Elgohary, 2008; Jones-Jordan *et al.*, 2012; Lin *et al.*, 2014). A Sydney based study by Rose *et al.* (2008) found a significantly higher myopia prevalence in East Asian children living in Singapore compared to those living in Sydney (29.1% and 3.3%, respectively). The East Asian children in Sydney spent 14 hours per week outdoors in comparison to three hours per week outdoors by their contemporaries in Singapore. Children living in Sydney were reported to be undertaking a greater amount of near vision activities than those in Singapore, indicating a protective effect of time spent outdoors, even in the presence of increased time spent in near work.

A systematic review and meta-analysis by Huang *et al.* (2015) recommended that additional longitudinal and randomized controlled trials should be performed to confirm

whether near work is a risk factor for the development of myopia (Huang, Chang and Wu, 2015). The researchers reported that the association between near work and myopia indicated a 2% increased odds of myopia per additional dioptre-hour of time spent on near work per week and that myopic children spend more time reading for pleasure than non-myopes. However, there was no significant difference in time spent studying, watching TV, or using a computer between the myopes and non-myopes.

In summary, there are some unanswered questions regarding the associations between near work and myopia, including:

- **Is increased near work activity an independent risk factor for myopia after accounting for time spent outdoors?**
- **Is there evidence for a difference between the effect of traditional near tasks on myopia in comparison to screen time based near tasks?**
- **What is the mechanism behind the association between near activity and myopia?**

2.3. Screen Time

Screen time describes time spent on handheld electronic devices such as smartphones and tablets as well as time spent on computers or laptops, and time spent watching TV. It is important to note that from previous studies there is inconsistent evidence for computer usage as a risk factor for childhood myopia (Lanca and Saw, 2020). However, the lack of consistent association between time spent on computer and myopia applies to the use of a desktop computer/laptop. In recent years, screen time also relates to the use of smartphones and tablets, which are held at a much closer working distance than laptop and desktop computers (Liu *et al.*, 2019). While the rise in popularity and access to handheld screens led the public and media to draw conclusions about a link to childhood myopia, the limited time during which digital handheld devices have been available limit the strength of the available evidence (Lanca and Saw, 2020).

Electronic devices have become an integral part of childhood in the 21st Century, both in an educational setting and for leisure purposes. Therefore, it is important to scrutinise whether handheld electronic devices constitute a modifiable risk factor for myopia. There is currently a lack of research and knowledge evaluating links between the use of handheld electronic devices and myopia as these devices are relatively new and have grown considerably in popularity in the past decade. There is a tendency of handheld

device users to adopt a close working distance (Bababekova *et al.*, 2011; Yoshimura *et al.*, 2017), and use devices for extended periods of time (Morgan, French and Rose, 2020). The combination of close working distance and extended periods of use raise a concern in relation to myopia because of the proposed link between extensive near work and childhood myopia.

Nonetheless, it is also possible that screen time could be an independent risk factor for myopia due to the blue light from the handheld devices before sleep suppressing melatonin production and subsequently delaying sleep onset, therefore disrupting circadian rhythms. Some studies have used blue blocking filters (Leger *et al.*, 2019) and a comparison between LED backlit and non-LED screens (Cajochen *et al.*, 2011) to investigate the effect of blue light on melatonin production. The findings were that the suppression of melatonin was significantly reduced, sleep duration was extended, sleep onset was earlier and sleep quality was improved with blue blocking filters when compared to no filters (Leger *et al.*, 2019), and that the LED screen supressed melatonin more, sleepiness was decreased and cognitive performance increased in comparison with the non-LED screen (Cajochen *et al.*, 2011). Therefore, it is important to determine whether the use of handheld devices is a risk factor for myopia and if this is simply by falling under the blanket of near work as whole, or as an independent risk factor for myopia.

As shown by Bullimore *et al.* (1992) a change from passive viewing (e.g., reading or scrolling on social media) to active viewing (e.g., watching a video or playing a game) requires a significant cognitive-induced increase in accommodative response over a range of viewing distances. The authors also found that myopes have a significantly lower accommodative response than emmetropes when in the passive condition, also known as accommodative lag. Other researchers report that accommodative lag is a feature rather than a cause of myopia as lags are not evident until after the onset of myopia (Mutti *et al.*, 2006). Bhandari and Ostrin (2020) examined viewing distances and viewing patterns on adult participants. The authors reported mean viewing distance for passive printed tasks was 33.2 cm, for active printed tasks was 29.5 cm, for passive electronic tasks was 40.8 cm, and for active electronic tasks was 35.4 cm. The findings were that viewing distances were closer for active tasks versus passive tasks, and participants tended to take fewer breaks (looking at a distance >1 metre) when using electronic devices as opposed to using printed materials. This further supports the theory that handheld electronic

devices such as smartphones and tablets are being used for longer periods of time than printed materials, hence increasing the accommodative demand.

The recent Ireland Eye Study (IES) reported an increased risk of myopia with increased time spent on all types of screens via questionnaire data. They found that in children aged 6-7-years old myopia prevalence increased five-fold from 3.0% amongst those who reported <1 hour of screen time per day group to 15.5% in the group who reported using screens for >3 hours per day (Harrington, Stack and O'Dwyer, 2019). A Chinese study with 59.2% of 6-14-year-olds being myopic, found that the use of electronic devices was not associated with the prevalence of myopia. However, the authors reported that children who spent more time using smart phones and computers had higher levels of myopia and longer axial lengths but, time spent on tablets or watching TV were not associated with the participants refractive error or axial length (Liu *et al.*, 2019). Nonetheless, two recently published viewpoints proposed the theory that increased screen time is simply a surrogate for less time outdoors and/or more sedentary time, and that it is the societal shift to indoor activities while using these devices that is leading to a worldwide increase in myopia prevalence (Dirani, Crowston and Wong, 2019; Zadnik and Mutti, 2019).

As discussed, there are conflicting findings which regards to the impact of screen use on the prevalence or progression of myopia. The previously mentioned systematic review by Lanca and Saw (2020) concluded that further studies incorporating objective measures of screen time were warranted. Another literature review by Morgan *et al.* (2020) established that there is currently no evidence to suggest that use of digital devices increases the likelihood or risk of the development or progression of myopia in comparison to, for example, reading a book for the same length of time. However, the authors acknowledge that digital devices are increasing the appeal of near work activities and indoor lifestyles.

At present, most studies use questionnaires/diaries for self-reporting screen time usage (Lanca and Saw, 2020). However, since the majority of screen time usage by children and young adults is now performed on smartphones or tablets, researchers can benefit from the use of screen time monitoring apps to access objective measures of participants' screen usage patterns. On the other hand, a diary or questionnaire remains the most viable option for assessing time spent on computers, laptops, or TV. A study in Taiwan on young adults' usage of a smartphone screen time monitoring app alongside self-reported screen time, found an average daily usage on the app of 4.20 hours and weekly usage of 29.39

hours. By contrast, the self-reported screen time was significantly lower (20.11 hours per week). The study also found that participants who spent the greatest time on smartphones had the greatest discrepancy between the objective measures and self-reported screen time usage, consistently underestimating their screen use (Lin *et al.*, 2015).

One limitation to self-reported screen time measures could be the growing negative attitude towards screen time which could potentially encourage participants and parents to underestimate and under-disclose the full extent of screen usage due to fear of judgement. Some examples of appropriate apps for commonly used smartphones/tablets include, 'Moment- Screen Time Control' (Moment Health Inc) and 'Apple Screen Time' (Apple Inc) on iPhone/iPad devices and 'Quality Time My Digital Diet' (ZeroDesktop Inc) on Android devices. The use of these apps alongside a near viewing distance monitor like the Clouclip could enable researchers to tease out time spent in near viewing of smart technology from that spent on more traditional near vision tasks such as reading and writing, providing an opportunity to differentiate between the two types of near vision task to determine independent associations.

A study in the US by Christensen *et al.* (2016) into the relationship between adults' screen time usage and mood, physical activity and sleep quality found that increased screen time was statistically significantly associated with reduced sleep efficiency and shorter sleep durations but not associated with mood or levels of physical activity. The exposure to blue light from backlit screens has been proposed to suppress the production of the sleep-promoting hormone melatonin, thereby delaying sleep onset, and reducing sleep duration and sleep quality. However, the authors of the study noted that they could not exclude "effect-cause" i.e., poor sleep could encourage increased used of screens. These findings present another possible mechanism for screen time and a potential association with myopia, via an interruption of the body's circadian rhythms.

In summary, there are some questions that remain to be answered with regards to increased screen time and its potential effect on myopic eye growth, including:

- **Does the effect of screen time on myopic eye growth differ to time spent on traditional near vision tasks?**
- **Is increased screen time linked to myopia due to the interruption of circadian rhythms when using backlit electronic devices immediately before sleep?**

- **Is increased screen time simply a surrogate for increased time spent in a sedentary state or reduced time spent outdoors, both of which have been previously reported risk factors for myopia?**
- **Is it possible that the active nature of some screen use affects the accommodative effort when compared to some passive traditional near tasks, and could the nature of the task have a differential impact on the risk of myopia?**

2.4. Physical Activity Levels

2.4.1. Questionnaire Data

There have been conflicting reports over whether physical activity (PA) influences the development and progression of myopia in recent years. It is widely appreciated that higher levels of physical activity have benefits for systemic health and physical wellbeing, and that too much sedentary behaviour can cause several adverse health outcomes. However, little is known about the relationship between PA and the regulation of eye growth. To date there have been a few different ways that researchers have assessed children's PA in relation to refractive error; the most common methods being parent- and/or child-reported questionnaires, interviews, or diaries.

One such study is the Northern Ireland Childhood Errors of Refraction (NICER) study 1.0, where the researchers discovered that in 12-13-year old children, self-reported, 'regular' PA was significantly associated with a lower prevalence of myopia compared to the prevalence of myopia measured in children leading more sedentary lifestyles (O'Donoghue *et al.*, 2015). The Ireland Eye Study used an identical sampling framework to that used by the NICER study and the authors reported that the prevalence of myopia in 6-7-year-olds with predominantly sedentary lifestyles was 8.1% but this dropped to 3.1% for those 6-7-year-olds involved in regular after-school PA. This trend was also present in the 12-13-years old cohort, in which 35.2% of participants with sedentary lifestyles were myopic, with the prevalence decreasing to 14.4% among participants involved in regular after-school PA (Harrington, Stack and O'Dwyer, 2019).

The major limitation in most studies investigating the association between PA and myopia is failing to differentiate between indoor and outdoor PA (Khader *et al.*, 2006; Jones-Jordan *et al.*, 2011; Theophanous *et al.*, 2018). Lower levels of PA could primarily be a surrogate for increased time spent indoors and less time spent outdoors, with time

spent outdoors having been found to have a protective effect on the development of myopia (Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018). A consideration for future studies should be the importance of separating PA and time spent outdoors to assess whether PA is independently associated with myopia.

2.4.2. Objective Data

Objective measures of PA can be recorded with the use of accelerometers or via a physical fitness test. Widely used devices that have been used to measure PA include, Actiwatch2, Actiwatch Spectrum, Actical (all 3 Phillips, NV, USA), and Actigraph (Pensacola, Florida). Section 2.7. of this chapter will be used to explain each device in more detail.

Accelerometers are used to measure both PA and sleep through assessment of gross motor activity. A core accelerometer is typically worn around the waist for accurately predicting energy expenditure, while an accelerometer worn on the wrist uses smaller movements of the wrist to classify time asleep and awake. Rowlands (2007) determined that accelerometer devices are a feasible method of assessing PA, particularly when assessing children's PA, due to the sporadic nature of their activity patterns. Data output from accelerometers allow the analysis of PA beyond total or mean activity alone, e.g., they allow the categorization of type of activity- sedentary all the way to vigorous PA, as well as the timing of PA.

Two literature reviews on the use of accelerometers to measuring children's PA specifically note the importance of short recording epochs (<1 minute), which allow capture of short bursts of moderate-vigorous activity, and help to properly estimate PA in this age group (Trost, McIver and Pate, 2005; Rowlands, 2007). One review also recommended that a 4-5 day monitoring protocol for children was sufficient as children exhibit less day-to-day variability in daily habitual PA than adolescents (Trost, McIver and Pate, 2005). Herrmann *et al.* (2014) also determined that a wear time of more than 12 waking hours per day was necessary to ensure accurate reflection of an individual's PA.

Muhamedagić *et al.* (2013) assessed myopic university student's PA with both questionnaires and a fitness test, and their cycloplegic autorefraction was assessed at baseline and a year later. The authors report that in this cohort of young adults, those with

greater physical competence and more active PA levels had less myopic shift over 12 months than those with less physical competence and less active PA levels. The authors concluded that higher levels of PA were linked with less myopia progression. However, this study did not control for time spent outdoors which could also have the protective effects of myopic progression.

In Australia, researchers found a significant association between average daily light exposure and children's average daily PA level, indicating a tendency to perform PA when outdoors. However, there was no significant association between PA and myopia in these 101 10-15-year old children (Read, Collins and Vincent, 2014). The authors suggest that a lack of association between PA and myopia indicates that increased light exposure was the significant variable influencing the incidence of myopia rather than the level of PA.

The Avon Longitudinal Study of Parents and Children (ALSPAC) study based in the UK assessed the PA of 4880 children via accelerometers when they were 12-years old. The authors found that non-myopes have significantly higher levels of moderate-vigorous PA in comparison with their myopic peers, with myopes spending more time in a sedentary state (Deere *et al.*, 2009).

A recent systematic review concluded that while there was evidence of a slight association between PA and myopia, more studies are required which concentrate on objective measurements of PA alongside a robust evaluation of childhood refractive status (Suhr Thykjær, Lundberg and Grauslund, 2017). The authors also suggest that future studies should clearly distinguish between the PA and outdoor light exposure to further explore the association between PA and myopia.

In summary, the questions that remain unanswered in relation to physical activity and myopia include:

- **Does physical activity remain an independent risk factor for myopia after distinguishing between physical activity and time spent outdoors?**
- **Are objectively measured higher levels of physical activity protective against the onset of myopia in the same way that they are protective against other systemic health problems?**

2.5. Circadian Rhythms and Sleep

Circadian rhythm is also known as the body's natural biological clock. The human biological clock has a period of approximately 24-hours and is generated by autonomous cell-based molecular timing mechanisms known as circadian clocks. Circadian clocks regulate daily rhythms of sleep and alertness, blood pressure and heart rate, locomotor activity, hormone secretion, body temperature, metabolism, and many other physiological processes. Most of these rhythms are controlled directly or indirectly by the 'master clock' in the suprachiasmatic nuclei (SCN) of the hypothalamus which receives direct input from retinal photoreceptors (Klein et al., 1992). Light is the most important Zeitgeber for regulating circadian activity. A Zeitgeber is an environmental agent that provides the cue for setting or resetting a biological clock, promoting a 24-hour cycle. Light activation of the intrinsically photosensitive retinal ganglion cells (ipRGCs) in the retina supresses the secretion of the circadian hormone, melatonin, by the SCN and conversely, during night-time, melatonin secretion is promoted by low light levels. With known relationships between light exposure and the release of melatonin, and increasing evidence that light exposure is protective for myopia, speculation exists regarding whether melatonin and circadian rhythms may also play a role in refractive error development (Chakraborty *et al.*, 2018). Melatonin is considered a robust biomarker of circadian rhythm and sleep quality and quantity, both of which are outputs of the circadian system and have been used as indicators of circadian rhythm.

2.5.1. Questionnaire Data

Part of the Korea National Health and Nutrition Examination (KNHANE) Survey of 3625 12–19-year-olds, without cycloplegia, found that the odds of having myopia were 41% less in adolescents reporting an average of >9 hours of sleep compared with those reporting <5 hours of sleep, after adjusting for other factors including age, education level, economic status, and physical activity. Jee, Morgan and Kim (2016) also found that the risk of being myopic decreased by 10% per hour increase in sleep per night. They report that high myopia (defined as ≤−6.0 D) was not associated with sleep duration, after adjustment for these factors. These findings indicate that chronic sleep deprivation in Korean adolescents is associated with myopia in Korea (Jee, Morgan and Kim, 2016). Light exposure or time spent outdoors were not examined in this study.

The Pittsburgh Sleep Quality Index (PSQI) has been widely used in many sleep studies and more recently in refractive error studies to subjectively determine sleep quality. One

such study by Ayaki *et al.* (2016) in Tokyo evaluated sleep quality in myopic and non-myopic adults and children aged 10-59-years old. The subjects were grouped into myopes (−5.75D to −0.50D), high myopes (≤-6.00D) and non-myopes (−0.25D to + 2.75D). The researchers found that children with high myopia had the highest PSQI scores, translating to the poorest sleep quality. However, no correlation was found between sleep quality and refractive error amongst adult participants. The children's sleep quality was significantly correlated with myopic refractive error, with high myopes most affected. The high myopes displayed the shortest sleep duration, latest bedtime, as well as the poorest subjective sleep score in PSQI (Ayaki *et al.*, 2016). This study did not control for near work or outdoor activity, and cycloplegic refraction was not performed on all participants.

In Beijing, China, researchers found that the prevalence rate of myopia was 68.45% in children (aged 7-18-years) who slept <7 hours on average in the month previous, dropping to 34.80% in children who slept for >9 hours on average by parental report (Gong *et al.*, 2014). They also found that for every hour increase in sleeping time, there was a 0.09 D shift in refraction toward less myopic values ($p<0.001$). Researchers found that sleep duration was independently associated with myopia independent of the parental-reported hours per day of near work and of sport. The authors concluded that this association between sleep duration and myopia needed further investigation in studies to distinguish any cause-effect relationship (Gong *et al.*, 2014; Xu *et al.*, 2017). These studies used non-cycloplegic refraction and did not control for amount of outdoor activity.

As previously mentioned, all the studies discussed above included non-cycloplegic refraction, which may have overestimated the prevalence of myopia by not controlling accommodation with cycloplegia. In addition, the amount of near work, outdoor activity and sunlight exposure were not evaluated in all studies. Therefore, the relative contribution of these risk factors to the presence or magnitude of myopia could not be assessed.

2.5.2. Objective Data

Objective data on circadian rhythms in relation to sleep can be gathered using accelerometer devices which measure several sleep parameters such as bedtime, get up time, total time in bed, total sleep time, sleep onset, minutes spent awake during the night, sleep efficiency and awakenings after sleep onset. Another objective method for

assessment of circadian rhythms is using clinical biomarkers including, measuring circulating and salivary melatonin and/or dopamine levels.

Kearney *et al.* (2017) assessed circulating serum concentrations of melatonin and dopamine from fasting blood samples and found that adult myopes exhibited significantly higher melatonin and lower dopamine concentrations than non-myopes. These findings indicate an association between disrupted circadian rhythms and myopia. They did however acknowledge that the findings warranted further investigation. This is due to some limitations from the investigation, namely, serum was collected at two time points, but both were in the morning, and sleep patterns, time spent outdoors, and menstrual cycles were not controlled for which could all impact on the levels of serum melatonin and dopamine. Therefore, the authors could not conclude if the difference between refractive groups was phasic, as the entire day was not profiled, and the other factors not examined could have had bearing on the magnitude of this difference. The authors concluded that measures of serum melatonin and dopamine from children would prove valuable in order to ascertain any link between disrupted circadian rhythm and the incidence or progression or myopia, or to clarify if the difference appears after the onset of myopia (Kearney *et al.*, 2017).

In Texas, researchers measured adult morning saliva melatonin levels and subjectively assessed sleep quality and light exposure using the Pittsburgh Sleep Quality Index (PSQI) and a questionnaire (Abbott, Queener and Ostrin, 2018). Sleep quality and light exposure were also assessed objectively using the Actiwatch Spectrum on both myopic and non-myopic adults. Increased time outdoors during the previous week was associated with higher morning melatonin concentration but the melatonin differences between the refractive groups were not significantly different, even though the myopes had a trend towards higher levels of melatonin. However, melatonin levels were assessed from saliva rather than serum, and the authors reported that saliva measures demonstrate more variability. Some studies have shown that the proportion of salivary melatonin decreases as the proportion of serum melatonin increases in those individuals with lower serum melatonin concentrations, and therefore the melatonin concentration measured in saliva may not consistently reflect the serum melatonin concentration, although the correlation between the two methods increases as serum melatonin levels increase (Laakso *et al.*, 1990; Gooneratne *et al.*, 2003). Abbott *et al.* (2018) found that PSQI scores were significantly lower for emmetropic subjects than myopic subjects indicating that the

myopes tended to have poorer subjective sleep quality. Despite this self-reported difference between myopes and non-myopes in terms of sleep quality, the objectively measured sleep duration and efficiency by the Actiwatch did not differ significantly between myopes and non-myopes.

Christensen *et al.* (2016) examined the relationship between adults' screen time usage and mood, physical activity and sleep quality and they found that increased screen time was statistically significantly associated with reduced sleep efficiency and shorter sleep durations but not associated with mood or levels of physical activity. The exposure to blue light from backlit screens has been proposed to suppress the production of the sleep-promoting hormone melatonin, thereby delaying sleep onset, and reducing sleep duration and sleep quality. However, the authors of the study noted that they could not exclude "effect-cause", i.e., poor sleep could encourage increased used of screens. This study highlights a modern-day potential cause of poor sleep, and potential subsequent interruption to circadian rhythm.

A literature review by Hale and Guan (2015) concluded that a gold standard method to assess the effect of screen usage on sleep quality would be via an intervention study using actigraphy to monitor sleep behaviours rather than self-report. This conclusion could also be applied when investigating any potential relationship between refractive error and sleep quality.

Further research is still required to investigate the currently speculative link between melatonin, circadian rhythm and eye growth in human myopia, and whether this relationship is part of the pathway through which light exposure has a protective effect on the development and progression of myopia (Ostrin, 2019). Currently there are no published studies exploring the association between objectively measured sleep parameters and refractive error in myopic and pre-myopic children. Studies investigating childhood myopia and its relationship with sleep have all utilised questionnaires and data are therefore subject to recall bias. In addition, those studies into sleep and childhood myopia have not undertaken the examination of refractive error using the gold standard cycloplegic refraction therefore they could be overestimating the prevalence of myopia by failing to control participants accommodation.

In summary, some of the unanswered questions that remain regarding the association between sleep and myopia include:

- **Is sleep quality reduced in myopes due to decreased bright light exposure during the day?**
- **Is sleep quality affected using screens before bedtime via inhibiting the release of melatonin?**
- **Is the link between poor sleep quality and childhood myopia causal, or simply correlated?**

2.6. Methods which could be used to Evaluate Modifiable Environmental and Lifestyle Risk Factors for Childhood Myopia

2.6.1. Clouclip

Figure 2.6.1. Clouclip attached to a pair of spectacles. Image from http://www.clouclip.com

The Clouclip M2 (Glasson Technology Co. Ltd., Hangzhou, China) is a relatively new device developed to quantify near working distances and light exposure at eye level. The Clouclip has a built-in infrared distance sensor (ranging from 5-120cm) and light intensity sensor (ranging from 1−65536 lux) used to measure near viewing distance and ambient light intensity, respectively. The Clouclip device is attached to the right side of the participant's spectacles and records near viewing distance every five seconds and ambient illuminance every two minutes. The infrared distance sensor emits an infrared beam and receives the reflected signal. The sensor then processes the time difference between transmission and reception of the infrared signal to calculate the working distance of a near object. The Clouclip is also equipped with a three-axis accelerometer (X, Y, Z axis) to distinguish when it is worn or not. If the triaxial accelerometer does not detect any movement for more than 40 seconds, the Clouclip enters "sleep mode" and no data are recorded. The data collected by Clouclip are stored in the internal memory of the device and then sent to the cloud platform via a smartphone application (Wen *et al.*, 2020). A previous study showed that the Clouclip is highly accurate when compared to

actual measures, with good repeatability for measurements of light intensity and near viewing distance (Wen *et al.*, 2016).

Bhandari and Ostrin (2020) also assessed the correlation between the actual working distance and the near viewing distance recorded by the Clouclip at a range of different distances and found the two measures to be highly correlated ($r=0.996$, $p<0.001$). The study also reported that the light exposure measurements recorded in lux from the Clouclip were highly correlated to that measured with a lux meter ($r=0.96$, $p<0.001$), and that the Clouclip was able to accurately distinguish between indoor (<1000 lux) and outdoor (>1000 lux) environments (Bhandari and Ostrin, 2020).

2.6.2. Daysimeter

Figure 2.6.2. Daysimeter mounted via a headband. Image from https://www.newswise.com/articles/media-article/525641

The Daysimeter is a head-mounted device with two eye level photosensors for measuring photopic light and 'blue' light (wavelengths shorter than 570nm only The Daysimeter measures illuminance at the eye at light levels from 1 lux to more than 100 000 lux and spectrally weighted blue radiation at the eye over a similar dynamic range, enabling measurements both indoors and outdoors (Bierman, Klein and Rea, 2005). However, researchers found the Daysimeter to be cumbersome and uncomfortable for the adult participants to wear (Jardim *et al.*, 2011), giving rise to concerns about compliance and participation rates in studies involving children.

2.6.3. Fastrak

Fastrak (Polhemus, USA) is an electromagnetic motion-tracking system which is commonly used for near posture measurements (Bao *et al.*, 2015). The Fastrak tracking system uses electromagnetic fields to determine the position and orientation of an object. This device is composed of an emitter and several receivers. One receiver is attached to the head of the participant by means of a headband, and the others can be fixed to the task materials (reading and writing materials for example). This device allows complete freedom of movement throughout the near tasks. Working distance is defined as the distance from the base of the participants nose to the centre of each line (for reading or writing) or to the centre of the screen (for a handheld screen). Head declination is defined as the angle in the sagittal plane between the head and the vertical upright position. However, this device would need to be used in the presence of the researcher to attach the receivers to task materials, therefore is not a practical option for research in free-living settings.

2.6.4. Actigraph

Figure 2.6.3. Image of an Actigraph with a wrist strap. Image from https://www.actigraphcorp.com

Actigraphy is a non-invasive, cost-effective method of monitoring human rest/activity cycles and is also used to study sleep/wake patterns. Actigraph (Pensacola, Florida) manufacture some of the most widely used commercially available accelerometer devices which have been frequently used in physical activity (PA) research since the 1990s. Researchers in laboratory and field-based studies have used Actigraphs to derive energy expenditure prediction equations and establish criteria to distinguish between light, moderate, and vigorous activity (Trost, McIver and Pate, 2005). The latest version

(GT1M) uses a Micro-Electro-Mechanical-System capacitive accelerometer, which has a lower sampling frequency and better memory capacity than previous models. The Actigraph can be worn on the waist or wrist, depending on the desired measurement, activity, or sleep.

2.6.5. Actical

Figure 2.6.4. Actical device with options of multisite wear. Image from http://www.actigraphy.com/solutions/actical

Actical by Phillips Respironics is a non-invasive, omni-directional accelerometer that has been validated to accurately measure a subjects energy expenditure (Heil, 2006) and step count (Oliver *et al.*, 2011). The Actical is lightweight, waterproof, durable and offers real-time ambulatory monitoring in epochs as short as 1 second and can be worn on the waist, wrist, or ankle.

2.6.6. Actiwatch 2

Figure 2.6.5. Actiwatch 2 wrist worn device. Image from https://www.usa.philips.com/healthcare/product

The Actiwatch 2 is a wrist-worn 'actigraphy' device that contains a silicone photodiode light sensor to measure visible light illuminance (lux) and a solid-state piezoelectric accelerometer to measure physical activity ("activity counts per minute" [cpm]). The device is lightweight (16g including the band) and waterproof for up to 30 minutes in water. The Actiwatch 2 can be programmed to record light and activity measurements

and data on sleep quality. These wrist-worn devices have been used successfully in previous research studies investigating refractive error and light exposure (Read *et al.,* 2014; Ostrin, 2017). The Actiwatch is worn on the non-dominant wrist 24-hours a day during data collection and the participants are instructed to ensure that the watch is not covered by clothing during wear. The benefit of the Actiwatch device is the ability to use just one instrument for measuring light exposure, sleep, and activity, therefore simplifying the collection of data with minimal cost and less burden on the participant.

2.6.6.1. Physical Activity (PA)

A validity, comparability and reliability study of the Actiwatch was carried out on children in Sweden (Ekblom *et al.*, 2016). The authors found the correlation between total energy expenditure (the number of calories an individual uses in a day) and Actiwatch activity counts to be significantly correlated (correlation coefficient of 0.80), and significantly correlated with the widely used Actigraph (correlation coefficient of 0.67 However, the Actiwatch was found to underestimate activity levels in active children and overestimate activity levels in less active children. However, the high correlation with the Actigraph suggests that the Actiwatch has acceptable validity for measuring PA in children. Metabolic equivalents (METS) are used to estimate the energy expenditure for different physical activities, enabling us to define PA as sedentary, light, moderate or vigorous with cut-offs <1.5 METS to be sedentary, 1.5-3 to be light, 3-6 to be moderate and >6 to be vigorous (Mansoubi *et al.*, 2015). Ekblom *et al.* (2016) also established cut-off values for the Actiwatchs activity counts per 15 seconds. These cut offs were 80, 262, 406 for light, moderate and vigorous PA, respectively, which were deemed equivalent to 1.5, 3 and 6 METs, respectively.

Two validation studies of the Actiwatch and Actigraph devices against energy expenditure values found the accelerometery-based devices useful for the assessment of children's PA. These studies found high correlations between activity counts and energy expended in activity and measures of heart rate, and concluded that both devices were valid and useful in classifying PA into sedentary, light, moderate and vigorous intensity levels (Puyau *et al.*, 2002, 2004).

2.6.6.2. Light Exposure

Outdoor light exposure typically been described as >1000 lux (Read *et al.,* 2014; Ostrin, 2017). Ulaganathan *et al.* (2017) assessed the effect of measurement duration and frequency of sampling on estimates of daily light exposure and suggest that a measurement duration of at least one week and measurement frequency of two minutes or less provides the most reliable estimates of personal outdoor light exposure in both children and young adults. An advantage of the Actiwatch 2 is the ability to measure luminance's <1 lux to provide data on the full scotopic and mesopic light range. This feature is not available on either the Daysimeter (Lighting Research Centre, Rensselaer Polytechnic Institute, New York), or Clouclip, both have a minimum of 1 lux.

A validation study of eye-level and wrist-level light exposure using an Actiwatch (wrist) and a Daysimeter (eye-level) found that the mean difference between the two devices was less than 10 lux at light levels less than 5000 lux, but that agreement between the devices decreased as eye-level light exposure increased (Jardim *et al.*, 2011). Measurements at eye-level of 5000 lux or more were on average 100 lux greater than those on the wrist. This discrepancy is not a concern in most refractive error related research studies which use a cut-off of >1000 lux to identify outdoor light exposure.

Okudaira *et al.* (2017) demonstrated that measurements of lux at eye-level and wrist-level were highly correlated (r=0.76). Therefore, measurements at wrist-level can be considered representative of eye-level light exposure, except for night-time wear when bedding tends to cover the wrist. Despite the wrist-level Actiwatch being shown to underestimate light exposure at higher levels of light (>5000 lux), it is well tolerated by participants in the clinical setting. In contrast, the eye-level Daysimeter was found to be cumbersome and uncomfortable for patients to wear (Jardim *et al.*, 2011). These findings suggest that wrist-level monitoring using the Actiwatch provides an adequate estimate of light exposure whilst being acceptable and well tolerated by wearers.

While there are ample validated studies on both physical activity and sleep from the Actiwatch, there is limited information on the validation of the Actiwatch for measuring light exposure. Therefore, if this device was to be used in research studies to assess an individual's light exposure and/or the amount of time spent outdoors the Actiwatch 2 would need to be validated to do so (See Chapter 3 for validation of the wearable devices)

2.6.6.3. Sleep Quality

A number of groups have researched the validity of actigraphy devices in measuring sleep/wake intervals compared with polysomnography (PSG) (see section 2.6.7.) and have found the devices to be a reliable (Hyde *et al.,* 2007; Weiss *et al.,* 2010*)*. One notable limitation is that the Actiwatch is unable to differentiate between periods of quiet wakefulness and sleep therefore it may overestimate total sleep time. However, actigraphy is accepted as a useful, non-invasive tool for continuous prolonged recordings of sleep patterns in the natural environment. Hyde *et al.* (2007) compared the sensitivity and specificity of the Actiwatch in predicting sleep/wake intervals in comparison to PSG. The authors found that sensitivity to sleep was high, with values ranging from 90.1% to 97.7%, but in contrast, specificity to wake was low ranging between 39.4-68.9%.

A validation study of the Actiwatch alongside two other actigraphy devices with PSG found a strong correlation (r=0.836) between the Actiwatch and the PSG, with the proviso that the Actiwatch overestimated total sleep time (Weiss *et al.*, 2010).

Another validation study of the Actiwatch 2 with PSG presented the limits of repeatability for total sleep time, sleep efficiency, wake after sleep onset (WASO) and sleep onset latency. The limits of repeatability were 48.8 minutes, 9.9%, 28.8 minutes and 33.7 minutes respectively. The authors found the Actiwatch 2 to be a valid method in assessing sleep onset latency, total sleep time and sleep efficiency but found that the Actiwatch significantly overestimated WASO in comparison with the PSG (Shin *et al.,* 2015).

A literature review by Meltzer *et al.* (2012) suggests that in the measurement of sleep in a childhood population, all reports should include a basic amount of information on the device used including; name of the device, the specific model, and the name (and location) of the manufacturer. The authors also recommended that detail such as device placement (wrist, ankle or waist and left or right side), epoch length, mode of data collection, wake sensitivity threshold and the type and version of software used should also be reported.

2.6.7. Polysomnography (PSG)

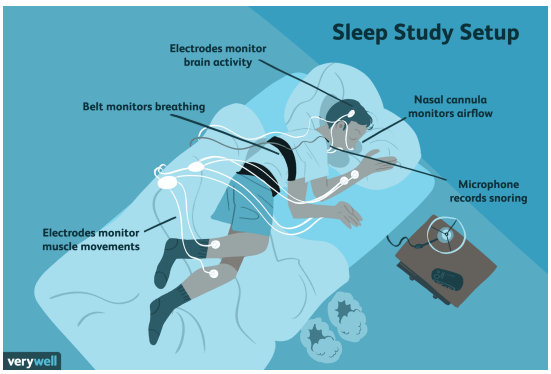

Figure 2.6.6. Image depicting the processes being measured during a sleep study using PSG. Image from https://www.verywellhealth.com/what-to-expect-in-a-sleep-study-3015121

Polysomnography (PSG) is the "gold standard" method for diagnosing sleep disorders. PSG measures brain waves, muscle activity, blood oxygen levels, heart rate, breathing rate, snoring and eye movement and is typically carried out within a specialist sleep centre or hospital. PSG also registers the body's shift between different sleep cycles; non-rapid eye movement sleep (NREM) and rapid eye movement (REM) sleep. However, limitations of using polysomnography in research include expenses incurred, as well as the lack of ability to assess sleep in a free-living setting.

Regardless of the method used to monitor sleep, it is important that the method is validated for monitoring sleep within the population under test; correlation statistics alone are not appropriate. Sensitivity and specificity are the most appropriate statistical method for validity assessment. The ideal test accurately identifies 100% of both positive cases (is highly sensitive) and negative cases (is highly specific). When it comes to actigraphy, researchers have established a convention of considering sensitivity to be the proportion of epochs scored as 'sleep' using gold standard PSG that are accurately identified as 'sleep' by actigraphy. Specificity, on the other hand, is the proportion of polysomnography-scored 'wake' epochs accurately identified as 'wake' by actigraphy. An actigraph, or algorithm, that incorrectly scores 'sleep' as 'wake' has low sensitivity, and an actigraph, or algorithm, that incorrectly scores 'wake' as 'sleep' has low specificity. Another method commonly used to examine instrument validity is the Bland–Altman agreement method where the new instrument (actigraphy) is plotted visually against the gold standard (PSG). The difference between the measures for each participant are fitted to lines that represent the ideal (no difference) and standard deviations to show

each participant's deviation from the ideal (Meltzer *et al.*, 2012). From these data limits of agreement (LOA) between the gold standard and the new device can be calculated.

A literature review by Meltzer *et al.* (2012) found high sensitivity and low specificity for a number of different actigraphy devices with a sensitivity range of 82.2–90.1% and a specificity range of 50.9–72.8%. The authors concluded that regardless of the device, where it was placed, algorithm or wake sensitivity threshold used, all devices consistently and accurately identified 'sleep' periods but, were less accurate at identifying 'wake after sleep onset' amongst children.

2.7. Questionnaires for Subjective Measures of Potential Risk Factors for Myopia

2.7.1. Children's Sleep Habits Questionnaire (CSHQ)

The CSHQ is a retrospective, 45-item parent questionnaire that has been used in several studies to examine sleep behaviour in young children. The CSHQ includes items including, bedtime behaviour and sleep onset; sleep duration; anxiety around sleep; behaviour occurring during sleep and night waking; sleep-disordered breathing; parasomnias; and morning waking/daytime sleepiness. Parents are asked to recall sleep behaviours occurring over a "typical" recent week. Items are rated on a three-point scale: "usually" if the sleep behaviour occurred five to seven times per week; "sometimes" for two to four times per week; and "rarely" for zero to one time per week. A cut-off total CSHQ score of 41 has been shown to correctly yield a sensitivity of 0.80 and specificity of 0.72 in the determination of childhood sleep problems (Owens, Spirito and McGuinn, 2000).

2.7.2. Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a validated and repeatable tool for assessing an individual's sleep quality over the month prior to completion. The PSQI consists of 19 self-rated questions. The 19 self-rated questions assess a wide variety of factors including estimates of sleep duration, latency, and frequency and severity of specific sleep-related problems. These 19 items are grouped into seven component scores, each weighted equally on a 0-3 scale. The seven component scores are then summed to yield a global PSQI score, which has a range of 0-21, with higher scores indicating poorer sleep quality. The components of the PSQI

are subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. The entire index requires 5-10 min for the participant (or their parent if they are a young child) to complete. A global PSQI score ≥5 has been shown to provide a sensitive and specific measure of poor sleep quality, relative to clinical and laboratory measurements; a PSQI score ≥5 is expected to yield a sensitivity of 89.6% and a specificity of 86.5% in identifying poor sleep quality (Buysse *et al.*, 1989).

2.7.3. Physical Activity Questionnaire for Children (PAQ-C)

The PAQ-C is a simple validated, reliable questionnaire that is used to assess the activities a child has performed over the last seven days. The overall result of the test is a score of 1 to 5 points that provides a graded level of PA for the 7-day period (Kowalski, Crocker and Faulkner, 1997; Voss, Ogunleye and Sandercock, 2013). The PAQ-C can be adapted by researchers to replace the original American sporting terminology with more relevant sports and activities applicable to the population under test (e.g., changing 'recess' to 'breaktime', 'American football' to "soccer/ Gaelic football'). This questionnaire is particularly useful for estimating PA on occasions that an accelerometer device is removed, for example during swimming lessons.

2.7.4. Screen Time Diary

A screen time diary can be used to obtain a subjective assessment of time spent using hand-held digital screens as well as the use of computer/laptop and TV watching. This could be usefully applied in conjunction with screen-time monitoring apps for a comparison between objectively measured and subjectively reported screen-time. The diaries may also be useful for reporting the use of multiple screens and screen use directly before bedtime (as there is some indication of a link between screen use and sleep (Christensen *et al.*, 2016)). A screen time diary may be particularly relevant to younger children who do not have their own phone or tablet. Ofcom Communications Market Report (2021) found 14% of children aged 5-7-years have their own smartphone and 57% have their own tablet, whereas 91% of children aged 12-15-years have their own smartphone and 59% have their own tablet. One limitation of screen time monitoring apps for younger children is that using data from a shared family phone or tablet may overestimate an individual's total screen time.

2.7.5. NICER 1.0 Questionnaires

NICER 1.0 used a participant questionnaire for the 12-13-year-old participants, which was designed to identify risk factors for myopia, including amount of time spent on near work, level of physical activity, and time spent indoors and outdoors. A parental questionnaire was also designed to elicit further details of myopic risk factors including, classification of parental myopia, socioeconomic status, birth history and birth order of the participant, in addition to lifestyle questions. The NICER questionnaire was completed and returned directly to the university via a freepost envelop (O'Donoghue *et al.*, 2010). 100% of the 12-13-year-old children completed their questionnaire and 70.7% of the children's parents returned the parental questionnaire (from Lisa O'Donoghue's Thesis Section 9.3.2.).

2.8. Conclusion

In summary, there are many new and viable means for objectively recording the potential risk factors for myopia that have been previously mentioned. Objective measures of the potential risk factors for myopia are optimum as they will reduce the limitation of recall-bias via subjective measures which have been widely used in this field of research. This approach will be beneficial in determining independent risk factors for childhood myopia as well as the contribution of each risk factor to the presence and magnitude of myopia. This review also includes some questionnaire-based methods of collecting data. These can be used to subjectively quantify some of the risk factors and to compare between objectively and subjectively measured risk factors to determine the accuracy of self-report or parental reported activities.

Chapter 3:
Validation Study of the Wearable Devices

Chapter 3. Validation Study of the Wearable Devices

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3.1. Introduction

Wearable devices which monitor aspects of daily living such as light exposure (Read, Collins and Vincent, 2014; Ostrin, Sajjadi and Benoit, 2018), sleep (Rosenberger *et al.*, 2016), physical activity (Read, Collins and Vincent, 2014; Rosenberger *et al.*, 2016) and near work behaviours (Wen *et al.*, 2016; Bhandari, Lan and Ostrin, 2019; Cao *et al.*, 2020) are increasingly being used by researchers to provide objective data pertinent to systemic (Humphreys, McLeod and Ruseski, 2014) and ocular health issues (Sherwin *et al.*, 2012; French *et al.*, 2013; Read, Collins and Vincent, 2015; Cao *et al.*, 2020; Ostrin *et al.*, 2020) including obesity, diabetes, hypertension, mental well-being, and the development of myopia (short-sightedness).

Research from around the world has identified that based on current trends, half the world's population will be myopic by 2050 (Holden *et al.*, 2016), and that modern lifestyles could be contributing to the rise in myopia worldwide (Morgan *et al.*, 2018). Ulster University's Northern Ireland Childhood Errors of Refraction (NICER) study has demonstrated that the prevalence of myopia amongst white UK teenagers has more than doubled in the last 50 years and is appearing in children at a younger age than in previous decades (McCullough, O'Donoghue and Saunders, 2016). An earlier onset of myopia results in an increased risk of progression to high myopia, inflating the risk of secondary sight threatening ocular pathologies (Haarman *et al.*, 2020). The prevalence of myopia is increasing at a rate that cannot solely be attributed to genetic pressures and is therefore a cause for global concern (Wu *et al.*, 2016; Morgan *et al.*, 2018). Researchers are seeking a better understanding of the environmental and lifestyle factors that may contribute to the earlier incidence of myopia in order that strategies for delaying myopia onset may be applied. The potentially modifiable risk factors for childhood myopia include; spending less time spent outdoors (Sherwin *et al.*, 2012; French *et al.*, 2013; Read, Collins and Vincent, 2014), increased educational pressure (Saw *et al.*, 2007; Guggenheim and Williams, 2015; Mountjoy *et al.*, 2018), spending more time on near activities (Saw *et al.*, 2002; Saw *et al.*, 2007; Ip *et al.*, 2008), leading less active lifestyles (Deere *et al.*, 2009; O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019), having poor

sleep quality (Gong *et al.*, 2014; Ayaki *et al.*, 2016; Jee, Morgan and Kim, 2016; Kearney *et al.*, 2017; Xu *et al.*, 2017), and increased time spent using hand-held electronic devices (Harrington, Stack and O'Dwyer, 2019; Liu *et al.*, 2019).

Wearable devices can provide objective measures of multiple risk factors and remove the limitation of recall-bias from self-/parental-reports of childhood behaviours collected through questionnaire or diaries (Alvarez and Wildsoet, 2013; Ostrin, 2017; Ostrin, Sajjadi and Benoit, 2018). Wearable devices are generally lightweight, easy to wear and allow for data collection in the free-living setting (Verkicharla *et al.*, 2017; Smith *et al.*, 2018). These features make wearable devices an attractive method with which to collect myopia-related risk factor data. Furthermore, self-reported measures of time spent outdoors are not able to record the intensity of the light to which the individual is exposed and previous research has determined that time spent outdoors is often misreported and poorly correlated to objective sensor-derived data (Alvarez and Wildsoet, 2013; Ostrin, Sajjadi and Benoit, 2018). To date, it is not clear which elements of the outdoor experience are beneficial in relation to reducing the risk for myopia, but further information on children's light exposure in terms of timing of exposure to different levels of illumination and the duration and frequency of these exposures is needed. Therefore, it is important to determine which devices are valid and reliable for estimating the intensity of light as well as the amount of time spent outdoors. Time spent in illumination levels >1000 lux is often used as a proxy for time spent outdoors (Read, Collins and Vincent, 2014; Ostrin, 2017; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020).

The devices employed to objectively measure illumination in the present study were the Respironics Actiwatch 2 (Philips, NV, USA), the Clouclip Model M2 (HangZhou Glasson Technology Co) and the Hagner Universal Photometer S2 (B Hagner AB, Solna, Sweden). The Actiwatch 2 is a wristworn device which records physical activity and illumination. The Clouclip is a spectacle-mounted device which records near viewing distance and eye-level illumination.

The inter-device reliability of the Actiwatch 2 for illumination and activity measures has been reported as excellent; with intraclass correlation coefficients of 0.99 and 0.98 for light and activity, respectively (Read, Collins and Vincent, 2014). The Actiwatch brand refers to a family of wearable devices including; the Actiwatch 2, Actiwatch-L, Actiwatch Spectrum and Actiwatch 64, and this family of devices have previously been validated

against both ‘gold standard’ polysomnography and room respiration calorimetry (measures total energy expenditure) and found to be a reliable method for measuring sleep (Hyde *et al.*, 2007; Weiss *et al.*, 2010) and physical activity, respectively (Puyau *et al.*, 2002, 2004; Ekblom *et al.*, 2016; Neil-Sztramko *et al.*, 2017). Actiwatch 2 measures of illumination have also been compared with a ‘gold standard’ photometer in both laboratory and outdoor lighting conditions by Joyce *et al*. (2019). The authors found that the Actiwatch 2 underestimated the ‘true’ level of illuminance in comparison to the photometer. However, the linear relationship illustrated between the two devices suggests that it may be possible to apply a conversion factor in order to estimate ‘true’ illumination (Joyce *et al.*, 2019). The Actiwatch-L has also been compared to eye-level illumination from a Daysimeter. Comparison between these devices demonstrated that their measures were correlated under 5000 lux, but that at higher illuminations the Actiwatch-L underestimated the light exposure by more than 100 lux. In contrast, at night in lower illuminations the Actiwatch-L was found to overestimate the illumination compared to the Daysimeter (Jardim *et al.*, 2011). Two other studies compared the Actiwatch Spectrum measures to calibrated photometer measures, with one study also comparing readings between the Actiwatch Spectrum and Daysimeter. Both studies found the Actiwatch Spectrum to consistently overestimate illumination in comparison to the calibrated photometers (Figueiro *et al.*, 2013; Markvart, Hansen and Christoffersen, 2015), and the Daysimeter devices (Figueiro *et al.*, 2013). Another study by Okudaira *et al.* (2017) using photoconductive cells found a high correlation between the eye-level and wrist-level measures (0.76). There are currently no data examining how well the Actiwatch 2 can categorise illumination into scotopic, mesopic, and photopic (indoor/outdoor) levels.

Previous published abstracts (Wen *et al.*, 2016; Bhandari, Lan and Ostrin, 2019) and a recently published paper (Bhandari and Ostrin, 2020) have shown that the Clouclip is highly accurate for measurements of illumination and viewing distance in a laboratory setting, and that the Clouclip could accurately distinguish between indoor (<1000 lux) and outdoor (>1000 lux) environments (Bhandari, Lan and Ostrin, 2019; Bhandari and Ostrin, 2020). As the Clouclip is relatively new there are currently no studies where the inter-device reliability of the Clouclip is investigated; hence the consistency of measures taken by different Clouclip units is unknown. Recently, Bhandari and Ostrin (2020) reported that the Clouclip slightly underestimated ‘true’ illumination in comparison to a photometer in a range of real-world conditions in Houston, Texas (29°N, 95°W). It is not

yet clear how well the device discriminates between indoor photopic and mesopic levels of illumination.

Landis *et al.* (2018) reported significant differences in the light exposure profiles experienced by myopic and non-myopic children in Australia and hypothesise that these differences suggest that both scotopic and outdoor photopic light have a potential role in the prevention of myopia development. However, at present we have limited information on how accurately either the Clouclip M2 or the Actiwatch 2 classify illumination into different categories.

Additionally, seasonal differences in light exposure may also play a role in eye growth patterns. A number of studies have found a slower progression of myopia in summer compared to winter (Deng, Gwiazda and Thorn, 2010; Donovan *et al.*, 2012; Gwiazda *et al.*, 2014; Ulaganathan *et al.*, 2019) and have postulated that this is due to the increased daylight hours leading to increased time outdoors, but it could also be a result of increased light intensity. It seems necessary then to understand the difference in light exposure patterns throughout summer and winter months in order to examine if they have any impact on seasonal eye growth. In Houston, Texas, Ostrin *et al.* (2017) examined the environment ambient illumination under different conditions and found large differences between the outdoor light exposure between winter and summer and between indoors and outdoors. It may not be appropriate to assume that the measurements taken by Ostrin *et al*. (2017) in Texas reflect indoor and outdoor ambient light exposures in Northern Ireland (UK) due to differences in climate and daylight hours between Texas and Northern Ireland.

3.1.1. Aims and Objectives

The present study aims to:

- Compare the ambient illumination experienced in a range of indoor and outdoor locations in Northern Ireland in winter vs summer
- Assess the inter-device reliability of the Clouclip M2 for illumination and viewing distance measures.
- Assess the inter-device reliability of the Actiwatch 2 for light exposure and physical activity measures.
- Assess the ability of the Actiwatch 2 and Clouclip M2 to measure and accurately categorise illumination using ‘gold standard’ photometry as the reference.

3.2. Methods

3.2.1. Ambient Illumination Measures in Winter and Summer

Environment ambient illumination was measured using a calibrated photometer in several locations in order to best represent the normal day-to-day range of lighting conditions in the UK. A Hagner Universal Photometer S2 was calibrated prior to data collection, on the 16th October 2019 by the manufacturing company B Hagner (Sweden). The photometer is an illuminance meter designed to measure the incident light on a surface over a range of 0.025-100,000 lux with a 10mm sensor. Light sensitive components of the device are filtered to give a spectral response matching that of a human eye. The illuminance detector within the photometer is cosine-corrected thus eliminating measurement errors which may arise when the light source is not directly above the sensor, but at any angle within the hemisphere of measurement.

Measurements of illuminance were taken in the same locations in both winter and summer, to allow comparisons between both extremes of light exposure in Northern Ireland. The locations where measurements were taken are listed as follows:

Daytime:

- Indoors by window
- Indoors away from window
- Outside on a sunny day
- Outside sunny day with sunglasses/hat covering the sensor
- Outside on a cloudy/rainy day
- Outside either side of school hours, before 9am and after 2pm/3pm

Evening:

- Living room with lights on
- Living room with TV only on

Night:

- Bedroom in complete darkness
- Bedroom with main lights on
- Bedroom with night light on
- Bedroom with ambient light (from street/hall)
- Bedroom with tablet/phone screen only on

Six measurements were taken at 0, 2, 4, 6, 8 and 10 minutes after the photometer was placed in location. This protocol was an extended version of the Houston protocol, whereby photometer readings were taken every minute for five minutes by (Ostrin, 2017). The average illuminance of each location in the present study was calculated for both winter and summer.

3.2.2. Inter-Device Reliability: Actiwatch 2

Thirteen Actiwatch 2 devices (Philips, NV, USA) were used to evaluate the inter-device reliability of illumination (lux) and physical activity (cpm) measures. The devices were programmed using Actiware software, to record light exposure (lux) and activity (cpm) every 30 seconds for 60 minutes, with all devices synced to start and end recording simultaneously. The devices were mounted on a solid board (see Figure 3.2.1.) and exposed to a range of lighting conditions and activity movements. The board was sized to ensure it could be transported efficiently through a variety of spaces over a 60-minute period of data collection whilst maintaining the vertical orientation of each Actiwatch's light sensor. Light levels were not manipulated; they represented the normal variation

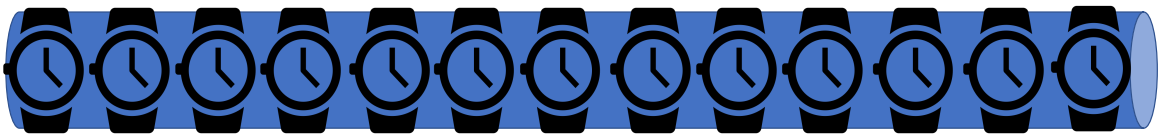


Figure 3.2.7. Schematic drawing of all the Actiwatches mounted on a solid board for inter-device reliability measures. Diagram not to scale.

experienced in a range of real-world settings both indoors and outside (spanning the illumination categories under investigation; scotopic through to outdoor photopic). The synchronised 60-minute sample of both the illumination and activity data was extracted from each device and the inter-device intraclass correlation coefficients for both illumination (lux) and physical activity (cpm) were calculated.

3.2.3. Inter-Device Reliability: Clouclip M2

Five Clouclip M2 devices (HangZhou Glasson Technology Co.) were used to evaluate the inter-device reliability of illumination (lux) and viewing distance (cm) measures. The number of Clouclips under evaluation was restricted to five in order that the spectacle frames on which they were mounted, could be fixed to a moveable surface in such a way that the devices would receive uniform illumination (see Figure 3.2.2.). The moveable surface was sized to ensure it could be transported efficiently through a variety of spaces

over a 60-minute period of data collection whilst maintaining the horizontal orientation of each Clouclips' light sensor. Again, light levels were not manipulated.

Clouclips are activated through a mobile phone app, and it was not possible to simultaneously start recording on all the devices. In order to ensure that the time of data logging of the Clouclips matched one another, each unit was activated consecutively and then all devices were left in darkness before illumination was introduced, and the test protocol commenced. The point at which the devices detected the onset of illumination was used to synchronise data after download. To evaluate the reliability of viewing distance measures the board was held at a range of distances from a solid, flat surface (e.g., a wall or door). The actual distances from the solid surface to the Clouclips were not independently recorded. Data were uploaded from each device to a cloud location using the Clouclip app. A synchronised 60-minute sample of both the illumination and viewing distance data was extracted from each device and the inter-device intraclass correlation coefficients for both illumination (lux) and viewing distance (cm) were calculated.

Figure 3.2.8. Schematic drawing of the Clouclips mounted on spectacle frames attached to a solid, portable board for inter-device reliability measures. Diagram not to scale.

3.2.4. Validity of Actiwatch 2 and Clouclip M2 Measures and Categorization of Illumination: Comparison with Hagner-S2 Universal Photometer

In order to evaluate how well the two wearable devices classified ambient illumination into previously published categories (Table 3.2.1.), a free-standing anatomically accurate adult-sized skeleton (height: 176cm [comparable to UK average male height of 175.3cm (Moody, 2012)]) was employed to 'wear' the devices. A skeleton was chosen in order to maintain consistent, device-appropriate positioning of each devices' light sensors throughout data collection. To enable measures of illumination to be taken by the photometer at the same plane as each wearable device's light sensor, the two devices could not be compared to the photometer at the same time and were not worn concurrently. The skeleton was stationed in a range of locations spanning all four light exposure categories (Table 1) over a period of 100 minutes per device, including locations with illumination close to the boundaries of each category. The locations included indoor and outdoor locations in a family home (e.g., cupboard without windows, living room, kitchen by window, outdoors in shade, outdoors in bright light) providing a range of illuminations from near darkness indoors to outdoor sunshine (nine conditions in total), and included locations with illumination close to the boundaries of each light exposure category.

LIGHT EXPOSURE CATEGORIES	LUX VALUE	REFERENCES
SCOTOPIC LIGHT	≤0.01 lux	SolarLight (2014)
MESOPIC LIGHT	0.02-3 lux	Rosenfield and Logan (2009)
INDOOR PHOTOPIC LIGHT	>3-1000 lux	Bhandari and Ostrin (2020)
OUTDOOR PHOTOPIC LIGHT	>1000 lux	Ulaganathan *et al.* (2019)

Table 3.2.1. Categories used to classify light exposure.

Clouclip vs. Photometer: The photometer's light sensor was held at eye level, to match the position of the Clouclip mounted on a pair of spectacles worn by the skeleton (Figure 3.2.3.), and readings taken for periods of 12 minutes (an expansion of Bhandari and Ostrin's (2020) four minute measuring period) in each condition. The Clouclip has a fixed illumination collection epoch of two minutes, and the photometer readings were taken every 15 seconds. Coinciding time points from the Clouclip raw data sheets were matched with the photometer's readings (averaged across two minutes) to reflect the two-minute measurement epoch of the Clouclip. As noted by Bhandari and Ostrin (2020) the skeleton's head needed to be 'wobbled' from side to side between illumination

measurements in order to prevent the Clouclip from going into sleep mode (if no motion detected for 40 seconds).

Actiwatch 2 vs Photometer: The protocol described above was repeated with the skeleton wearing an Actiwatch 2. The photometer's light sensor was held at wrist level, to match the position of the Actiwatch 2 (Figure 3.2.3), and readings taken for periods of 12 minutes in each condition. The Actiwatch 2 illumination epoch was set to 15 seconds throughout and recordings were taken from the photometer every 15 seconds. Data were extracted from the Actiwatch 2 raw data sheets and matched with measures taken by the photometer at corresponding time points.

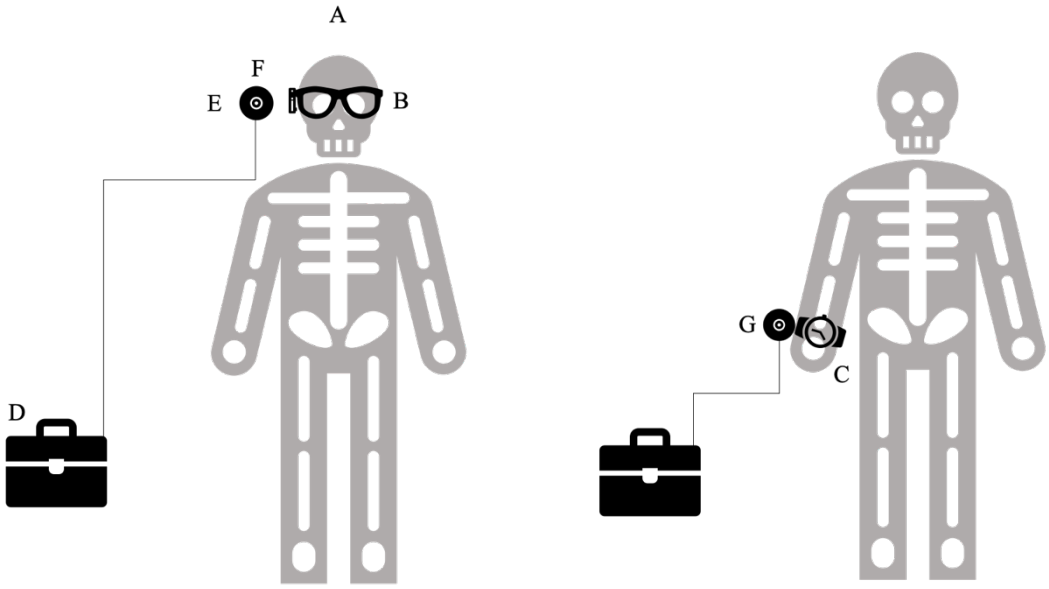


Figure 3.2.9. The skeleton (A) setup with the spectacle mounted Clouclip (B) and Actiwatch 2 (C). The photometer (D) was setup with the light sensor (E) held at eye-level (F) and wrist-level (G) to allow comparison of outputs with the Clouclip and the Actiwatch 2, respectively. Diagram not to scale.

3.3. Statistical Analysis

3.3.1. Ambient Illumination Measures in Winter and Summer

SPSS Version 25 was used for all statistical analysis. The average illumination in each condition in both winter and summer were reported in their raw format in Table 3.4.1. along with the mean +/- standard deviation (SD) and paired sample T-test results between seasons.

3.3.2. Inter-Device Comparability: Actiwatch and Clouclip

Reliability analysis using two-way mixed, average measures, absolute agreement models were used to calculate the inter-device intraclass correlations for the Clouclip (illumination and viewing distance) and Actiwatch (illumination and activity) metrics under test. This enabled comparison of the 60-minute sample of illumination, viewing distance and activity for all five Clouclips and 13 Actiwatches under investigation.

3.3.3. Validity of Actiwatch 2 and Clouclip M2 Measures and Categorization of Illumination: Comparison with Hagner-S2 Universal Photometer

Scatterplots were constructed to illustrate the relationship between measures made with the Actiwatch 2 and the photometer, and the Clouclip and the photometer across a range of illuminations. Illumination data from the photometer, Actiwatch 2 and Clouclip were tested for normality using the Shapiro-Wilk test and were found to follow a non-normal distribution (all $p<0.001$) therefore, Spearman's Rank Order Correlations were used. Illumination category 'cut-offs' were included in a graphical representation to illustrate the capability of the Actiwatch 2 to successfully categorise ambient light levels into each of the four categories described in Table 3.2.1.; scotopic (≤0.01 lux), mesopic (0.02-3 lux), indoor photopic (>3-1000 lux) and outdoor photopic (>1000 lux) light. As the Clouclip cannot measure illumination below 1 lux, environmental illuminations of ≤1 lux are recorded as 1 lux on the output Excel file. Therefore, Clouclip is unable to differentiate between scotopic and low mesopic illumination. Hence for the purpose of this study, the scotopic and mesopic categories were combined and the ability of the Clouclip to successfully categorise ambient light levels within its operating range was evaluated in terms of the following categories, scotopic/mesopic (≤3 lux), indoor photopic (>3-1000 lux) and outdoor photopic (>1000 lux) light and was also presented in graphical and numerical format. The agreement between measures recorded by the wearable devices and the photometer were compared using Bland and Altman (1986) analyses. The mean difference in illumination measures and 95% limits of agreement (LOAs) were plotted for each wearable device against the photometer and regression analyses were used to check for proportional bias. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the area under curve (AUC), sensitivity and specificity of the photometer, Actiwatch 2 and Clouclip in identifying a measurement taken indoors and outdoors using the traditional cut-off >1000 lux.

3.4. Results

3.4.1. Ambient Illumination Measures in Winter and Summer

	WINTER	SUMMER	
	Mean +/- SD	**Mean +/- SD**	**Significant Difference**
DAYTIME			
Indoors by Window	1216.67 +/- 132.92	3316.67 +/- 98.32	p= 0.000*
Indoors away from Window	520 +/- 0	545 +/- 87.35	p= 0.515
Outside Sunny Day- Noon	74000 +/- 7974.96	90500 +/- 1673.32	p= 0.002*
Outside Rainy/Cloudy Day-Noon	2383.33 +/- 487.51	34666.67 +/- 4718.76	p= 0.000*
Outside Morning-9am	2350 +/-126.49	14000 +/- 632.46	p= 0.000*
Outside Afternoon-2pm	2125 +/- 464.49	45666.67 +/- 6121	p= 0.000*
Outside Afternoon-3pm	2341.67 +/- 193.43	32500 +/- 5648.01	p= 0.000*
Hat Partly Shading Photometer	46833.33 +/- 883.19	51416.67 +/- 1655.8	p= 0.002*
Sunglasses Over Photometer	13500 +/- 1760.68	22500 +/- 1378.41	p= 0.000*
EVENING			
Living Room with Lights On	36.5 +/- 0.55	25.5 +/- 0.55	p= 0.000*
Living Room with TV Only On	6.33 +/- 1.37	7.17 +/- 0.26	p= 0.250
NIGHT			
Bedroom Complete Darkness	0 +/- 0	0 +/- 0	p= n/a
Bedroom Main Lights On	67.67 +/- 2.25	74.5 +/- 0.55	p= 0.000*
Bedroom Phone/Tablet Screen Light On	0.63 +/- 0.08	0.92 +/- 0.21	p= 0.038*

Bedroom with Night Light Only On	1.6 +/- 0	3 +/- 0	p= n/a
Bedroom Ambient Light (from street/hall)	0.78 +/- 0.08	0.4 +/- 0	p= 0.000*

Table 3.4.1. Average ambient illumination levels in winter and summer. All the above measurements are in lux. Descriptive statistics along with the significant difference values between measures during winter vs. summer are also presented.

3.4.2. Inter-Device Reliability: Actiwatch and Clouclip

The inter-device intraclass correlation coefficients (ICC) for the Actiwatch and Clouclip are shown in Table 3.4.2. below. The ICCs indicate good inter-device reliability for the Clouclip illumination measures, and excellent inter-device reliability for the Clouclip viewing distance and both the Actiwatch illumination and activity measures.

DEVICE AND PARAMETER	INTER-DEVICE INTRACLASS CORRELATION COEFFICIENTS
ACTIWATCH LIGHT	0.999
ACTIWATCH ACTIVITY	0.999
CLOUCLIP LIGHT	0.853
CLOUCLIP VIEWING DISTANCE	0.958

Table 3.4.2. Inter-device intraclass correlation coefficients for the Actiwatch and Clouclip parameters.

3.4.3. Validity of Actiwatch 2 and Clouclip M2 Measures and Categorization of Illumination: Comparison with Hagner-S2 Universal Photometer

The natural light measured (by the photometer) ranged between 0-3700 lux and 0-6850 lux when comparing the photometer and Clouclip and photometer and Actiwatch 2, respectively. Strong correlations were found between 'true' photometer-measured illumination and both the Actiwatch 2 ($\rho=0.99$, $p<0.0001$) and the Clouclip ($\rho=0.991$, $p<0.0001$) measures (Figure 3.4.1.). Both devices underestimated the illumination levels in comparison to the photometer when exposed to high levels of outdoor light (>2500 lux). However, the Actiwatch 2 consistently underestimated the illumination in all lighting conditions to a greater degree than the Clouclip (Figure 3.4.1.). The disparity between both wearable devices' recordings and the photometer output increased with increasing illumination. Table 3.4.3. presents how successfully the Actiwatch 2 and Clouclip devices categorised illumination levels, using the photometer reading as the reference value.

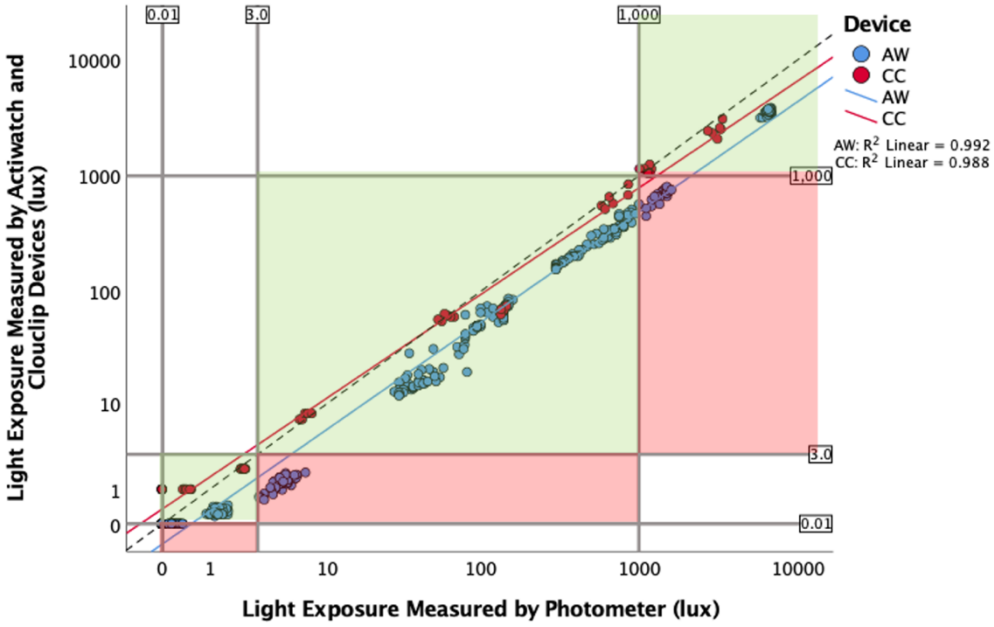


Figure 3.10.1. Illumination measures taken with the photometer vs Clouclip (CC) and the photometer vs Actiwatch 2 (AW) plotted on a logarithmic scale. The measures taken by the Clouclip every 2 minutes, and the photometer measures averaged over the corresponding 2 minutes are represented by a single data point (red). The measures taken by the Actiwatch 2, and photometer every 15 seconds are also represented by a single data point (blue). The black dashed line represents the line of unity (1:1). The solid red and blue lines indicate the correlation between the photometer and Clouclip measures and the photometer and Actiwatch 2 measures, respectively. Data points falling in the shaded green areas represent the measurements made by the wearable devices provided a classification of light level which agreed with the photometer, while the shaded red areas represent incorrect classification by the wearable devices. The Actiwatch 2 and photometer are unable to differentiate between illumination levels lower than 0.01 and 0.1 lux, respectively. Lower illuminations are recorded as 0.01 lux and 0 lux, respectively. The Clouclip is unable to differentiate between illumination levels less than or equal to 1 lux. Lower illuminations are recorded by the Clouclip as 1 lux.

LIGHT EXPOSURE MEASUREMENT BY PHOTOMETER	CATEGORY	ACTIWATCH 2 CATEGORISATION
≤ 0.01 LUX	Scotopic	100% (44/44)
0.02-3 LUX	Mesopic	50% (44/88)
>3-1000 LUX	Indoor Photopic	77.3% (150/194)
> 1000 LUX	Outdoor Photopic	62.9% (44/70)
OVERALL	All categories	71.2% (282/396)

LIGHT EXPOSURE MEASUREMENT BY PHOTOMETER	CATEGORY	CLOUCLIP CATEGORISATION
≤3 LUX	Scotopic/Mesopic	100% (18/18)
>3-1000 LUX	Indoor Photopic	100% (24/24)
> 1000 LUX	Outdoor Photopic	100% (12/12)
OVERALL	All categories	100% (54/54)

Table 3.4.3. The agreement between the photometer and both wearable devices when categorising illumination levels with the number of measures in each condition noted. The scotopic and mesopic categories are combined for the Clouclip due to the device's floor effect preventing it from distinguishing between scotopic and low mesopic illuminations.

As seen in Figure 3.4.1., while the Clouclip outputs are more closely aligned with the photometer's categorisation, neither the Actiwatch 2 nor the Clouclip correctly categorised all the illumination levels to which they were exposed. Adjusted cut-off criteria for scotopic, mesopic, indoor and outdoor photopic categories calculated from application of the linear fit equations from Figure 3.4.1 are presented in Table 3.4.4. for both devices.

LIGHT EXPOSURE CATEGORIES (LUX)	**EMPIRICALLY DERIVED ACTIWATCH 2 CRITERIA (LUX)**
SCOTOPIC ≤ 0.01	≤0.01
MESOPIC 0.02-3	0.02-0.78
INDOOR PHOTOPIC 3-1000	>0.78-533.15
OUTDOOR PHOTOPIC >1000	>533.15

LIGHT EXPOSURE CATEGORIES (LUX)	**EMPIRICALLY DERIVED CLOUCLIP CRITERIA (LUX)**
SCOTOPIC/MESOPIC ≤3	≤3
INDOOR PHOTOPIC 3-1000	>3-850
OUTDOOR PHOTOPIC >1000	>850

Table 3.4.4. The adjusted criteria for Actiwatch 2 and Clouclip devices to better align classification with that defined by the photometer. These criteria were derived from the application of linear fit equations from Figure 3.4.1. A combined 'scotopic/mesopic' category for measures ≤3 lux has been applied to the Clouclip because the operating range of the device does not allow for measurements ≤1 lux to be differentiated.

Figures 3.4.2. and 3.4.3. illustrate the Bland and Altman analyses evaluating the agreement between measures of illumination taken with the photometer and the two wearable devices. The mean differences between the Actiwatch 2 and photometer, and Clouclip and photometer are 430.92 and 79.35 lux, respectively. The limits of agreement (LOAs) between measures made with the Actiwatch 2 compared with the photometer (±1828.74 lux) are wider than those derived by the Clouclip comparison with the photometer (± 407.33 lux). Regression analyses demonstrated significant proportional bias for both the Actiwatch 2 compared to the photometer ($r=0.998$, $p<0.001$) and the Clouclip compared to the photometer ($r=0.778$, $p<0.001$).

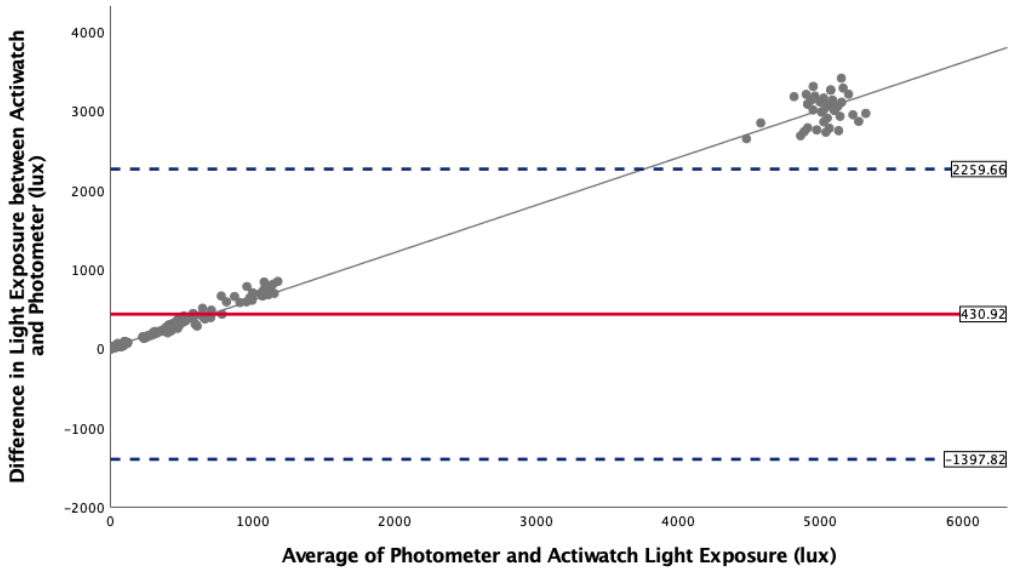


Figure 3.4.2. Bland and Altman plot for illumination measures recorded with the photometer and Actiwatch 2. The red line represents the mean difference between illumination measures. The dashed blue lines represent the upper and lower limits of agreement, and the grey line illustrates the proportional bias (r=0.998, p<0.001).

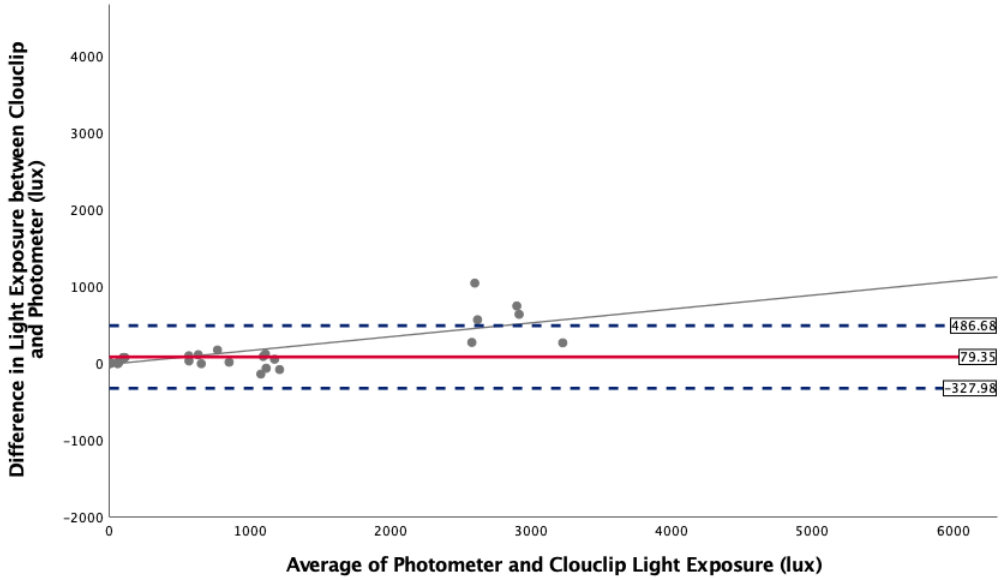


Figure 3.4.3. Bland and Altman plot for illumination measures recorded with the photometer and Clouclip. The red line represents the mean difference between illumination measures. The dashed blue lines represent the upper and lower limits of agreement, and the grey line illustrates the proportional bias (r=0.778, p<0.001).

During testing it was noted that light levels of >1000 lux were occasionally recorded in indoor environments such as when the skeleton was situated adjacent to a window/door. ROC curve analysis was carried out to determine the sensitivity (i.e., a measurement of >1000 lux results in correct identification of an outdoor position) and specificity (i.e., a measurement of ≤1000 lux results in correct identification of an indoor position) of each

device, for determining between an indoor and outdoor setting using the traditional cut-off of >1000 lux. The results are presented in Table 3.4.5.

DEVICE USED	AREA UNDER CURVE (AUC)	SENSITIVITY (%)	SPECIFICITY (%)
PHOTOMETER	1.00	90.5	100
ACTIWATCH 2	1.00	99.7	100
CLOUCLIP	1.00	91.7	100

Table 3.4.5. The results of ROC curve analysis reporting the sensitivity and specificity of using >1000 lux to identify whether the measurement was taken outdoors or indoors for each of the devices.

DEVICE USED	AREA UNDER CURVE (AUC)	SENSITIVITY (%)	SPECIFICITY (%)
ACTIWATCH 2 (533.15 LUX)	1.00	100	93.2
CLOUCLIP (850 LUX)	1.00	100	87.5

Table 3.4.6. The results of ROC curve analysis reporting the sensitivity and specificity of the newly derived cut-offs to identify whether the measurement was taken outdoors or indoors for each of the devices.

3.5. Discussion

This is the first study that has examined the Clouclip's inter-device reliability for both near viewing distance and illumination measures. Moreover, this is the first to investigate the ability of the Actiwatch 2 and the Clouclip to identify different illumination categories (scotopic, mesopic, indoor photopic and outdoor photopic) used by researchers to explore and compare children's activity and light exposure profiles.

The ambient illumination recorded in a range of locations differ significantly between summer and winter in this Northern Ireland (UK) study, and this difference is apparent on both sunny and rainy/cloudy days. As expected, the illumination present outdoors in summer is significantly higher than that experienced in winter for all conditions listed; sunny day, rainy/overcast day, before school, after school and with hat or sunglasses covering the photometer. As the measurements were taken at the same time in both seasons the significant differences between summer and winter are likely to be a result of

a combination of differing weather conditions, daylight hours, and sun position in the sky across the seasons in the UK. The daytime measures of light exposure received by a classroom window were higher in summer than winter, but away from the window there was no difference between the light exposure recorded in the different seasons. The indoor light exposure readings taken during the evening/night revealed less disparities between winter and summer, but some significant differences were apparent (Table 3.4.1.). When comparing the Northern Ireland measures of light exposure to those from Houston, Texas it is evident that the average outdoor light exposure is significantly higher in Texas particularly in summer (176,497 lux vs 90,500 lux in summer sun) with the indoor readings being more similar (248 lux vs 520 lux in a classroom) (Ostrin, 2017). The geographical differences are as expected given the climatic differences and difference in latitude (Northern Ireland (UK) 55 degrees north, Houston, Texas 29 degrees north) between the two locations.

The present real-world data clarifies the strengths and limitations of using the Clouclip to study illumination measures in Northern Ireland (UK, 55° North), demonstrating for the first time good and excellent inter-device reliability with intraclass correlation coefficients of 0.853 and 0.958 for illumination and near viewing distance measures, respectively (Koo and Li, 2016). The Actiwatch 2 had excellent inter-device reliability with intraclass correlation coefficients of 0.999 for both illumination and activity measures, which agrees strongly with the findings of Read *et al.* (2014). Bhandari and Ostrin (2020) report that the Clouclip slightly underestimated 'true' illumination in comparison to a photometer. Our findings support those of Bhandari and Ostrin, illustrating that the Clouclip underestimates 'true' lux values in higher levels of illumination, but to a lesser degree than the Actiwatch 2 outputs.

Underestimation of the 'true' illumination value results in the Actiwatch 2's relatively poor ability to successfully identify environmental light as scotopic, mesopic, indoor photopic or outdoor photopic. Misclassification was most prevalent in dimmer illumination; low levels of mesopic light were classified by the Actiwatch 2 as scotopic, indoor photopic light as mesopic, and outdoor photopic light as indoor photopic (Figure 3.4.1.). Given that outdoor photopic light is generally in the range 1000 to 10000 lux (ATP Instrumentation, 1989), but can be as high as 100,000 lux on a very bright summer day (Ostrin, 2017), the opportunities for misclassification of outdoor light (between 1000-2500 lux) by the Actiwatch 2 are likely to be limited to measures made at dusk or dawn,

particularly in the winter months. The empirically calculated criteria presented in Table 5 can be applied to both Actiwatch 2 and Clouclip outputs to allow categorisation that aligns more closely with photometer measures. Joyce *et al.* (2019) also recommended the use of a conversion factor when using the Actiwatch 2 to accurately quantify ambient illumination.

In findings similar to the present study, Joyce *et al.* (2019) found that the Actiwatch 2 underestimated the true illumination in comparison with a calibrated photometer, but that the relationship between the illumination outputs by the Actiwatch 2 and photometer was strongly linear. Jardim *et al.* (2011) also report that both eye-level (Daysimeter) and wrist-level (Actiwatch-L) illumination measures were correlated with each other at <5000 lux but above that, the Actiwatch-L underestimated the illumination. The average difference across the entire day between the eye-level and wrist-level illumination was 130 lux, with a range of differences of 5-1000 lux. In contrast to two previous studies which found the Actiwatch Spectrum to consistently overestimate illumination in comparison to calibrated photometers (Figueiro *et al.*, 2013; Markvart, Hansen and Christoffersen, 2015), our data demonstrate consistent underestimation of the 'true' illumination value by the Actiwatch 2. The Actiwatch-L and Actiwatch 2 both have a silicon photodiode light sensor while the Actiwatch Spectrum has colour sensitive photodiodes which could explain the variation in under- and overestimation of illumination when compared to photometer measures.

The present study demonstrates that the Clouclip measures of illumination are more comparable to the 'true' illumination measured by a calibrated photometer than those achieved with the Actiwatch 2. The relationship between the Clouclip and photometer measures found in the present study (ρ=0.991) are similar to those reported by Bhandari and Ostrin (2020) who also report a strong relationship between measures made by the Clouclip and photometer (r=0.96). In higher levels of illumination (>2500 lux), the Clouclip underestimates the 'true' lux value in comparison with the photometer, but this is unlikely to result in misclassification of the outdoor photopic light category. The Clouclip is unable to distinguish between scotopic and mesopic light ≤1 lux, and therefore is not a useful tool to explore exposure to extremely low light levels as it cannot discern between scotopic and low mesopic illumination. However, when used to distinguish between mesopic and indoor photopic, and indoor and outdoor photopic light levels, the Clouclip performed more successfully than the Actiwatch 2 (Table 3.4.3.). Classification

by the Clouclip remained accurate even when illumination levels measured by the photometer were close to the category borders. Bhandari and Ostrin (2020) report that the Clouclip could reliably detect outdoor illumination (defined as >1000 lux) in a more southerly location than (Houston, Texas 29° North) than the present study.

Several studies have used the Actiwatch 2 to quantify differences between myopes and non-myopes in terms of time spent in different lighting conditions (Read, Collins and Vincent, 2014, 2015; Landis *et al.*, 2018). However, the criteria used to delineate one type of illumination from another has been inconsistent, making comparison between data sets challenging. Landis *et al.* (2018) report that non-myopes spent a greater amount of time in scotopic light conditions compared with myopic children. When combined with the rather extended definition of scotopic used by Landis et al (<1-1 lux) compared to more commonly accepted values (≤0.01 lux) (SolarLight, 2014) as used in the present study and the underestimation of illumination by the Actiwatch 2 reported here, the light levels in Landis *et al.*'s study attributed as 'scotopic' could have been anywhere between scotopic and low mesopic. While the non-myopic children spent more time in these lower lighting levels than their myopic peers it is not clear whether the illumination was truly rod activating as the authors suggest. It has also been reported using Actiwatch 2 data that non-myopes spend more time in outdoor photopic (>1000 lux) light levels than myopes (Read, Collins and Vincent, 2014, 2015; Landis *et al.*, 2018). The results of the present study suggest that the amount of time exposed to light of >1000 lux is likely to have been underestimated using a cut-off of >1000 lux measured by these wristworn devices, although the effect will be consistent across refractive groups. For researchers wishing to evaluate time spent in different light levels including the very dimmest illumination, the broader measurement range of the Actiwatch 2 makes it a more useful tool than the Clouclip, but researchers should be aware of, and calibrate for, the underestimation of true illumination using empirically derived cut-offs.

The Bland and Altman analysis comparing illumination measures between the Actiwatch 2 and photometer (Figure 3.4.2.), and the Clouclip and photometer (Figure 3.4.3.), indicate the superior ability of the Clouclip to determine 'true' illumination compared to the Actiwatch 2, as illustrated by the smaller mean difference and narrower LOAs for the Clouclip (79.35 ± 407.33 lux) compared to the Actiwatch 2 (430.92 ± 1828.74 lux). However, there is significant proportional bias for both devices, illustrating that as the

illumination increases the measures recorded by the wearable devices deviate more from the 'true' value.

A notable finding of the present study was that readings >1000 lux were recorded by the photometer in indoor domestic locations, when the sensor was near a window/door with bright sunlight streaming in. Illumination readings of >1000 lux are commonly used by researchers to denote time spent outdoors (Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018; Ulaganathan *et al.*, 2019). The present field study determined that even when using a calibrated photometer to measure illumination, a value of >1000 lux does not always indicate an outdoor location. Using this cut-off to indicate an outdoor location as measured by the calibrated photometer has a sensitivity (i.e., a measurement of >1000 lux results in correct identification of an outdoor position) of 90.5% and specificity (i.e., a measurement of ≤1000 lux results in correct identification of an indoor position) of 100% (Table 3.4.5.). The Clouclip suffers from a similar limitation, but because the Actiwatch 2 consistently under-estimates 'true' lux, the >1000 lux values recorded with the Actiwatch 2 will reflect outdoor location more consistently than when recorded by the other devices used in the present study, with a sensitivity of 99.7% and specificity of 100%. When the empirically derived cut-offs for each wearable device were applied the sensitivity increased to 100% for both the Actiwatch and Clouclip. The specificity however reduced to 93.2% and 87.5% for the Actiwatch and Clouclip, respectively, indicating the increased accuracy of determining an outdoor position but not indoor. Time spent outdoors not only confers higher light levels, but also more varied spectral content as well as differences in dioptric demand and spatial content experienced by the eye. Given that there is still debate about the mechanisms by which time spent outdoors protects against myopia (Flitcroft, 2012; Ngo *et al.*, 2013), this distinction may be important. If researchers want to accurately discriminate between time spent indoors and outdoors, activity may need to be certified by video or GPS data when using the Clouclip. The use of activity diaries can also support objectively gathered data in profiling time spent outdoors.

The results of the present study highlight some benefits and limitations of the Actiwatch 2 and Clouclip devices for measuring illumination. Both devices are wearable and therefore ideal for field-use. The Actiwatch 2 can record illumination across a wider range of light levels and is therefore useful when investigating time spent in conditions ranging from near-dark scotopic illumination through to bright outdoor photopic light levels.

However, the Actiwatch 2 underestimates light levels to a greater extent than the Clouclip and more often misclassifies illumination than the Clouclip if the traditional criteria for categorisation are applied. The empirically derived cut-offs for illumination described in Table 3.4.4. are likely to be more appropriate for determining time spent in different types of illumination if researchers are using a categorical approach to analyse environmental light exposure. The Clouclip outputs more closely resemble 'true' illumination as measured by the photometer, and the spectacle mounted device accurately classifies light exposures >1 lux. However, the Clouclip's utility is limited by a short battery life, a restricted recording epoch and an inability to determine between scotopic and low mesopic light levels as illumination ≤1 lux is recorded as 1 lux in the output Excel. Additionally, the restricted two-minute recording epoch could result in under- or over-estimation of time spent in different categories of illumination if the wearer is moving rapidly between different environments. This may be particularly relevant when conducting research aimed at understanding light exposure profiles of children; the Clouclip will not capture dynamic changes in environment as readily as the Actiwatch 2, which has the option of shorter recording epochs (15, 30 or 60s).

The present study was intentionally carried out in the field rather than a laboratory setting to gain insight into the real-world utility of the devices. However, the non-laboratory setting resulted in reliance on the natural light conditions encountered and it was not possible to control the specific lux range to which the devices were exposed. The outdoor illumination values are reflective of the real-world light levels experienced in the present study's location (Northern Ireland, UK 55° North). Interpretation of the results is restricted to evaluation of the devices' performance in these naturally occurring light conditions. It should also be recognised that the two devices were not compared with the photometer under identical conditions due to practical constraints, including the need to continually 'wobble' the skeleton's head to prevent the Clouclip entering 'sleep mode'. The Clouclip wasn't exposed to the same high illuminations that were available when undertaking testing with the Actiwatch 2, and therefore the two devices' outputs could not be directly compared to each other.

3.6. Conclusion

The present data illustrate that the Actiwatch and Clouclip devices produce comparable measures of illumination, viewing distance and activity in a real-world setting. Both

Actiwatch 2 and Clouclip devices underestimate illumination in the field when compared to ‘gold standard’ photometer measures. This disparity increases at higher levels of illumination and is greater for the Actiwatch 2 measures. For researchers interested in categorising light exposure into different classifications from mesopic through to outdoor photopic levels, the Clouclip is a more useful tool, but when scotopic and low mesopic differentiation is required, the Actiwatch 2’s broader measurement range is required. Empirically calculated criteria for defining scotopic, mesopic, indoor and outdoor photopic illuminations are presented for the Actiwatch 2 devices and empirically calculated criteria for defining scotopic/mesopic, indoor and outdoor photopic illuminations are presented for the Clouclip devices. These could be applied by researchers to improve the accuracy of categorisation, or researchers may consider undertaking such calibration activity for the devices used in their own research. Finally, caution should be applied when using a cut-off of >1000 lux as a proxy for outdoor settings.

3.6.1. Key Points

- Both the Actiwatch and the Clouclip demonstrate good or excellent inter-device reliability for measuring light exposure, physical activity and viewing distance.
- Illumination measures taken in real-world settings by Clouclip more closely reflect ‘true’ illumination measured by photometer than those obtained with the Actiwatch 2, particularly at higher levels of illumination.
- Clouclip more accurately classifies illumination levels ≥2 lux than the Actiwatch 2, but the restricted operating range means it cannot discriminate between time spent in scotopic vs low mesopic light.
- Photometry measurements of >1000 lux were obtained from indoor as well as outdoor locations. This should be considered when using illumination measures as a proxy for time spent outdoors.

Chapter 4: Comparison of Objective Measures of Physical Activity, Light Exposure, Sleep and Near Viewing Behaviours when gathered over 7- vs 14-Days

Chapter 4: Comparison of Objective Measures of Physical Activity, Light Exposure, Sleep and Near Viewing Behaviours when gathered over 7- vs 14-Days

4.1. Introduction

Previous research has determined that two weeks of data collection is the "gold standard" for assessing sleep metrics (Van Someren, 2007). Ulaganathan *et al.* (2017) also notes that the 14-day 'gold standard' sampling period of light exposure measures by the Actiwatch 2 is primarily determined by the memory capacity of the device. The authors then suggested that at least seven days of data collection provides the most reliable estimates of personal light exposure in both children and young adults. Trost *et al.* (2000) reported than 7-days of physical activity monitoring using an accelerometer provided reliable estimates of normal physical activity in children, but that 8-9 days of monitoring would increase this reliability further.

The Northern Ireland Childhood Errors of Refraction (NICER) Study 2.0 as discussed in Chapter 5 aims to investigate the prevalence of myopia in children aged 6-7-years-old in 2019-2021 alongside objectively measuring potential risk factors for myopia such as light exposure, sleep quality, physical activity and near viewing behaviours including, screen time use. However, a 14-day data collection period is a logistical challenge for the NICER 2.0 study, with a large sample size (n=100) and young participants (aged 6-7-years old).

The screen time recorded in this study is defined as screen time on handheld devices such as phones/tablets alone. There are currently challenges regarding the assessment of screen time on laptops, work computers, or shared devices such as a family TV or games console. In addition, a grey area with screen time assessment is the use of multiple devices at once (media multitasking) where someone has the TV on in the background while doing some work on the laptop and intermittently checks their phone notifications (Kaye *et al.*, 2020).

4.1.1. Aims

The aims of the study were:

- To understand how average measures taken over one week (including five weekdays and two weekend days) compare with measurements taken over a two-week period (including ten weekdays and four weekend days)
- To determine whether obtaining seven days' worth of data is a valid way of profiling a persons' lifestyle in relation to their physical activity, light exposure, sleep quality and near viewing behaviours using the Actiwatch 2, Clouclip and screen time monitoring apps.

4.2. Recruitment and Participants

The sample size for this study was determined using the formula for "agreement between two methods" (McAlinden, Khadka and Pesudovs, 2011). The desired confidence interval of limits of agreement=$1.96\sqrt{3s^2}/n$. Fourteen counts per minute (cpm) was determined as the desired confidence interval for the physical activity measure with a standard deviation of 19.6 cpm (derived from (Routen *et al.*, 2012). A confidence interval of 14 cpm is a conservative estimate of the minimum value between wake and sleep on the Actiwatch 2. Using these data, a sample size of 23 participants was required.

Twenty-three healthy adult participants aged between 18-60 years, that were full time spectacle wearers were recruited from friends and family of the researcher and the staff and postgraduate students within the Optometry Department in Ulster University. Written consent was given by the participants after reading an information sheet on the nature and any possible consequences of the study.

4.3. Methods

4.3.1. Wearable Devices

The devices being employed to objectively measure light exposure, sleep quality, physical activity and near viewing distances are the Respironics Actiwatch 2 (Philips, NV, USA) and the Clouclip Model M2 (HangZhou Glasson Technology Co). The Actiwatches have been used successfully in previous research studies investigating refractive error and light exposure (Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018). The Clouclips are relatively new devices but have been used in studies to examine light exposure and viewing behaviours in children (Cao *et al.*, 2020; Wen *et al.*, 2020).

4.3.1.1. Respironics Actiwatch 2

The Actiwatch 2 is a lightweight (16g) and waterproof (for up to 30 minutes) wrist-worn 'actigraphy' device measuring 43 x 23 x10 mm. The Actiwatch 2 that contains a silicone photodiode light sensor to measure visible light illuminance with a range of 0.01-100,000 lux and a solid-state piezoelectric accelerometer to measure physical activity ranging from 0.35-7.5 Hertz (recorded as activity counts per minute [cpm]). The Actiwatch has an adjustable epoch from 15, 30, or 60 seconds. The device is connected to a computer contained the Actiware software using a docking station for charging and data retrieval.

The data is uploaded onto the Actiware software and from here can be exported as a CSV file and converted to an Excel (Microsoft, www.microsoft.com) spreadsheet for further analysis. The Actiwatch 2 was programmed to record light and activity measurements, and data on sleep/wake intervals every 30 seconds for two weeks of participant wear. Participants were instructed to wear the device on their non-dominant wrist for 24 hours a day over the 2-week period, to ensure that the watch was not covered by clothing during wear and to remove it for any water-based activities of greater than 30 minutes.

4.3.1.2. Clouclip M2

The Clouclips were provided by Aeir Eye Hospital Group, China. The Clouclip M2 is a 45.3 x 13.4 x 8.0 mm device, designed for attachment to the right temple of a spectacle frame using a rubber sleeve. The devices have a built-in infrared distance sensor to determine near viewing distance (ranging from 5-120 cm), a light intensity sensor to record eye-level ambient illumination (ranging from 1-65536 lux) and a three-axis accelerometer (X, Y, Z axis) to distinguish when it is being worn. The Clouclip records near viewing distance every 5 seconds and illumination every 2 minutes. The device is Bluetooth capable and has a magnetic USB charger for syncing the device to an app and uploading the data to the cloud, from here raw data can be downloaded as an Excel spreadsheet using login credentials (Wen *et al.*, 2016; Bhandari and Ostrin, 2020) and a number of parameters are already calculated for download (average duration of near work, maximum duration of near work, average near work distance, average illumination during near work, sunlight exposure duration per day and sunlight exposure frequency per day). As the spectacles were removed at night for the device to be charged and sometimes removed for certain activities (e.g., showering/sports), the parameters were only analysed for when the participant was wearing the Clouclip (determined by the accelerometer information).

4.3.2. Screen-Time Monitoring Applications

Screen-time monitoring applications on participants phones/tablets were used to monitor the time spent on these devices over the course of the data collection period. The apps were Apple Screen Time (built-in app) or Moment Balance Screen Time for iPhone, and Quality Time-My Digital Diet for Android.

4.3.3. Data Collection Procedure

On Day one of data collection, participants were fitted with a wristworn Actiwatch 2 and the Clouclip M2 was attached to their spectacles on day one of data collection. The Clouclip has a maximum capacity of eight days therefore, on day seven the participants returned with the device for data upload and the Clouclips were re-initialised for the second week of wear. On day 14 both devices, along with data from the apps were collected. The data collection procedure has been outlined in Figure 4.3.1.

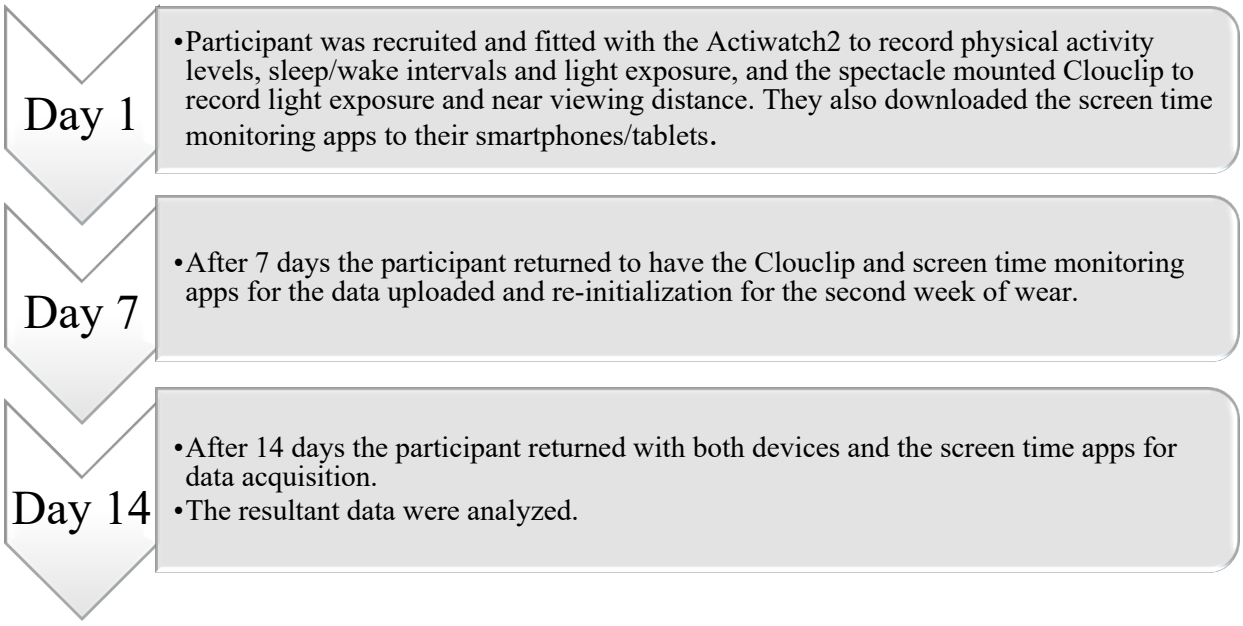


Figure 4.3.11. A flow chart of the data collection procedure.

4.3.4. Data Extraction and Categorisation

Following two-weeks of device wear, the physical activity, sleep quality and light exposure data were downloaded from the Actiwatch 2 using Actiware software and the raw data were exported to Excel (Microsoft, www.microsoft.com) for categorising the parameters as described below. The Clouclip data on light exposure and near working distance were downloaded via the Clouclip Medical app and exported to Excel for categorising the parameters. The app data were also recorded. The average values for each of the parameters were calculated as well as the time spent under different lighting conditions, at different working distances or varying physical activity levels over 7- and 14-days. The inclusion criteria of wear time were at least four full days of data from both wearable devices (including at least one weekend day) per week, with at least eight hours wearing time per day of the Clouclip.

Compliance (i.e., wear) with Clouclip is indicated by the accelerometer output. This allows the researcher to determine the number of hours which the Clouclip has been worn

during the study period. Actiwatch data were initially screened to remove any invalid data, i.e., where it was evident that the watch was removed for more than 15 minutes, or the light sensor was covered by clothing.

Tables 4.3.1. and 4.3.2. describe how the measured parameters were categorised in the present study. All the parameters were calculated as an average per day. The binning of data into categories helps describe the patterns of light exposure levels (Rosenfield and Logan, 2009; SolarLight, 2014; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020), viewing distances (Bilton, 2010; Long *et al.*, 2017) and physical activity levels (Neil-Sztramko *et al.*, 2017) throughout the course of the data collection period. Read *et al.* (2014) pointed out that quantifying of activities is likely to provide a more comprehensive understanding of the intensity, duration and frequency of light exposure and physical activity metrics, which may provide new insights into the potential mechanisms underlying the protective influence of outdoor activity on myopia, which enhances the richness of the data compared to average and total values alone (Rowlands, 2007).

Parameters for Actiwatch 2	**Categories**	**Derived from/References**
Time spent in Scotopic Light (mins)	mins in ≤0.01 lux	SolarLight (2014)
Time spent in Mesopic Light (mins)	mins in 0.02-3 lux	Rosenfield and Logan (2009)
Time spent in Photopic Light (mins)	mins in >3-1000 lux	Bhandari and Ostrin (2020)
Time spent Outdoors (mins)	mins in >1000 lux	Ulaganathan *et al.* (2019)
Time spent Indoors (mins)	mins in ≤1000 lux	Ulaganathan *et al.* (2019)
Time Spent in Mesopic Light (mins)	mins in 0.02-0.78 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Time spent in Photopic Light (mins)	mins in >0.78-533.15 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Time spent Outdoors (mins)	mins in >533.15 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Time spent Sedentary (mins)	mins spent at <160 cpm	Neil-Sztramko *et al.* (2017)
Time spent on Light Activity (mins)	mins spent at 160-524cpm	Neil-Sztramko *et al.* (2017)
Time spent on Moderate Activity (mins)	mins spent at 524-812cpm	Neil-Sztramko *et al.* (2017)

Time spent on Vigorous Activity (mins)	mins spent at >812cpm	Neil-Sztramko *et al.* (2017)
Daytime Light Exposure (lux)		Average lux with sleep time excluded
Night Light Exposure (lux)		Average lux with active time excluded
Daytime Physical Activity (cpm)		Average cpm with sleep time excluded
Sleep Time (mins)		Output from Actiware Software
Sleep Onset (mins)		Output from Actiware Software
Sleep Efficiency (%)		Output from Actiware Software
Wake After Sleep Onset (WASO) (mins)		Output from Actiware Software
Number of Awakenings		Output from Actiware Software

Table 4.3.2. This table presents all the parameters determined by the Actiwatch, and how they were calculated, included references for the cut-offs where appropriate.

Parameters for Clouclip/Apps	**Categories**	**Derived from/References**
Time spent in Mesopic Light (mins)	mins in 1-3 lux	Rosenfield and Logan (2009)
Time spent in Photopic Light (mins)	mins in >3-1000 lux	Bhandari and Ostrin (2019)
Time spent Outdoors (mins)	mins in >1000 lux	Ulaganathan *et al.* (2019)
Time spent Indoors (mins)	mins in ≤1000lux	Ulaganathan *et al.* (2019)
Time spent in Mesopic Light (mins)	mins in 2-3 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Time spent in Photopic Light (mins)	mins in >3-850 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Time spent Outdoors (mins)	mins in >850 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Daytime Light Exposure (lux)		Average lux with non-wear time excluded
Daytime Viewing Distance (cm)		Average cm with non-wear time excluded
Screen Time (mins)		App data
Time spent at very close (mins)	≤30cm	(Long *et al.*, 2017)
Time spent at near (mins)	31-49cm	(Bilton, 2010)
Time spent at intermediate (mins)	50-119m	(Bilton, 2010)
Time spent at distance (mins)	≥120cm	(Bilton, 2010)

Table 4.3.3. This table presents all the parameters determined by the Clouclip and screen-time monitoring apps, and how they were calculated, including references for the cut-offs where appropriate.

4.3.5. Ethical Approval

The study was in compliance with the Helsinki Declaration and was approved by the Ulster University's Research and Ethics Committee on 29th November 2018, application number: FCBMS-18-180-A.

4.4. Statistical Methods

Data were entered into SPSS Version 25 which was used for statistical analysis. Descriptive statistics were used to describe data for each devices' parameters over the course of 7- and 14-days. The agreement between measures over 7- and 14-days were compared using Bland and Altman analyses (Bland and Altman, 1986). The normality of the data was tested using a Shapiro-Wilk test, and a paired T-test or Wilcoxon matched pairs signed rank test were used to evaluate statistically significant differences between 7- and 14-days parameters where normality or non-normality were present, respectively. The within participant standard deviation was compared for data collected from 7- and 14-days separately. The difference in measures for 7- and 14-day data were calculated for each participant as the value for 14 days data minus 7-days data. Regression analysis was used to check for proportional bias, i.e., a relationship between the size of the difference between 7- and 14-days measures and the magnitude of the measure.

4.5. Results

4.5.1. Descriptive Statistics

Data collection was carried out between January 2019 and November 2020. Twenty-three participants were recruited with an average age of 32.9 years (range 19.3-57.8 years). Complete Actiwatch 2 and screen time data were available for 21/23 (91%) of participants and Clouclip data were available for 12/23 (52%) of participants.

Two participants had less than four days' worth of data on both the Actiwatch and Clouclip and hence were removed from all analyses. A further nine participants did not meet the inclusion criteria of wear from the Clouclip for one and/or both weeks, and so were removed from the Clouclip analyses. One outlier had data removed for analysis.

4.5.2. Comparison of 7- and 14-days of Data

Table 4.5.1. presents the mean and standard deviation along with the range for each parameter for both 7- and 14-day periods. The mean difference, standard deviation and 95% upper and lower limits of agreement (LOAs) for both sampling periods are also reported in Table 4.5.1. In addition, the results of paired T-tests or Wilcoxon matched pairs signed rank tests for each parameter were reported to evaluate statistically significant differences between the results from 7- and 14-day periods. Additionally in Table 4.5.1. are the results of the regression analyses where each parameter was assessed for demonstrating proportional bias between the two sampling periods.

	Mean +/SD 7 days	Range 7 days	Mean +/- SD 14 days	Range 14 days	Mean Difference 14 days - 7 days	SD	95% Upper LOA	95% Lower LOA	Significant Difference in 7- and 14- days	Proportional Bias
Clouclip Light Exposure (lux)	177.35 +/- 92.31	68.18-400.54	171.90 +/- 68.78	71.73-290.38	-5.45	42.88	78.59	-89.49	p=0.668	r=0.563 p=0.057
Viewing Distance (cm)	106.55 +/- 21.46	83.88-155.26	109.11 +/- 19.52	85.02-156.76	2.56	10.08	22.32	-17.20	p=0.398	r=0.199 p=0.536
Time spent at Very Close (mins)	95.12 +/- 45.69	7.78-161.19	91.01 +/- 42.55	10.22-154.48	-4.11	22.14	39.28	-47.50	p=0.533	r=0.147 p=0.650
Time spent at Near (mins)	103.95 +/- 61.69	21.65-270.27	107.38 +/- 64.16	23.53-263.57	3.43	18.36	39.42	-32.56	p=0.695†	r=0.136 p=0.674
Time spent at Intermediate (mins)	153.06 +/- 64.05	57.13-248.28	161.54 +/- 60.29	74.68-263.56	8.48	13.52	34.98	-18.02	p=0.053	r=0.280 p=0.379
Time spent at Distance (mins)	271.94 +/- 106.59	138.33-489.43	276.65 +/- 101.00	157.34-516.50	4.71	30.87	65.22	-55.80	p=0.607	r=0.183 p=0.569
Actiwatch Light Exposure Day (lux)	208.20 +/- 360.45	27.76-1732.74	207 +/- 331.59	32.41-1589.14	0.76	33.33	66.09	-64.57	p=0.455†	r=0.149 p=0.543

Actiwatch Light Exposure Night (lux)	12.11 +/- 53.26	0.01-244.52	11.82 +/- 51.79	0.04-237.84	0.02	0.45	0.90	-0.86	p=0.835†	r=0.026 p=0.912
Physical Activity (cpm)	165.55 +/- 36.08	71.44-222.08	163.35 +/- 31.17	72.72-211.04	-2.20	10.38	18.14	-22.54	p=0.342	r=0.477 p=0.029*
Sleep Time (mins)	436.49 +/- 72.80	268.85-565.42	436.85 +/- 70.59	271.35-538.28	0.35	15.17	30.08	-29.38	p=0.916	r=0.147 p=0.526
Sleep Onset (mins)	27.03 +/- 27.18	7.79-125.60	23.25 +/- 14.72	9.32-73.02	-1.34	8.44	15.20	-17.88	p=0.455†	r=0.728 p<0.001*
Sleep Efficiency (%)	81.89 +/- 8.41	54.75-91.33	82.20 +/- 8.01	56.11-89.54	0.31	2.48	5.17	-4.55	p=0.876†	r=0.164 p=0.478
WASO (mins)	47.18 +/- 22.21	24.21-98.36	50.17 +/- 26.50	27.81-125.82	2.99	9.58	21.77	-15.79	p=0.274†	r=0.455 p=0.038*
Number of Awakenings	36.20 +/- 8.85	24.83-55.57	37.83 +/- 8.42	23.06-55.93	1.64	2.67	6.87	-3.59	p=0.011**	r=0.164 p=0.476
Screen Time (mins)	149.96 +/- 124.93	24.28-556.00	210.48 +/- 130.57	28.14-587.50	3.65	17.85	38.64	-31.34	p=0.987†	r=0.309 p=0.161
Scotopic Actiwatch (mins)	573.43 +/- 148.15	0.00-746.22	578.87 +/- 146.68	0.00-719.28	5.44	22.09	48.74	-37.86	p=0.296†	r=0.067 p=0.773

Mesopic Actiwatch (mins)	204.60 +/- 120.44	81.94-642.62	194.91 +/- 66.78	92.77-321.31	5.45	20.66	45.94	-35.04	p=0.556	r=0.329 p=0.157
Photopic Actiwatch (mins)	630.57 +/- 83.53	489.22-791.16	634.40 +/- 108.36	506.00-956.76	3.83	65.99	133.17	-125.51	p=0.205†	r=0.397 p=0.075
Outdoor Actiwatch (mins)	31.41 +/- 36.23	1.36-133.29	31.82 +/- 41.90	0.90-161.94	-1.64	7.13	12.33	-15.61	p=0.274†	r=0.210 p=0.375
Indoor Actiwatch (mins)	1408.59 +/-36.23	1306.71-1438.64	1408.18 +/- 41.90	1278.07-1439.11	1.64	7.13	15.61	-12.33	p=0.274†	r=0.210 p=0.375
Validation Mesopic Actiwatch (mins)	87.31 +/- 40.60	13.57-176.16	86.50 +/- 34.62	22.07-148.07	-0.82	22.87	44.01	-45.65	p=0.872†	r=0.274 p=0.230
Validation Photopic Actiwatch (mins)	726.99 +/- 103.49	569.60-1061.41	720.62 +/- 104.72	594.14-1069.36	-6.37	22.23	37.20	-49.94	p=0.244	r=0.056 p=0.811

Validation Outdoor Actiwatch (mins)	52.27 +/- 51.54	2.93-202.43	54.01 +/- 64.39	3.07-282.56	-1.91	9.15	16.02	-19.84	p=0.614	r=0.104 p=0.661
Sedentary Activity (mins)	1058.57 +/- 95.38	868.72-1288.30	1062.23 +/- 83.93	902.13-1283.95	3.66	26.21	55.03	-47.71	p=0.530	r=0.441 p=0.046*
Light Activity (mins)	185.92 +/- 45.50	96.51-281.90	185.16 +/- 40.10	97.74-257.32	-0.75	12.03	22.83	-24.33	p=0.777	r=0.452 p=0.039*
Moderate Activity (mins)	162.66 +/- 49.58	51.18-284.04	161.93 +/- 44.43	54.16-268.23	-0.73	13.36	25.46	-26.92	p=0.805	r=0.388 p=0.082
Vigorous Activity (mins)	32.85 +/- 14.88	4.02-58.29	30.67 +/- 13.64	4.16-51.17	-2.18	5.30	8.21	-12.57	p=0.074	r=0.239 p=0.297
Mesopic Clouclip (mins)	72.63 +/- 43.43	24.52-151.60	68.53 +/- 34.14	24.08-128.79	-4.10	14.32	23.97	-32.17	p=0.343	r=0.655 p=0.021*
Photopic Clouclip (mins)	569.91 +/- 128.14	355.54-751.66	581.97 +/- 126.95	352.92-786.97	12.07	31.48	73.77	-49.63	p=0.211	r=0.038 p=0.906
Outdoor Clouclip (mins)	21.84 +/- 13.27	2.00-42.23	20.37 +/- 10.94	4.55-37.30	-1.47	5.51	9.33	-12.27	p=0.375	r=0.432 p=0.161
Indoor Clouclip (mins)	642.54 +/- 133.66	386.98-811.84	650.50 +/- 132.12	376.99-845.94	7.97	29.39	65.57	-49.63	p=0.368	r=0.053 p=0.870

Validation Mesopic Clouclip (mins)	21.94 +/- 10.22	11.19-40.17	21.12 +/- 9.04	9.44-40.71	-0.82	4.21	7.43	-9.07	p=0.513†	r=0.287 p=0.366
Validation Photopic Clouclip (mins)	566.22 +/- 127.90	353.73-747.27	578.25 +/- 126.47	350.74-783.79	12.03	32.45	75.63	-51.57	p=0.221†	r=0.045 p=0.890
Validation Outdoor Clouclip (mins)	25.52 +/- 15.24	3.00-48.77	24.09 +/- 12.40	5.72-43.71	-1.43	6.60	11.51	-14.37	p=0.468†	r=0.440 p=0.153

*Table 4.5.1. Means, standard deviations (SD), ranges, mean differences and SD between 7- and 14-days, 95% upper and lower limits of agreement (LOAs), significant differences between 7- and 14-days ($p<0.05$) and regression analyses for proportional bias ($p<0.05$). † Parametric testing * Significant proportional bias on regression analyses ** Significant difference in 7- and 14-days.*

There was a statistically significant difference between the number of night-time awakenings between 7- and 14-days as measured by the Actiwatch, with more awakenings over 14-days than over 7-days ($p=0.011$). For all other parameters there were no statistically significant differences between 7- and 14- days averages (Paired t-test/Wilcoxon signed rank test, all $p>0.05$) (Table 3).

The mean difference and 95% limits of agreement (LOA) are plotted on the graphs (Figures a-ab) and regression lines are plotted where regression analysis showed a statistically significant proportional bias. Proportional bias was found for the Clouclip parameter of time spent in mesopic light ($r=0.655$, $p=0.021$) and for the Actiwatch parameters of average physical activity ($r=0.477$, $p=0.029$), sleep onset ($r=0.728$ $p<0.001$), WASO ($r=0.455$, $p=0.038$), time spent sedentary ($r=0.441$, $p=0.046$) and time spent at light physical activity ($r=0.452$, $p=0.039$).

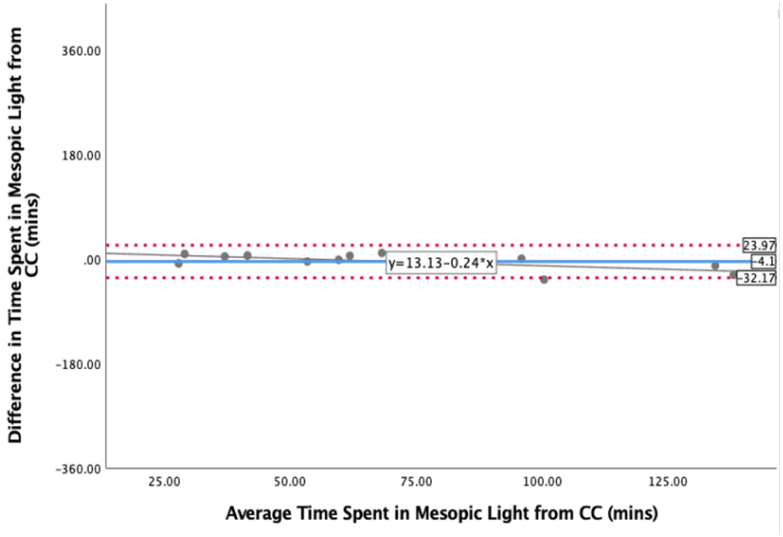
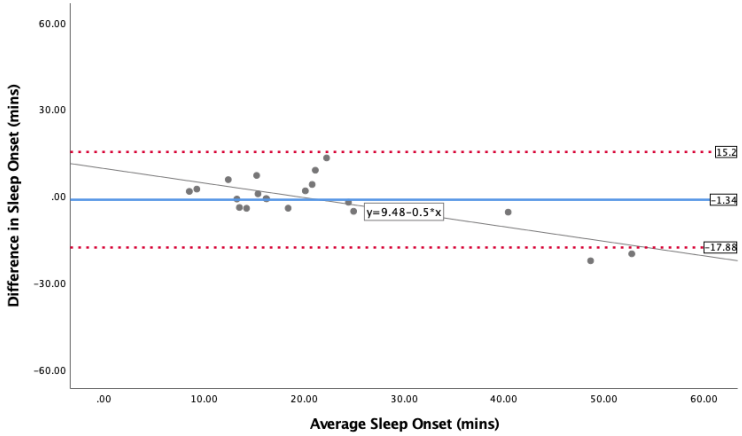
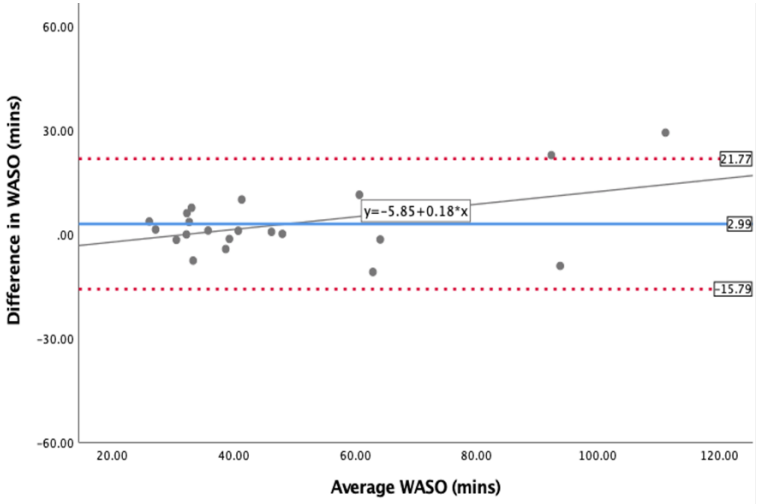
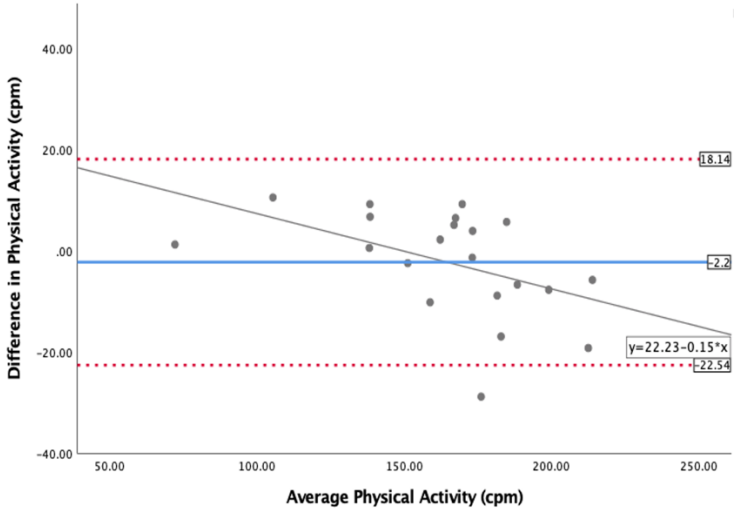


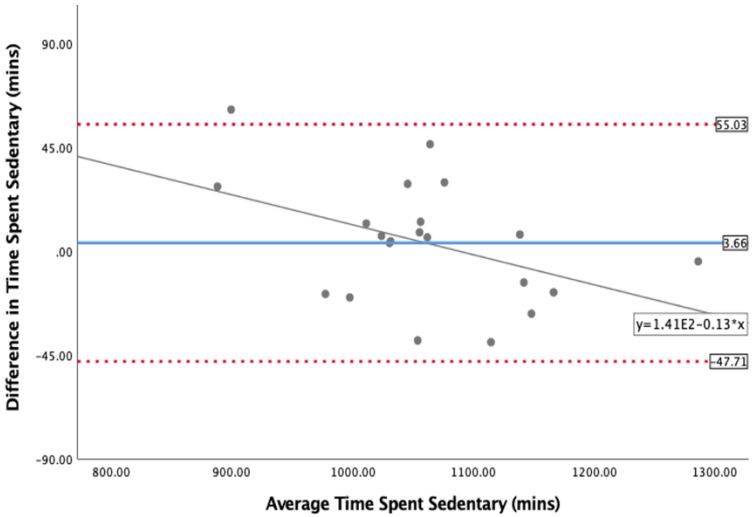
Figure 4.5.1. is a Bland and Altman plot for the Clouclip. The blue line indicates the mean difference between 7- and 14-days of data and the dashed red lines indicate the 95% upper and lower LOAs. The solid grey line represents a significant proportional bias for time spent in mesopic light measured by the Clouclip (r=0.665, p=0.021).

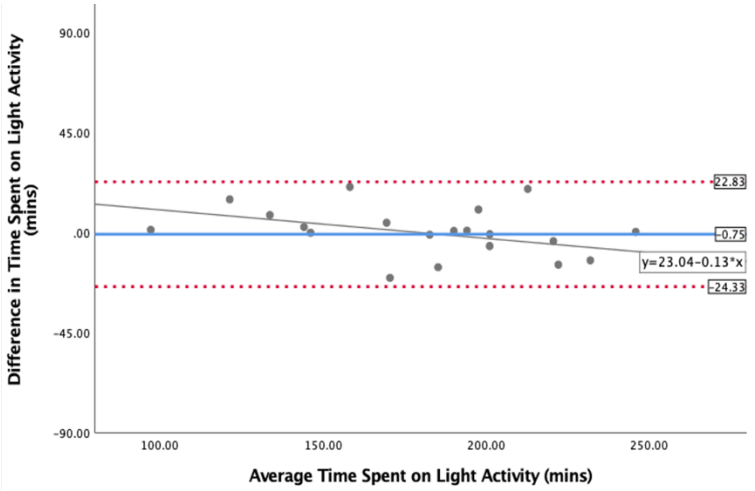




Figures 4.5.2. and 4.5.3. are Bland and Altman plots for some sleep parameters from the Actiwatch. The blue lines indicate the mean difference between 7- and 14-days of data and the dashed red lines indicate the 95% upper and lower LOAs. The solid grey line represents a significant proportional bias for sleep onset (r=0.728, p<0.001) and WASO (r=0.455, p=0.038).







Figures 4.5.4.-4.5.6. are Bland and Altman plots for some physical activity parameters from the Actiwatch. The blue lines indicate the mean difference between 7- and 14-days of data and the dashed red lines indicate the 95% upper and lower LOAs. The solid grey line represents a significant proportional bias for physical activity (r=0.477 p=0.029), time spent sedentary (r=0.441 p=0.046) and on light activity (r=0.452 p=0.039).

4.6. Discussion

This is the first study to our knowledge conducted to investigate if 7-days of data collected from the wearable devices, the Actiwatch 2 and Clouclip and the screen time monitoring apps was a useful representation of a person's lifestyle, when compared with the 'gold standard' measurement duration of 14-days. There is a growing need within the myopia research field for precise sampling of potentially modifiable risk factors for childhood myopia in order to understand the role of these risk factors in the development and/or progression of myopia. Previous research has relied heavily on subjective methods which have their limitations namely, recall bias and over- or under estimation of activities. The NICER study (Chapter 5) aims to collect objective data on children's sleep patterns, physical activity, light exposure, viewing behaviours and screen time over a 7-day period, hence this study was designed to determine if 7-days of data collection was representative of a longer data collection period. The two wearable devices (Actiwatch 2 and Clouclip) alongside screen time monitoring apps enable objective assessment of participants sleep patterns, physical activity, light exposure, viewing behaviours and screen time with minimal invasive testing.

Previous research had determined that two weeks of data collection is the "gold standard" for assessing sleep metrics (Van Someren, 2007), and at least 1 week for sampling light exposures (Ulaganathan *et al.* (2017), and physical activity monitoring (Trost *et al.* (2000).

The results of the present study show a statistically significant difference between the number of night-time awakenings between 7- and 14-days as measured by the Actiwatch, with more average awakenings over 14-days than over 7-days (36.20 vs 37.83, p=0.011) However, this difference seems clinically insignificant. For all other parameters averages and time spent in different lighting and PA intensities there were no statistically significant differences between 7- and 14- days (all p>0.05).

4.6.1. Actiwatch Parameters

4.6.1.1. Light Exposure

The mean difference for 7- vs 14-days of daytime light exposure was 0.76 lux with 95% LOAs of -64.57 to 66.09 lux. This is unlikely to compromise the ability of 7-days' worth of data to distinguish between indoor and outdoor light exposure, which is the one of the primary reasons for exploring this parameter in the NICER study. Time spent outdoors

has been shown, in other geographical areas, to be a protective factor against myopia onset. Time spent outdoors has been widely accepted as >1000 lux (Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018). However, our recent validation study (Chapter 3) highlighted that illumination levels >1000 lux can also be found indoors by a window or door with light streaming in, therefore >1000 lux might not always be indicative of an outdoor position. Therefore, we calculated the time spent in different light exposure categories using new category cut-offs determined by empirically derived criteria from the validation study (Chapter 3) in addition to the previously determined categories.

The mean difference for night-time light exposure was 0.02 lux with 95% LOAs of -0.86 to 0.90 lux which are very narrow but, could compromise the ability of the Actiwatch to determine a difference between scotopic (≤0.01 lux) and mesopic light (0.02-3 lux) exposure at night.

The mean differences (and 95% LOAs) for time spent in the original light exposure categories over 7- vs. 14-days were, 5.44 (-37.86-48.74), 5.45 (-35.04-45.94), 3.83 (-125.51-133.17), -1.64 (-15.61-12.33) and 1.64 (-12.33-15.61) (all in mins) for time spent in scotopic, mesopic, photopic, outdoors and indoors light, respectively. The mean differences and 95% LOAs tended to increase with increased time spent in in each condition, demonstrating more variability between 7- and 14-days.

The mean differences (and 95% LOAs) for time spent in the new empirically derived light exposure categories over 7- vs. 14-days were, -0.81 (-45.65-44.01), -6.37 (-49.94-37.2) and -1.91 (-19.84-16.02) (all in mins) for time spent in mesopic, photopic, outdoor light, respectively. The mean differences and 95% LOAs were quite consistent among these new empirically derived categories.

The mean differences between 7- and 14-days were very narrow for all the Actiwatch light exposure parameters leading to the conclusion that measurements of a participants light exposure profile are reliable over a 7-day period. This is important for the 7-day protocol for collecting NICER study data, as time spent outdoors is one of the widely reported protective factors against the development and/or progression of childhood myopia (Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018).

4.6.1.2. Physical Activity

The mean difference for 7- vs 14-days of average physical activity was -2.20 cpm with 95% LOAs of -22.54 to 18.14 cpm which falls within the default wake threshold value of 40 cpm and a range of 20-80 cpm to score wake (Phillips Respironics, 2008). This indicates that 7-days of physical activity data is an accurate and reliable way to profile a persons' average physical activity when compared 14-days' worth of data.

The mean differences (and 95% LOAs) for time spent in different levels of physical activity over 7- vs. 14-days were, 3.66 (-47.71-55.03), -0.75 (-24.33-22.83), -0.73 (-26.92-25.46) and -2.18 (-12.57-8.21) (all in mins) for time spent sedentary, on light, moderate and on vigorous physical activity, respectively. The 95% LOA tended to be narrower with increasing levels of physical activity, indicating that the more time spent on higher levels of physical activity the increased accuracy of results over the course of 7- compared to 14-days.

Regression analysis demonstrated significant proportional bias for average physical activity ($r=0.477$, $p=0.029$). Regression analysis also demonstrated significant proportional bias for time spent sedentary ($r=0.441$, $p=0.046$) and time spent on light physical activity ($r=0.452$, $p=0.039$). Average physical activity, time spent sedentary, and time spent on light physical activity were all higher over 7-days compared to 14-days, indicating that 7-days of data collection could result in overestimation of these parameters.

There was no proportional bias for time spent on moderate or vigorous physical activity. This means that when assessing moderate-vigorous physical activity as a risk factor for myopia, 7-days' worth of data would be sufficient. Physical activity is a potentially modifiable risk factor for myopia. Therefore the ability to accurately measure higher levels of physical activity is important as these higher levels of physical activity have been previously reported to be protective over myopia development (Deere *et al.*, 2009; Holton *et al.*, 2019). The LOAs for time spent sedentary are within the validated LOAs for time spent sedentary on another accelerometer device (the Actigraph GT3X) with published 95% LOAs of 207 mins (Clemes *et al.*, 2012). This could indicate that the Actiwatch 2 is reliable for assessing time spent sedentary over the course of 7-days compared to 14-days. The LOAs for average physical activity fall within the wake

threshold value, and time spent sedentary falls within the validated LOAs for sedentary time on the Actigraph GT3X, therefore average physical activity and time spent sedentary can be reliably assessed over 7-days of data collection regardless of the proportional bias on regression analysis. Time spent sedentary has been reported as a risk factor for myopia from subjective data in the past (O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019) therefore it is important to examine if objectively measured sedentary time is a risk factor for childhood myopia.

4.6.1.3. Sleep

The mean differences (and 95% LOAs) for sleep time, sleep onset, sleep efficiency, wake after sleep onset (WASO) and number of awakenings over 7- vs. 14-days were, 0.35 mins (-29.38-30.08 mins), -1.34 mins (-17.88-15.20 mins), 0.31% (-4.55-5.17%), 2.99 mins (-15.79-21.77 mins) and 1.64 awakenings (-3.59-6.87 awakenings), respectively.

Regression analysis also demonstrated significant proportional bias for sleep onset ($r=0.728$, $p<0.001$), WASO ($r=0.455$, $p=0.038$). Individuals with faster sleep onset had slower sleep onset over 14-days compared to 7-days, therefore 7-days of data collection could overestimate their sleep onset. On the contrary, individuals with higher WASO had higher WASO over 14-days compared to 7-days, therefore 7-days of data collection could underestimate an individual's WASO.

Shin *et al.* (2015) have published limits of repeatability for the Actiwatch 2 sleep parameters. The limits of repeatability are 48.8 mins for total sleep time, 33.7 mins for sleep onset, 28.8 mins for WASO and 9.9% for sleep efficiency. The LOAs for all the parameters are within the publishing limits of repeatability for the Actiwatch 2 hence, 7-days' worth of sleep data could be deemed reliable in comparison to 14-days of data regardless of the proportional bias for sleep onset and WASO. There are currently no published limits of repeatability for the number of awakenings. The ability to measure sleep parameters is important due to new research reporting decreased sleep time (Gong *et al.*, 2014; Jee, Morgan and Kim, 2016), poor sleep quality (Zhou *et al.*, 2015; Ayaki *et al.*, 2016) and disrupted circadian rhythms (Kearney *et al.*, 2017) as increased risk factors of myopia.

4.6.2. Clouclip Parameters

4.6.2.1. Light Exposure

The mean difference for 7- vs 14-days of average light exposure was -5.45 lux with 95% LOAs of -89.49 to 78.59 lux. This is again unlikely to compromise the ability of 7-days' worth of data to distinguish between indoor and outdoor light exposure. The mean difference in 7- vs 14-days of average light exposure is slightly larger for the Clouclip than the Actiwatch 2, however the LOAs are narrower for the Clouclip than the Actiwatch 2 indicating superior reliability and accuracy of the Clouclip when measuring average light exposure than the Actiwatch 2 over 7-days when compared to the 14-days.

The mean differences (and 95% LOAs) for time spent in the original light exposure categories over 7- vs. 14-days were, -4.10 (-32.17-23.97), 12.07 (-49.63-73.77), -1.47 (-12.27-9.33) and 7.97 (-49.63-65.57) (all in mins) for time spent in mesopic, photopic, outdoors and indoors light, respectively. Again, as noted for the time spent in different lighting conditions by the Actiwatch 2, the mean differences and 95% LOAs for the time spent in different lighting conditions by the Clouclip tended to increase with increased time spent in in each condition, demonstrating more variability between 7- and 14-days.

Regression analysis demonstrated significant proportional bias for the Clouclip parameter of time spent in mesopic light ($r=0.665$, $p=0.021$). Individuals who spent more time in mesopic light (measured by CC) had higher values over 7-days of data collection compared to 14-days, therefore 7-days of data collection could overestimate their time spent in mesopic light.

The mean differences (and 95% LOAs) for time spent in the new empirically derived light exposure categories over 7- vs. 14-days were, -0.82 (-9.07-7.43), 12.03 (-51.57-75.63) and -1.43 (-14.37-11.51) (all in mins) for time spent in mesopic, photopic, outdoor light, respectively. The mean differences and 95% LOAs tended to increase with increased time spent in in each condition, demonstrating more variability between 7- and 14-days. There was no significant proportional bias among these new empirically derived light categories. Again, this meant that those individual spending more time outdoors demonstrate longer time spent outdoors over 14-days compared to 7-days, thus a 7-day data collection period could underestimate the time spent outdoors even when using the cut-off of 533.15 lux rather than >1000 lux.

The LOAs for time outdoors as measured by the Actiwatch and the Clouclip were quite similar albeit slightly narrower for the Clouclip, but there are no published data on limits

of repeatability for time spent outdoors from the Actiwatch or the Clouclip to confirm whether the LOAs determined in the present study are acceptable. One reason for the narrower LOAs from the Clouclip than the Actiwatch 2 could be due to the wearing time, partly because the Actiwatch was worn full time and the Clouclip was removed with the participants spectacles at night or during exercise.

4.6.2.2. Viewing Distance

The mean difference for 7- vs 14-days of average viewing distance was 2.56 cm with 95% LOAs of -17.20 to 22.32 cm. The LOAs between 7- and 14-days of device wear are narrow with no proportional bias, hence 7-days of data collection is appropriate for measuring an individual's average viewing distance. However the LOAs in the present study fall outside the limits of repeatability of the Clouclip by Bhandari and Ostrin (2020) which ranged from -4.5 to 4.5 cm. Bhandari and Ostrin's (2020) mean differences between measures on day 1 and day 2, ranging between -0.1 and -1 cm, were more comparable to our mean difference of 2.56 cm between 7- vs 14-days of wear. However, these limits of repeatability were only measured between 5 and 120 cm in 5cm incremental steps, whereas the present study also included anything >120 cm as distance viewing which would naturally increase the LOA's.

The mean differences (and 95% LOAs) for time spent at difference viewing distances over 7- vs. 14-days were, -4.11 (-47.50-39.28), 3.43 (-32.56-39.42), 8.48 (-18.02-34.98), and 4.71 (-55.80-65.22) (all in mins) for time spent at very close, near, intermediate and distance viewing, respectively. All of these mean differences between 7- and 14-days are small and the LOAs narrow with no proportional bias; therefore 7-days of data collection is appropriate for measuring time spent at varying viewing distances.

It is important to establish a methodology to accurately measure the duration, frequency and intensity of near viewing habits as there are many studies reporting a positive association with close viewing distances and more myopic refractive error in childhood (Haro, Poulain and Drobe, 2000; Ip *et al.*, 2008; Lu *et al.*, 2009; Lee *et al.*, 2015; Li *et al.*, 2015; Guo *et al.*, 2016; Hsu *et al.*, 2016; Huang *et al.*, 2019). However, to date it is not known whether the link between myopia and close working distances is causal, or whether myopic children reduce their viewing distance alongside the development of their myopia, because myopia might make extended periods of near work less difficult in comparison to distance work.

4.6.3. Screen Time Data

The mean difference for 7- vs 14-days of time spent on screens 3.65 mins with 95% LOAs of -31.34 to 38.64 mins. These LOAs are narrow and there was no proportional bias for the app-measured screen time, indicating reliability of 7-days of data when assessing screen time.

As the increase in screen time has happened in recent years with the development of smartphones and tablets there is not enough evidence to link increased screen time with an increased risk of myopia despite the media seeking to 'blame' handheld electronic devices for the rising levels of myopia. Some researchers believe it to be the societal shift to indoor activities while using these devices that is linked to the increased levels of myopia rather than the devices themselves (Dirani, Crowston and Wong, 2019; Zadnik and Mutti, 2019; Morgan, French and Rose, 2020). Some questionnaire-based studies have reported a link between screen time and myopia prevalence (Hansen *et al.*, 2019; Harrington, Stack and O'Dwyer, 2019), but the need for objective measures of screen-time alongside measurements of other potential risk factors would enable researchers to determine the relative contribution of screen time to myopia risk.

4.6.4. General Discussion

This study is the first study to examine the influence of 7- vs 14 days' worth of data from both the Actiwatch 2 and the Clouclip as well as screen time monitoring apps. The results have confirmed the hypothesis that measures taken over 7-days provide average values which are not significantly different from those obtained over 14-days, except for number of night awakenings measured by the Actiwatch where there was a statistically significant difference between the two, with more average awakenings recorded over 14-days compared to 7-days (36.20 vs 37.83). However, this difference is not clinically significant. There were some parameters (measured by the Actiwatch 2 and Clouclip) which demonstrated significant proportional bias on regression analysis as previously mentioned. This suggests that for those parameters 7-days of data collection could result in an under- or overestimation of a participant's regular behaviours.

There were also wide limits of agreement for some parameters namely, time spent in mesopic and photopic light (both measured by the Actiwatch 2). For these parameters, 7-days' worth of data would need to be analysed with caution before drawing any

conclusions about myopic risk factors. The light exposure parameters are also measured using the Clouclip which exhibited narrower LOAs, therefore using the Clouclip measures might be a more accurate and reliable way of estimating an individuals' light exposure profile over the course of 7-days as opposed to the Actiwatch 2. Nonetheless, the Clouclip is limited when estimating time spent in mesopic light due to the 'floor effect' as the device cannot estimate illumination levels <1 lux.

The LOAs for the sleep parameters in the present study fall within published limits of repeatability of the Actiwatch 2 indicating reliability of just 7-days of data for the sleep parameters. The present study's findings regarding the sleep parameters are in agreement with the findings of Briscoe *et al.* (2014) who reported that one-week of sleep data provides similar outputs to two-weeks using an Actiwatch 4, despite subtle differences between the two weeks. The researchers also note that the one-week of data collection maximises the efficiency of data collection.

The participants in this study were all adults, and most adults tend to have less regimented lifestyles than children. Therefore, the findings that 7-days of collection is a reliable way to profile most of the parameters mentioned in this study should also be applicable to young participants when using the Actiwatch 2, Clouclip and the screen time monitoring apps. This is supported by Trost *et al.'s* (2005) literature review where they report that 4-5 days of data is sufficient for examining physical activity, as children exhibited less day-to-day variability in daily habitual physical activity than adolescents and adults.

The LOAs in the present study regarding average viewing distance from the Clouclip fell outside the limits of repeatability of the Clouclip by Bhandari and Ostrin (2020) which ranged from -4.5 to 4.5 cm. However, these limits of repeatability by Bhandari and Ostrin (2020) were only measured from 5 and 120 cm in 5cm incremental steps, whereas the present study also included anything >120 cm as distance viewing which would naturally increase the LOA's.

Ulaganathan *et al.* (2017) assessed the influence of duration and frequency of measuring light exposure on the Actiwatch 2. The researchers found that a measurement duration of at least 1-week and a measurement frequency of 2 minutes or less provides the most reliable estimates of personal outdoor light exposure measures in both children and young

adults. Thus, the findings of the present study reinforce that 7-days is an appropriate data collection period in order to evaluate an individuals' habitual light exposure patterns.

One limitation of the present study is the loss of 9 participants data from the Clouclip. This is likely due to the short battery life of the Clouclip (40 hours), therefore if the Clouclip is not charged every night, data can be lost. This could have reduced the statistical power of any findings from the Clouclip data. Additionally, the Clouclip as previously mentioned has a floor effect of 1 lux therefore cannot be used to examine scotopic or the lower end of the mesopic light range. Another limitation is the measurement of screen time on phones/tablets only as most participants were students or lecturers in the university, therefore were likely to spend a significant amount of time on other screens such as laptops or desktop computers at home or in university. This is a practical challenge that was highlighted in a recent literature review by Kaye *et al.* (2020).

4.7. Conclusion

To conclude 7-days of data collection proves to be a reliable and much more efficient way of examining an individual's habitual sleep, PA, light exposure, viewing distance and screen time habits, with several parameters LOAs in the present study falling within validated limits of repeatability or published LOAs for those metrics. The limits of agreement for Actiwatch measured time spent in mesopic and photopic light were wider compared to the Clouclip measures of the same parameters, indicating that using the Clouclip might be a more accurate and reliable way of estimating an individuals' light exposure profile, again limited by its battery life and inability to determine the lower end of the mesopic light range.

Chapter 5:
Profile of Environmental Risk Factors for Myopia and Future Myopia in Northern Irish School Children

Chapter 5: Profile of Environmental Risk Factors for Myopia and Future Myopia in Northern Irish School Children

5.1. Introduction

Ulster University's Northern Ireland Childhood Errors of Refraction (NICER) study has demonstrated that the prevalence of myopia amongst white UK teenagers has more than doubled in the last 50 years and is appearing in children at a younger age than in previous decades (McCullough, O'Donoghue and Saunders, 2016). Myopia is rising at a rate that cannot be explained by genetics alone (Wu *et al.*, 2016), therefore the influence of environment and lifestyle must be acknowledged (Morgan *et al.*, 2018).

Light exposure and time spent outdoors have been widely reported to have a protective effect on the development and/or progression of myopia in children (Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018). Landis *et al.* (2018) reported a protective effect of time spent in scotopic (very low) light as well as time spent outdoors on myopia among children aged 10-15-years. However, the authors recommended that further research on how scotopic light affects myopia in younger children would provide useful insight on the potential mechanisms such as retinal signalling via rod photoreceptors (Park *et al.*, 2014), that might precede myopia development. The authors also note that light exposure during sleep may have a role in myopia development and progression, but that they did not investigate this aspect of children's light exposure profiles (Landis *et al.*, 2018).

Many studies have reported increased near work activity such as reading for pleasure, and time spent on homework presents an increased risk for myopia onset among children (Mutti *et al.*, 2002; Saw *et al.*, 2002; Ip *et al.*, 2008; Deng, Gwiazda and Thorn, 2010; French *et al.*, 2013; Saxena *et al.*, 2015; Li *et al.*, 2015; Guo *et al.*, 2016; Hsu *et al.*, 2016; Williams *et al.*, 2018; Singh *et al.*, 2019; Han *et al.*, 2019; Harrington, Stack and O'Dwyer, 2019). There is also some evidence that individuals who habitually adopt close working distances (<30 cm) have an increased risk of myopia progression over a six month period when compared to individuals with longer working distances (>30 cm) (Huang *et al.*, 2019). In addition, there is strong evidence for more time spent in education

being associated with an increased prevalence of myopia (Mirshahi *et al.*, 2014; Lee *et al.*, 2015; Williams *et al.*, 2015; Mountjoy *et al.*, 2018; Han *et al.*, 2019). One such study discovered a linear relationship between time spent in education and the level of myopia, with Mendelian randomisation analysis showing that every additional year spent in education resulted in a more myopic refractive error of -0.27D (Mountjoy *et al.*, 2018).

The media often seeks to 'blame' handheld electronic devices such as tablets and smartphones when rising levels of myopia are reported but there is an insufficiency of research specifically teasing out time spent on handheld electronic devices from time spent in other near vision activities. Boots Opticians (2016) Green Paper on children's eye health notes the rise in childhood myopia and repeatedly suggests that 'managing screen time' is important for good eye health however there is little/evidence to support this assertion. A robust evaluation exploring associations between myopia and the use of handheld electronic devices (along with other near vision tasks) would provide much-needed information to support public health advice for parents, children, and eye care professionals.

The Northern Ireland Childhood Errors of Refraction (NICER) 1.0 study discovered that regular physical activity (>3 hr/week) was associated with a lower estimated prevalence of myopia in 12-13-year-olds compared to their peers leading more sedentary lifestyles (O'Donoghue *et al.*, 2015). The Ireland Eye Study (IES) used an identical sampling framework to that used by the NICER study and found that within their 6-7-year-old cohort, 8.1% of those with sedentary lifestyles were myopic, dropping to just 3.1% for those involved in regular after-school physical activity. In the 12-13-years-old cohort of the IES 35.2% of participants with sedentary lifestyles were myopic, decreasing to 14.4% among participants involved in regular after-school physical activity (Harrington, Stack and O'Dwyer, 2019). However due to the cross-sectional nature of these studies no casual effect can be determined and the direction of any effect cannot be determined.

Findings from East Asia have also recently identified associations between poor sleep quality and myopia (Zhou *et al.*, 2015; Ayaki *et al.*, 2016; Jee, Morgan and Kim, 2016) and significantly increased levels of circulating melatonin are reported in myopic adults compared with non-myopes (Kearney *et al.*, 2017). These reports may indicate an association between disrupted circadian rhythm and myopia.

To date, key environmental risk factors for myopia have primarily been assessed using a self-report rather than by objective methods. There is a scarcity of robust quantitative data which describe the relationship between myopia (assessed using cycloplegic techniques) and time spent outdoors, physical activity, sleep patterns, near viewing behaviours or screen time use for children living in the UK or Ireland. A systematic review regarding physical activity and myopia concluded that more studies are needed which include objective measurements of physical activity and robust evaluation of childhood refractive status (Thykjær *et al.* 2017).

The International Myopia Institutes white papers defines pre-myopia as "a non-myopic refraction in which a combination of risk factors and the observed pattern of eye growth indicate a high risk of progression to myopia" with a refractive state of an eye of ≤+0.75 D and >-0.50 D (Flitcroft *et al.*, 2019). The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study identified cycloplegic spherical equivalent refractive error as the single best predictor of future myopia. The authors defined cut-off points for certain age groups for which eye care professionals should consider providing advice regarding the onset of myopia as seen in Table 5.1.1. (Zadnik *et al.*, 2015). The NICER (1.0) Study found an SER of <+0.75 D at 6-7-years-old was relatively sensitive (75.56%) and specific (82.96%) for predicting the development of future myopia in a Northern Irish population (McCullough *et al.*, 2020).

Cut-Offs for Risk of Future Myopia (D)	Age (years)	Reference
<+0.75	6	(Zadnik *et al.*, 2015)
<+0.75	6-7	(McCullough *et al.*, 2020)
≤+0.50	7-8	(Zadnik *et al.*, 2015)
≤+0.25	9-10	(Zadnik *et al.*, 2015)
≤+0.00	11	(Zadnik *et al.*, 2015)

Table 5.1.1. SER Cut-offs per age category for which eye care professionals should be considering providing advice regarding the onset of myopia.

5.1.1. Aims

The aims of the study were:

- To profile, using device (Clouclip M2 and Actiwatch 2) measures of light exposure, physical activity levels, sleep patterns, near activity and screen time in 6-9-year-old children.

- To investigate the modifiable risk factors for myopia (light exposure/physical activity/sleep quality/near activity/screen time) in children aged 6-9-years old with a range of refractive errors.
- To determine whether there is evidence for differences in sleep quality between children with different refractive errors at 6-9-years of age.
- To determine the relative contribution of both modifiable and non-modifiable (parental myopia/ethnicity) risk factors to SER at 6-9-years-old.

5.2. Recruitment and Participants

A new prevalence study of refractive error in UK children (NICER 2.0) commenced in March 2019. NICER 2.0 was designed to establish the current prevalence of myopia at 6-7 years and 12-13 years using an identical sampling framework to that utilised in NICER 1.0, allowing a comparison of prevalence of myopia in 2006/8 to that in 2019/21. NICER 2.0 provided a platform from which suitable participants were identified for the current quantitative studies of environmental risk factors for myopia and future myopia. Children in Year 3 (aged 6-7-years) were invited to participate via information/consent leaflets sent out from school. Following informed parental consent, data collection occurred on the school premises, during the school day. Participants provided written assent prior to testing. Those children with a previous adverse reaction to cyclopentolate/proxymetacaine were excluded. Parents were notified where outcomes indicated a full eye examination or ophthalmological opinion was required. Additional recruitment (to augment participant numbers) was conducted through the Optometry Clinic at Ulster University, with an extended age range of 6-9-years.

Data collection was carried out by two PhD researchers, namely Rebecca Leighton (REL) and Colleen Howell (CMH) with each researcher consistently doing the same measurements on every child to control for inter-examiner differences. The measures pertinent to the present study were taken as follows:

- Cycloplegia was obtained by instilling one drop of 0.5% Proxymetacaine Hydrochloride followed by 1% Cyclopentolate Hydrochloride within 5 minutes. (CMH)
- Refractive error was assessed after 20 minutes by cycloplegic autorefraction using an open-field autorefractor (Shin-Nippon SRW-5000). (REL)

- Ocular biometry, including corneal curvature, anterior chamber depth, lens thickness and axial length was measured using the Zeiss IOL Master 700 (REL)
- The participants parents were asked to complete a questionnaire about their child's previous ocular/medical history and family demographics including questions on family ocular history, birth/medical history, ethnicity, and questions designed to elicit the family's socio-economic status. Where testing took place on school premises, the parents were provided a stamped and addressed envelope to return the questionnaire to the researchers at the university. (CMH)

Refractive error for each eye was defined using Spherical Equivalent Refraction (SER, sphere + cylinder/2). These data were used to select participants in the following refractive error groups (Flitcroft *et al.*, 2019; McCullough *et al.*, 2020) for the present study;

a) Pre-Myopes/Myopes (Children at high risk of developing myopia or already myopic): SER <+0.75DS in **EITHER** eye.
b) Emmetropes: (Children at low risk of developing myopia): SER ≥+0.75-<+2.00DS.
c) Hyperopes (Hyperopic children with no risk of developing myopia): SER ≥+2.00DS.

Children were only recruited into the above categories if astigmatism was less than -1.50DC and anisometropia was less than 1.50D.

Children who met the criteria above were invited to participate in an objective assessment of sleep quality, physical activity, light exposure and near vision activity. Following informed parental consent an appointment (either at the child's school or in the University eye clinic) was arranged to fit wearable devices. For children recruited through in-school testing this activity took place between 0-3 months after the initial in-school assessment. Where it was more than 3 months since cycloplegic autofraction had taken place, this measurement was repeated to ensure accurate attribution of children to the refractive groups under investigation. For the remainder of recruits all testing took place synchronously.

5.3. Methods

5.3.1. Wearable Devices

The devices being employed to measure light exposure, sleep quality, physical activity and near viewing distances were the Respironics Actiwatch 2 (Philips, NV, USA) and the Clouclip Model M2 (HangZhou Glasson Technology Co). The Actiwatches have been used successfully in previous research studies investigating refractive error and light exposure (Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018). The Clouclips are relatively new devices but have been used in studies to examine light exposure and viewing behaviours in children (Cao *et al.*, 2020; Wen *et al.*, 2020).

5.3.1.1. Respironics Actiwatch 2

The Actiwatch 2 (AW) is a lightweight (16g) and waterproof (for up to 30 minutes) wrist-worn 'actigraphy' device measuring 43 x 23 x10 mm. The Actiwatch 2 contains a silicone photodiode light sensor to measure visible light illuminance with a range of 0.01-100,000 lux and a solid-state piezoelectric accelerometer to measure physical activity ranging from 0.35-7.5 Hertz (recorded as activity counts per minute [cpm]). The Actiwatch has an adjustable epoch of either 15, 30, or 60 seconds. The device is connected to a computer containing the Actiware software using a docking station for charging and data retrieval. The Actiwatch 2 has a battery life between 8-30 days depending on the epoch chosen (longer epoch=longer battery life), therefore the researchers fully charged the Actiwatches prior to data collection and they did not require charging by the participants/parents. The data is uploaded onto the Actiware software and from here can be exported as a CSV file and converted to an Excel (Microsoft, www.microsoft.com) spreadsheet for further analysis. The Actiwatch 2 was programmed to record light and activity measurements, and data on sleep/wake intervals every 30 seconds for one week of participant wear. The 30 second epoch was chosen as it provided the best balance for battery life and regular sampling of children's activity levels.

5.3.1.2. Clouclip M2

The Clouclips were provided by Aeir Eye Hospital Group, China. The Clouclip (CC) M2 is a 45.3 x 13.4 x 8.0 mm device, designed for attachment to the right temple of a spectacle frame using a rubber sleeve. For those participants who did not routinely wear spectacles, 'dummy' spectacles were given to the participants to mount the Clouclip onto. These 'dummy' spectacles were glazed with a plano (0.00 D) prescription in both eyes and therefore did not affect the participants normal eyesight throughout the one-week of wear.

The devices have a built-in infrared distance sensor to determine near viewing distance (ranging from 5-120 cm), a light intensity sensor to record eye-level ambient illumination (ranging from 1-65536 lux) and a three-axis accelerometer (X, Y, Z axis) to distinguish when it is being worn. The Clouclip records near viewing distance every 5 seconds and illumination every 2 minutes. The device is Bluetooth capable and has a magnetic USB charger for syncing the device to an app and uploading the data to the cloud, from here raw data can be downloaded as an Excel spreadsheet using login credentials (Wen *et al.*, 2016; Bhandari and Ostrin, 2020) and a number of parameters are already calculated for download (average duration of near work, maximum duration of near work, average near work distance, average illumination during near work, sunlight exposure duration per day and sunlight exposure frequency per day [both time exposed to >1000 lux]).

5.3.2. Screen-Time Monitoring Applications

Screen-time monitoring applications on participants phones/tablets were used to monitor the time spent on these devices over the course of the data collection period. The apps were Apple Screen Time (built-in app) or Moment Balance Screen Time for iPhone, and Quality Time-My Digital Diet for Android.

5.3.3. Lifestyle Questionnaires

Participants parents completed two validated questionnaires namely, The Pittsburgh Sleep Quality Index (PSQI) and the Physical Activity Questionnaire for Children (PAQ-C). Both questionnaires were administered in previous research studies involving child participants (Crocker *et al.,* 1997; Ayaki *et al.,* 2016). These questionnaires allowed subjective assessment of sleep quality and physical activity which was useful for times when the devices are removed (e.g., swimming) or when the physical activity measures were not reflective of the exertion/effort of the activity (e.g., cycling). The questionnaires were also deployed to subjectively assess physical activity and sleep quality as a comparator with the objectively measured data.

The PSQI is a validated and repeatable tool (Buysse *et al.*, 1989) for assessing an individual's sleep quality over the previous month (Appendix F). The PSQI consists of 19 self-rated questions which assess a wide variety of factors including estimates of sleep duration, latency, frequency, and severity of specific sleep-related problems. These 19 items are grouped into seven component scores, each weighted equally on a 0-3 scale. The seven component scores are then summed to yield a global PSQI score, which has a

range of 0-21. The higher scores indicate poorer sleep quality. The components of the PSQI are subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. The entire index requires 5-10 min for completion. A global PSQI score >5 provided a sensitive and specific measure of poor sleep quality, relative to clinical and laboratory measures. The cut-off of 5 represents a sensitivity of 89.6% and a specificity of 86.5% to determine sleep quality (Buysse *et al.*, 1989).

The PAQ-C is a simple but valid and reliable questionnaire (Kowalski, Crocker and Faulkner, 1997; Voss, Ogunleye and Sandercock, 2013) that is used to assess a child's physical activity (PA) over the previous 7-days (Appendix E). The overall result of the test is a score of 1 to 5 points that allows for a graded level of PA performed by each participant (Kowalski, Crocker and Faulkner, 1997; Voss, Ogunleye and Sandercock, 2013). The PAQ-C was adapted by the researchers to replace typical American sports/terminology with sports/terminology applicable to a Northern Irish population (e.g., 'recess' to 'breaktime', 'American football' to "soccer/Gaelic football').

Each child, along with their parents, also filled out a screen time diary designed by the researchers to determine a subjective assessment of time spent on different screens over the course of the week of data collection along with time spent on devices prior to sleep (Appendix G).

5.3.4. Data Collection Procedure

On Day one of data collection, participants were fitted with the wearable devices and were given the questionnaires for their parents to complete and with a charger for the Clouclip M2.

Each participant had device measured sleep, physical activity, and light exposure over a one-week period (including the weekend) using the Phillips Respironics Actiwatch 2. Participants were instructed to wear the device on their non-dominant wrist for 24 hours a day, to ensure that the watch was not covered by clothing during wear, and to remove it for any water-based activities lasting >30 minutes. There were 13 Actiwatch's available which limited the data collection to a maximum of 13 children at a time.

Each participant also had their near working distance and their eye level light exposure measured using a spectacle mounted Clouclip over the same week. As the glasses would be removed at night/during certain activities (e.g., sleeping/showering/certain sports) these parameters were analysed during waking hours and when the device was worn only (determined by the accelerometer information). The participants were all given a charger and shown how to charge the Clouclip. Parents were advised this needed to be done nightly throughout the week of data collection as the Clouclip has a battery life of 40 hours.

On Day 8 participants returned the devices, screen time diaries, charging units and dummy spectacles (where appropriate) to the researchers.

The season during which the data collection occurred was noted (https://www.timeanddate.com/worldclock/uk/belfast). This step was undertaken to ensure that the season could be considered when evaluating the relationship between refractive error, light exposure and time spent outdoors.

5.3.5. Exclusion Criteria

Initially, participants were not invited to take part if they had >1.50 DC in either eye or if they had >1.50 D anisometropia between right and left eyes, to avoid misclassification of refractive grouping. Data were only included for each device if there were at least four days of data (including at least one weekend day), with at least eight hours wearing time of the Clouclip (Wen *et al.*, 2019).

5.3.6. Data Extraction and Categorisation

Physical activity, sleep quality and light exposure data were downloaded from the Actiwatch 2 using Actiware software and the raw data were exported to Excel (Microsoft, www.microsoft.com) for categorising the parameters as described below. The Clouclip data on light exposure and near working distance were downloaded via the Clouclip Medical app and exported to Excel for categorising the parameters. The average values for each of the parameters were calculated as well as the time spent under different lighting conditions, at different working distances or varying physical activity levels over the 7-day period. The night-time light exposure was calculated as the light exposure and time spent in differing levels of light during sleeping hours.

Compliance (i.e., wear) with Clouclip is indicated by the accelerometer output. This allows the researcher to determine the number of hours which the Clouclip has been worn during the study period. Actiwatch data were initially screened to remove any invalid data, i.e., where it was evident that the watch was removed for more than 15 minutes, or the light sensor was covered by clothing.

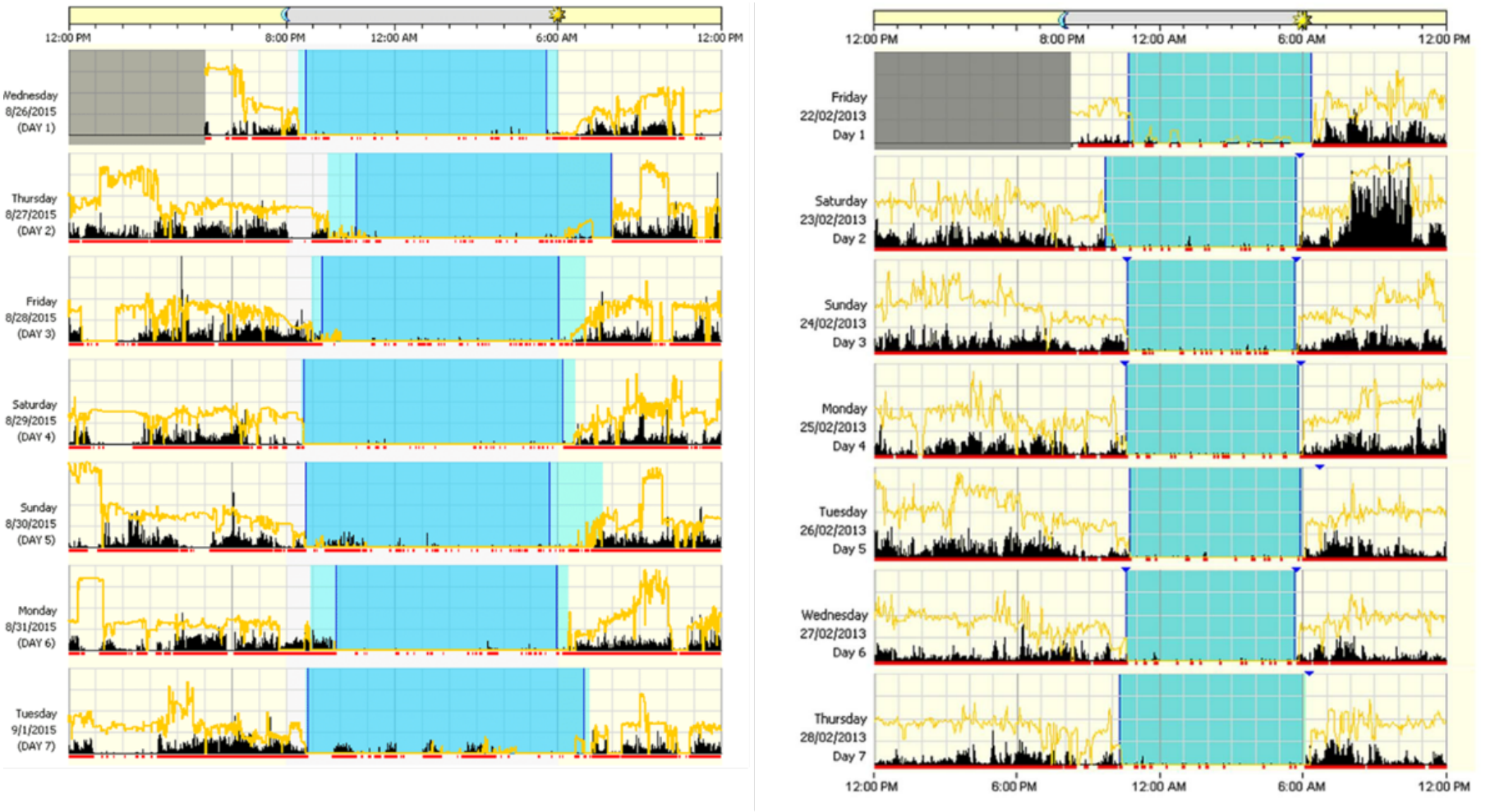


Figure 5.3.12. Two outputs from Actiwatch 2. The image on the left shows an output with evidence of the watch being removed for a certain period every day (broken red line). The image on the right shows a good quality output where the watch was not removed throughout the period of Actiwatch wear. The blue sections indicate periods of sleep. The yellow lines represent light exposure, and the black lines represent physical activity.

The categorisation of data helps describe the patterns of light exposure levels (Rosenfield and Logan, 2009; SolarLight, 2014; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020), viewing distances (Bilton, 2010; Long *et al.*, 2017) and physical activity levels (Read, Collins and Vincent, 2014; Ekblom *et al.*, 2016) over a defined period. Read *et al.* (2014) pointed out that quantifying activities is likely to provide a more comprehensive understanding of the intensity, duration and frequency of these potentially modifiable risk factors for myopia, therefore enhancing the richness of the data compared to average and total values alone.

Tables 5.3.1-5.3.3 below describe how the measured parameters were categorised in the present study. All the parameters were calculated as an average per day for this Chapter. Further interrogation of how these measures varied across the daytime (on weekdays and at the weekend) is presented in Chapter 6. In Chapter 3 the researchers validated the wearable devices for light exposure measures and due to underestimation of light exposure by both devices the cut-offs for illumination categorisation have been adjusted to compensate for this underestimation.

Parameters from Actiwatch 2	**Categories**	**Derived from/References**
Time spent in Scotopic Light (mins)	mins in ≤0.01 lux	SolarLight (2014)
Time spent in Mesopic Light (mins)	mins in 0.02-3 lux	Rosenfield and Logan (2009)
Time spent in Photopic Light (mins)	mins in >3-1000 lux	Bhandari and Ostrin (2020)
Time spent Outdoors (mins)	mins in >1000 lux	Ulaganathan *et al.* (2019)
Time spent Sedentary (mins)	mins spent at ≤145cpm	Ekblom *et al.* (2016)
Time spent on Light Activity (mins)	mins spent at 145-274cpm	Ekblom *et al.* (2016)
Time spent on Moderate Activity (mins)	mins spent at 275-597cpm	Ekblom *et al.* (2016)
Time spent on Vigorous Activity (mins)	mins spent at >597cpm	Ekblom *et al.* (2016)
Daytime Light Exposure (lux)		Average lux with sleep time excluded
Night-time Light Exposure (lux)		Average lux with active time excluded
Time Spent in Scotopic Light Night-time (mins)	mins in ≤0.01 lux	SolarLight (2014)

Time spent in Mesopic Light Night-time (mins)	mins in 0.02-3 lux	Rosenfield and Logan (2009)
Time spent in Photopic Light Night-time (mins)	mins in >3-1000 lux	Bhandari and Ostrin (2020)
Daytime Physical Activity (cpm)		Average cpm with sleep time excluded
Bedtime		Output from Actiware Software
Get Up Time		Output from Actiware Software
Total Time in Bed		Output from Actiware Software
Total Sleep Time		Output from Actiware Software
Sleep Onset (mins)		Output from Actiware Software
Sleep Efficiency (%)		Output from Actiware Software
Wake After Sleep Onset (WASO) (mins)		Output from Actiware Software
Number of Awakenings		Output from Actiware Software
Adjusted Daytime Spent in Mesopic Light (mins)	mins in 0.02-0.78 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Daytime spent in Photopic Light (mins)	mins in >0.78-533.15 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Daytime spent Outdoors (mins)	mins in >533.15 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Night-time Spent in Mesopic Light (mins)	mins in 0.02-0.78 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Night-time spent in Photopic Light (mins)	mins in >0.78-533.15 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)

Table 5.3.1. This table presents all the parameters determined by the Actiwatch, and how they were calculated, including references for the cut-offs where appropriate. The night-time spent in different lighting conditions was defined as time spent in these conditions during sleeping hours only.

Parameters from Clouclip M2	**Categories**	**Derived from/References**
Time spent in Mesopic Light (mins)	mins in 1-3 lux	Rosenfield and Logan (2009)
Time spent in Photopic Light (mins)	mins in >3-1000 lux	Bhandari and Ostrin (2019)
Time spent Outdoors (mins)	mins in >1000 lux	Ulaganathan *et al.* (2019)
Daytime Light Exposure (lux)		Average lux with non-wear time excluded
Daytime Viewing Distance (cm)		Average cm with non-wear time excluded
Time spent at Very Close (mins)	≤30cm	(Long *et al.*, 2017)
Time spent at Near (mins)	31-49cm	(Bilton, 2010)
Time spent at Intermediate (mins)	50-119m	(Bilton, 2010)

Time spent at Distance (mins)	≥120cm	(Bilton, 2010)
Average Duration of Near Work		Output from Clouclip Medical app
Maximum Duration of Near Work		Output from Clouclip Medical app
Average Near Work Distance		Output from Clouclip Medical app
Average Illumination During Near Work		Output from Clouclip Medical app
Sunlight Exposure Duration per Day		Output from Clouclip Medical app
Sunlight Exposure Frequency per Day		Output from Clouclip Medical app
Adjusted Time spent in Mesopic Light (mins)	mins in 2-3 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Time spent in Photopic Light (mins)	mins in >3-850 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)
Adjusted Time spent Outdoors (mins)	mins in >850 lux	Validation of Devices (Chapter 3) (Howell *et al.*, 2021)

Table 5.4.2. This table presents all the parameters determined by the Clouclip and how they were calculated, including references for the cut-offs where appropriate.

Parameters from Questionnaires	**Categories**	**Derived from/References**
Time in Bed at Night (hh:mm)		Pittsburgh Sleep Quality Index
Get up Time in Morning (hh:mm)		Pittsburgh Sleep Quality Index
Sleep Onset (mins)		Pittsburgh Sleep Quality Index
Hours of Sleep (hours)		Pittsburgh Sleep Quality Index
Pittsburgh Sleep Quality Index Score		Pittsburgh Sleep Quality Index
Sleep Quality	<5=Good or ≥5=Poor	Pittsburgh Sleep Quality Index
PAQ-C Score	1 to 5 (5 being more active)	PAQ-C
Number of Myopic Parents	0, 1 and 2 myopic parents	Screen Time Diary
Time Spent on TV/Video Games (hours)	0 hours, <1 hour, 1-2 hours, 2-3 hours, 3+ hours	Screen Time Diary
Time Spent on Phone/Tablet (hours)	0 hours, <1 hour, 1-2 hours, 2-3 hours, 3+ hours	Screen Time Diary
Time Spent on Computer/Laptop (hours)	0 hours, <1 hour, 1-2 hours, 2-3 hours, 3+ hours	Screen Time Diary
Device Usage Before Sleep (hours)	0 hours, 1-30 mins, 30 mins-1 hour, 1-2 hours, 2+ hours	Screen Time Diary

Table 5.3.3. This table presents all the parameters determined by the questionnaires.

5.3.7. Ethical Approval

The study was in compliance with the Declaration of Helsinki and was approved by the Ulster University's Research and Ethics Committee on 30th January 2019, application number: REC/18/0102.

5.4. Statistical Analysis

Data were entered into SPSS Version 25 which was used for statistical analysis. Descriptive statistics were used to describe data for each devices' parameters over the course of the 7-day data collection period and the data were presented in tabular form. Scatterplots of the spherical equivalent refraction (SER) and axial length (AL) against each of the potential risk factors for future myopia were constructed and Pearson's correlations were used to describe these relationships. Parametric testing was used due to the large sample size. Multiple regression analyses were performed to identify variables with a unique significant contribution to SER or AL. Univariate and multivariate logistic regression analysis was used to calculate odds ratios for the risk factors associated with pre-myopia/myopia. Independent samples t-tests were used to evaluate statistically significant differences between pre-myopes/myopes and non-myopes (emmetropes and hyperopes combined) and one-way between groups ANOVA was used to evaluate statistically significant differences in exposure to environmental risk factors between the three refractive groups (pre-myopes/myopes, emmetropes and hyperopes), with post hoc analysis for each parameter. Chi-Squared analyses were used to examine associations between categorical variables and refractive classification. Two-way ANOVAs were undertaken to examine if there were statistically significant differences between parameters measured during winter (Greenwich Mean Time [GMT]) and summer (British Summer Time [BST]). One-way ANOVAs were carried out for all parameters in winter and summer separately to determine if time of year had any impact on differences between refractive groups.

5.5. Results

5.5.1. Descriptive Statistics

Data collection was carried out between May 2019 and December 2020. 173 children were invited to participate initially, of which 119 (66.9%) agreed to participate. The majority of environment and activity data collection took place during British Winter Time (76.5% during Greenwich Mean Time [GMT]) (October-March). The time of year was defined using an online database *(www.timeanddate.com)*, and these data were considered during data analysis.

The descriptive data for the participants that agreed to participate in the wearing of devices and their success rates are presented in Table 5.5.1.

	Number	Age (Range)	Gender	Ethnicity	Number (%) of Participants Successfully Completing Data Collection					
					Actiwatch	Clouclip	Physical Activity Questionnaire for Children	Pittsburgh Sleep Quality Index	Screen Time Questionnaire	Screen Time Monitoring App
All participants	119	7.3 (6.1-8.9 years)	49 Male 70 Female	113 White 6 Non-White	100 (84.9%)	58 (48.7%)	115 (96.6%)	113 (95.0%)	87 (73.1%)	5 (4.2%)
Pre-myopes/Myopes	24	7.5 (6.3-8.9 years)	13 Males 11 Females	21 White 3 Non-White	20 (83.3%)	12 (50%)	23 (95.8%)	23 (95.8%)	17 (70.8%)	2 (8.3%)
Emmetropes	62	7.2 (6.3-8.4 years)	26 Males 36 Females	59 White 3 Non-White	51 (82.3%)	33 (53.2%)	60 (96.8%)	58 (93.5%)	48 (77.4%)	3 (4.8%)
Hyperopes	33	7.3 (6.1-8.4 years)	11 Males 22 Females	33 White 0 Non-White	29 (87.9%)	13 (39.4%)	32 (97.0%)	32 (97.0%)	22 (66.7%)	0 (0%)

Table 5.5.1. Table describes the success rate for participation and successful completion of the week of data collection with wearable devices, questionnaires, and app data. The table also presents the demographics of the participating children.

The ocular biometry and refractive error data for the participants are presented in Table 5.5.2.

	Spherical Equivalent Refraction (SER) RE (D)	Spherical Equivalent Refraction (SER) LE (D)	Axial Length (AL) RE (mm)	Axial Length (AL) LE (mm)	Anterior Chamber Depth (ACD) RE (mm)	Anterior Chamber Depth (ACD) LE (mm)	Lens Thickness (LT) RE (mm)	Lens Thickness (LT) LE (mm)	Corneal Curvature (R) RE (mm)	Corneal Curvature (R) LE (mm)
Average (Range) for All Participants	1.78 (-2.13-8.75)	1.85 (-1.50-10.00)	22.59 (19.93-24.86)	22.55 (19.73-24.81)	3.65 (3.08-4.20)	3.65 (3.09-4.23)	3.44 (3.17-3.88)	3.43 (3.12-3.86)	7.83 (7.12-8.70)	7.86 (7.26-8.87)
Average (Range) for Pre-Myopes/Myopes	0.09 (-2.13-1.00)	0.16 (-1.50-0.88)	23.14 (22.02-24.86)	23.07 (21.97-24.81)	3.76 (3.45-4.20)	3.76 (3.40-4.23)	3.40 (3.17-3.60)	3.39 (3.13-3.71)	7.76 (7.42-8.33)	7.67 (7.49-8.02)
Average (Range) for Emmetropes	1.43 (0.75-2.38)	1.43 (0.75-2.63)	22.71 (21.54-23.84)	22.72 (21.52-23.90)	3.69 (3.11-4.19)	3.69 (3.09-4.21)	3.43 (3.17-3.85)	3.41 (3.12-3.86)	7.83 (7.12-8.40)	7.86 (7.26-8.87)
Average (Range) for Hyperopes	3.71 (2.13-8.75)	3.85 (1.75-10.00)	21.92 (19.93-24.19)	21.84 (19.73-23.93)	3.48 (3.08-4.14)	3.49 (3.11-4.09)	3.49 (3.24-3.88)	3.48 (3.23-3.84)	7.88 (7.39-8.70)	8.01 (7.35-8.66)

Table 5.5.2. Table describing the average SER and biometric measures for all participants and for each refractive grouping for right and left eyes. There was a strong positive correlation between right and left eyes for SER (r=0.959), AL (r=0.983), ACD (r=0.982), LT (r=0.971), and R (r=0.871), all p<0.001.

As the right and left eyes were strongly correlated for all biometry parameters and SER, the right eye only was used for all further analyses. Therefore, when SER or ocular biometry parameters are reported henceforth it is the SER or ocular biometric measures of the right eye.

Once data collection began, we discovered that very few of the younger cohort owned their own phone or tablet, and a shared family device would lead to an overestimation of a child's screen time. Therefore, we ceased this collection of data and continued only with the parental-reported screen time diary for each child over the course of the week.

Chi-Squared tests for independence indicated no significant associations between refractive error classification and gender, ethnicity, season of the year, or the time of year (BST or GMT) the data were collected (all $p>0.05$). There was a significant association between refractive error classification and number of myopic parents, X^2 (2, n=87) =8.10, p=0.017 with a medium effect size, phi=0.305. Therefore, being classified as a pre-myope/myope was significantly associated with having at least one myopic parent. For the non-myopic cohort, 50%, 42.9% and 7.1% had no, one, and two myopic parents, respectively, whereas for the pre-myopes/myopes 23.5%, 47.1 % and 29.4% had no, one, and two myopic parents, respectively.

5.5.2. Comparison of Subjective and Objective Measures of Physical Activity and Sleep Parameters

Actiwatch Measured Parameter	Questionnaire-Reported Parameter	Correlation
Average Physical Activity	PAQ-C Score	r=0.237, p=0.020
Bedtime	PSQI Bedtime	r=0.638, p<0.001
Get-up Time	PSQI Get-up Time	r=0.411, p<0.001
Hours of Sleep	PSQI Hours of Sleep	r=0.198, p=0.054
Sleep Onset	PSQI Sleep Onset	r=-0.005, p=0.961

Table 5.5.3. Table describing the correlations between objectively and subjectively measured activity and sleep parameters with the Actiwatch and questionnaires, respectively.

Parental-reported bedtimes and get-up times have a strong correlation with the objectively measured bedtimes and get-up times. Parental reported physical activity using the PAQ-C was significantly correlated with the average physical activity over the week of data collection. The parental reported hours of sleep along with Actiwatch measured hours of

sleep approached significance. The parental reported sleep onset showed no correlation with the Actiwatch measured sleep onset.

5.5.3. Light Exposure Results (Actiwatch and Clouclip)

The light exposure parameters measured by both wearable devices, and their respective correlations with SER and AL are presented in Table 5.5.4.

Actiwatch Light Exposure Parameter	Average for all Participants	Correlation with SER	Correlation with AL
Light Exposure Daytime (lux)	371.84	r=0.006 p=0.955	r=0.071 p=0.483
Time Spent in Scotopic Light Daytime (mins)	84.30	r=0.033 p=0.743	r=-0.057 p=0.572
Time Spent in Mesopic Light Daytime (mins)	94.48	r=0.070 p=0.489	r=-0.079 p=0.437
Time Spent in Photopic Light Daytime (mins)	637.62	r=-0.054 p=0.591	r=0.047 p=0.644
Time Spent Outdoors Daytime (mins)	51.89	r=0.024 p=0.812	r=0.075 p=0.455
Time Spent in Scotopic Light Night-time (mins)	470.89	r=-0.030 p=0.769	r=0.054 p=0.594
Time Spent in Mesopic Light Night-time (mins)	56.54	r=-0.082 p=0.415	r=-0.144 p=0.154
Time Spent in Photopic Light Night-time (mins)	41.19	r=-0.028 p=0.780	r=0.004 p=0.968
Night-time Light Exposure (lux)	1.17	r=-0.122 p=0.227	r=-0.035 p=0.727
Clouclip Light Exposure Parameter	**Average for all Participants**	**Correlation with SER**	**Correlation with AL**

Light Exposure (lux)	347.65	r=0.176 p=0.186	r=-0.031 p=0.818
Time Spent in Mesopic Light (mins)	20.19	r=-0.147 p=0.271	r=0.135 p=0.312
Time Spent in Photopic Light (mins)	512.74	r=-0.077 p=0.566	r=-0.007 p=0.959
Time Spent Outdoors (mins)	47.97	r=0.198 p=0.135	r=-0.040 p=0.766
Illumination During Near Work (lux)	114.11	r=0.189 p=0.172	r=-0.057 p=0.680
Sunlight Exposure Duration (mins)	48.19	r=0.177 p=0.200	r=-0.021 p=0.882
Sunlight Exposure Frequency per Day	7.83	r=0.245 p=0.075	r=-0.066 p=0.638

Table 5.5.4. The average light exposure parameters for all the participants combined and the Pearson's correlations between each light exposure parameter with SER and AL. Light exposure was analysed in two ways; using the original cut-offs to define the category, and using the adjusted cut-offs determined by the validation study of the devices (Chapter 3), with the latter being presented in the table. There were no notable differences between the outputs using the original and new cut-offs hence the new classifications alone were used for all further analysis. Tables containing the results of the original light exposure data is available in Appendix J.

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the light exposure parameters are presented in Table 5.5.5.

Actiwatch Light Exposure Parameter	Pre-Myopes/Myopes Mean and (SD)	Non-Myopes Mean and (SD)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD)	Hyperopes Mean and (SD)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Light Exposure Daytime (lux)	400.32 (588.73)	364.72 (589.11)	p=0.809	320.02 (576.82)	443.31 (612.37)	p=0.650	
Time Spent in Scotopic Light Daytime (mins)	75.87 (61.50)	86.41 (41.70)	p=0.364	86.12 (39.26)	86.91 (46.41)	p=0.662	
Time Spent in Mesopic Light Daytime (mins)	92.77 (49.79)	94.91 (45.16)	p=0.853	93.89 (43.17)	96.72 (49.21)	p=0.950	

Time Spent in Photopic Light Daytime (mins)	652.37 (100.57)	633.94 (66.44)	p=0.444	634.83 (67.02)	632.36 (66.57)	p=0.609	
Time Spent Outdoors Daytime (mins)	60.62 (73.52)	49.71 (61.83)	p=0.499	43.81 (58.23)	60.09 (67.49)	p=0.441	
Time Spent in Scotopic Light Night-time (mins)	423.48 (183.44)	482.74 (147.14)	p=0.129	489.37 (135.61)	471.08 (167.41)	p=0.280	
Time Spent in Mesopic Light Night-time (mins)	44.21 (46.16)	59.63 (83.83)	p=0.431	65.70 (90.44)	48.94 (70.97)	p=0.480	
Time Spent in Photopic Light Night-time (mins)	90.68 (161.82)	28.82 (71.85)	p=0.110	20.25 (37.28)	43.90 (108.23)	*p=0.024*	*p=0.018 P/M vs E* p=0.220 P/M vs H p=0.542 E vs H

Night-time Light Exposure (lux)	4.86 (16.79)	0.25 (0.48)	p=0.235	0.18 (0.33)	0.36 (0.66)	p=0.051	
Clouclip Light Exposure Parameter	**Pre-Myopes/Myopes Mean and (SD)**	**Non-Myopes Mean and (SD)**	**Independent t-test (Pre-Myopes/Myopes vs Non-Myopes**	**Emmetropes Mean and (SD)**	**Hyperopes Mean and (SD)**	**One-Way ANOVA**	**Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)**
Light Exposure (lux)	476.91 (484.36)	313.94 (306.07)	p=0.287	237.15 (224.46)	508.84 (399.45)	*p=0.019*	p=0.092 P/M vs E p=0.969 P/M vs H *p=0.041 E vs H*
Time Spent in Mesopic Light (mins)	16.33 (13.29)	21.20 (14.06)	p=0.285	24.04 (14.00)	13.98 (11.80)	*p=0.046*	No significant difference between groups
Time Spent in Photopic Light (mins)	492.71 (85.20)	517.97 (86.16)	p=0.369	537.66 (83.30)	467.98 (74.57)	*p=0.028*	p=0.242 P/M vs E p=0.732 P/M vs H *p=0.032 E vs H*

Time Spent Outdoors (mins)	64.09 (61.07)	43.77 (41.05)	p=0.175	33.94 (29.17)	68.72 (55.75)	*p=0.025*	p=0.112 P/M vs E p=0.962 P/M vs H *p=0.048 E vs H*
Illumination During Near Work (lux)	123.92 (43.84)	111.31 (43.45)	p=0.380	102.07 (43.38)	131.92 (37.31)	p=0.079	
Sunlight Exposure Duration (mins)	61.00 (57.96)	44.52 (40.87)	p=0.269	34.14 (32.72)	67.69 (48.64)	*p=0.042*	No significant difference between groups
Sunlight Exposure Frequency per Day	9.42 (7.75)	7.38 (5.99)	p=0.336	5.76 (4.96)	11.00 (6.67)	*p=0.027*	p=0.196 P/M vs E p=0.793 P/M vs H *p=0.033 E vs H*

Table 5.5.5. The average light exposure parameters for the Actiwatch and Clouclip for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories.

Application of the original and newly derived cut-offs to define the light exposure categories (Chapter 3) did not influence the outcomes of any of the analyses exploring relations between light exposure profiles and ocular parameters (SER, AL, or refractive group). Therefore, the light exposure parameters reported in Tables 5.5.4 and 5.5.5. are using the newly derived cut-offs for both wearable devices.

The figures below (5.5.1-5.5.5) present the light exposure parameters with significant differences between refractive groups using one-way analyses of variance (ANOVAs).

There was a significant difference between refractive groups for night-time spent in photopic light between refractive groups (One-way ANOVA, $p=0.024$), with pre-myopes/myopes spending significantly more time in photopic light at night ($M=90.68$ mins) than the emmetropes ($M=20.25$ mins), $p=0.018$. There was no significant difference between the pre-myopes and the hyperopes ($M=43.90$ mins) or between the emmetropes and hyperopes using the new cut-offs (both $p>0.05$).

One-way ANOVA for average night-time light exposure approached statistical significance, $p=0.051$, with the pre-myopes/myopes having higher average light exposure ($M=4.86$ lux) during sleep than the emmetropes ($M=0.18$ lux).

There was a significant difference between groups for average light exposure from the Clouclip ($p=0.019$). The hyperopes had a significantly higher average light exposure ($M=508.84$) than the emmetropes ($M=237.15$), $p=0.041$. The pre-myopes/myopes average light exposure ($M=476.91$) was not significantly different to either the emmetropes or the hyperopes (both $p>0.05$).

There was a significant difference between daily sunlight exposure frequency per day between groups ($p=0.027$), with the emmetropes having significantly less daily sunlight exposure frequency ($M=5.76$) than hyperopes ($M=11.00$), $p=0.033$. There were no significant differences between the pre-myopes/myopes ($M=9.42$) and either the emmetropes or hyperopes (both $p>0.05$).

There was a significant difference between groups for time spent in photopic light ($p=0.028$), with emmetropes spending significantly more time in photopic light ($M=537.66$) than hyperopes ($M=467.98$), $p=0.032$. There were no significant differences

between the pre-myopes/myopes (M=492.71) and either the emmetropes or the hyperopes (both $p>0.05$).

There was significant difference between groups for time spent outdoors measured by the CC and using new cut-offs ($p=0.025$), with emmetropes spending significantly less time outdoors (M=33.94) than hyperopes (M=68.72), $p=0.048$. There were no significant differences between the pre-myopes/myopes (M=64.09) and either the emmetropes or the hyperopes.

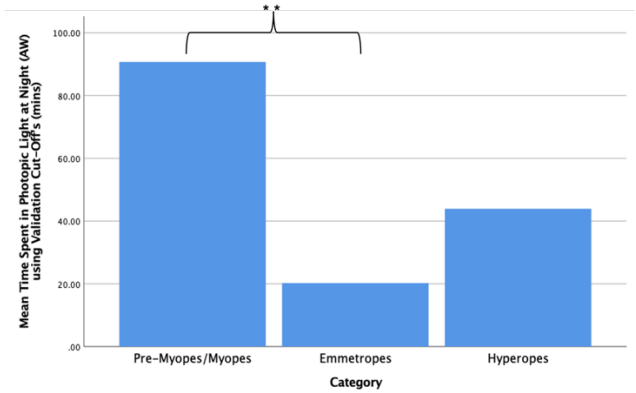


Figure 5.5.1. Bar chart showing the mean time spent in photopic light at night between refractive groups with the brace and stars indicating the significant difference.

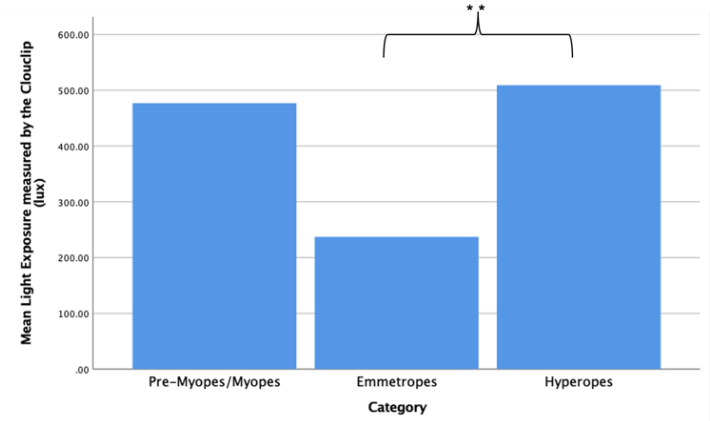


Figure 5.5.2. Bar chart showing the mean light exposure (measured by the Clouclip) between refractive groups with the brace and stars indicating the significant difference.

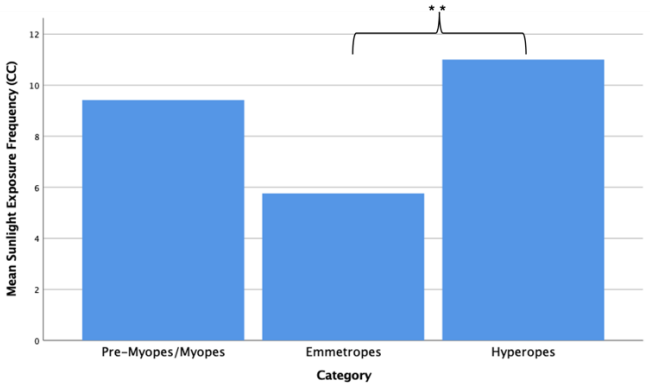


Figure 5.5.3. Bar chart showing the mean sunlight exposure frequency per day between refractive groups with the brace and stars indicating the significant difference.

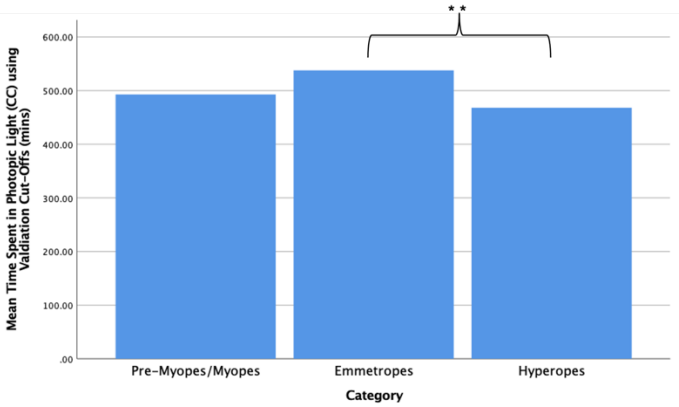


Figure 5.5.4. Bar chart showing the mean time spent in photopic light (measured by the Clouclip) between refractive groups with the brace and stars indicating the significant difference.

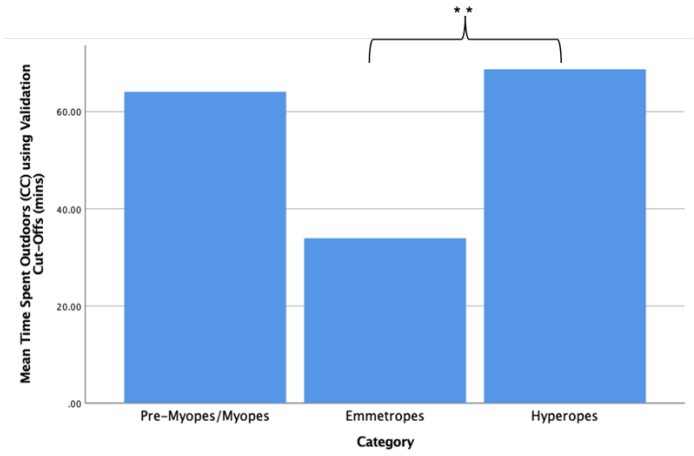


Figure 5.5.5. Bar chart showing the mean time spent outdoors (measured by the Clouclip) between refractive groups with the brace and stars indicating the significant difference.

Two-way ANOVAs found statistically significant differences between winter and summer for all light exposure parameters, all $p<0.001$. One-way ANOVAS were performed for each of the light exposure parameters in winter and summer measures separately. 25 children wore the devices during summer (DST) including seven pre-myopes/myopes, nine emmetropes and nine hyperopes. The devices were worn during the winter (GMT) by 75 children including thirteen pre-myopes/myopes, 42 emmetropes and 20 hyperopes. During the summer there were no statistically significant differences between refractive groups for any of the light exposure parameters ($p>0.05$). During winter there were several light exposure parameters which demonstrated statistically significant differences between refractive groups. Average daytime light exposure in winter was significantly higher for non-myopes (M=132.22 lux, SD=123.80) than pre-myopes/myopes (M=73.02, SD=68.00), $p=0.022$. Pre-myopes/myopes spent significantly more daytime in photopic light in winter (M=688.11, SD=100.23 mins) than non-myopes (M=644.58, SD=62.03 mins), $p=0.044$. Non-myopes spent significantly more time in scotopic light at night during sleep (M=484.71, SD=146.43 mins) than pre-myopes/myopes (M=385.11, SD=200.91) in winter, $p=0.041$. Pre-myopes/myopes spent significantly more time in photopic light at night during sleep (M=115.18, SD=191.22 mins) in winter than emmetropes (M=17.24, SD=105.07 mins), $p=0.007$. They also spent more time in photopic light at night during sleep than hyperopes (M=38.35, SD=105.07 mins) but the difference only approached statistical significance, $p=0.078$. Figures 5.5.6. and 5.5.7. describe these differences during winter.

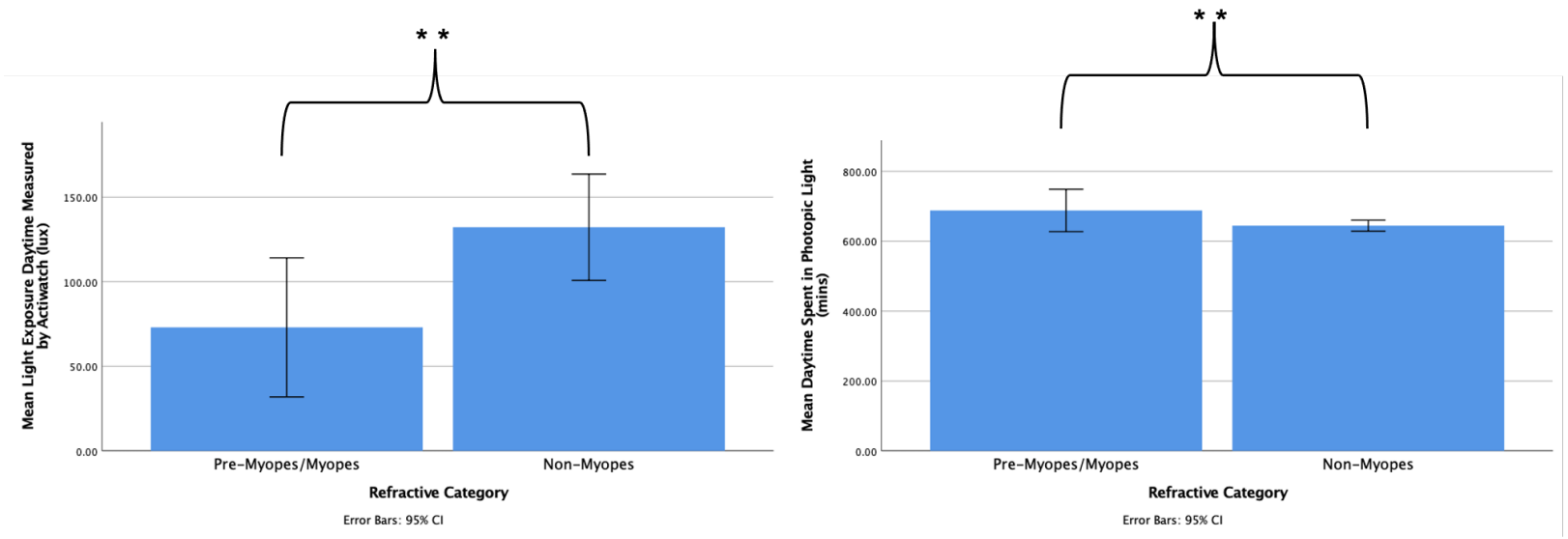


Figure 5.5.6. Bar charts showing the mean daytime light exposure and mean time spent in photopic light (both measured by the Actiwatch) during winter, between refractive groups with the brace and stars indicating the significant difference.

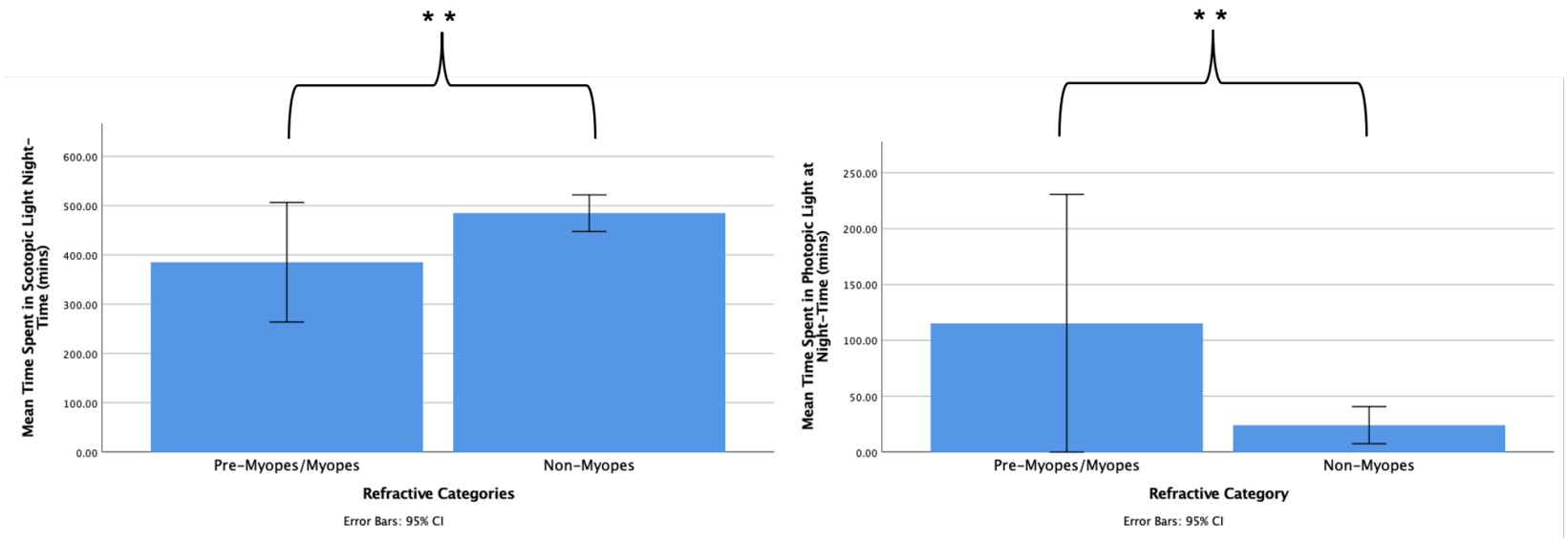


Figure 5.5.7. Bar charts showing the mean time spent in scotopic and mean time spent in photopic light at night-time during winter, between refractive groups with the brace and stars indicating the significant difference.

5.5.4. Physical Activity Results (Actiwatch and PAQ-C)

The physical activity parameters measured by the Actiwatch and PAQ-C, and their respective correlations with SER and AL are presented in Table 5.5.6.

Actiwatch Physical Activity Parameter	Average for all Participants	Correlation with SER	Correlation with AL
Physical Activity (cpm)	311.19	r=-0.073 p=0.471	r=0.155 p=0.123
Time Spent Sedentary (mins)	362.94	r=0.150 p=0.138	r=-0.146 p=0.147
Time Spent on Light Activity (mins)	351.92	r=-0.054 p=0.596	r=0.068 p=0.504
Time Spent on Moderate Activity (mins)	86.01	r=-0.129 p=0.201	r=0.134 p=0.185
Time Spent on Vigorous Activity (mins)	67.43	r=-0.063 p=0.531	*r=0.228* *p=0.022*
PAQ-C Score	3.07	r=-0.033 p=0.728	r=0.128 p=0.173

Table 5.5.6. The average physical activity parameters for all participants and the Pearson's correlations between each physical activity parameter and SER and AL.

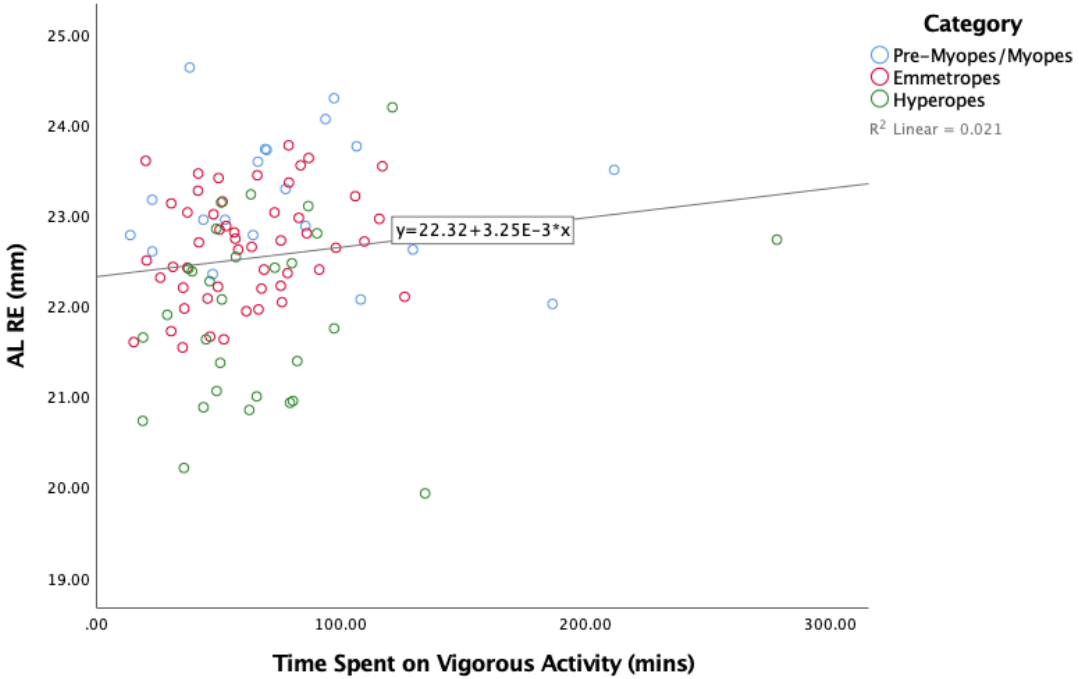


Figure 5.5.8. Scatterplot of time spent on vigorous activity against AL (mm). Pearson's correlation shows a statistically significant positive correlation (r=0.228, p=0.022).

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the physical activity parameters are presented in Table 5.5.7.

Actiwatch Physical Activity Parameter	Pre-Myopes/Myopes Mean and (SD)	Non-Myopes Mean and (SD)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD)	Hyperopes Mean and (SD)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Average Physical Activity (PA) (cpm)	332.26 (88.38)	305.92 (78.58)	p=0.194	298.60 (47.76)	318.79 (114.38)	p=0.242	
Time Spent Sedentary (mins)	355.37 (80.90)	364.84 (65.12)	p=0.582	364.53 (57.33)	365.37 (78.07)	p=0.859	
Time Spent on Light Activity (mins)	350.81 (53.55)	352.20 (45.54)	p=0.907	350.15 (46.72)	355.81 (43.96)	p=0.870	

Time Spent on Moderate Activity (mins)	95.21 (25.31)	83.70 (21.46)	*p=0.041*	82.71 (19.55)	85.45 (24.74)	p=0.110	
Time Spent on Vigorous Activity (mins)	80.23 (51.11)	64.22 (36.18)	p=0.108	61.26 (26.81)	69.44 (48.63)	p=0.187	
PAQ-C Score	3.09 (0.55)	3.07 (0.52)	p=0.835	3.04 (0.52)	3.11 (0.53)	p=0.821	

Table 5.5.7. The average physical activity parameters for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories.

The figure below (Figure 5.5.7.) shows the significant difference between the pre-myopes/myopes (M=95.21 mins) and non-myopes (emmetropes and hyperopes combined) (M=83.70 mins) for time spent on moderate activity using an independent samples t-test, p=0.041.

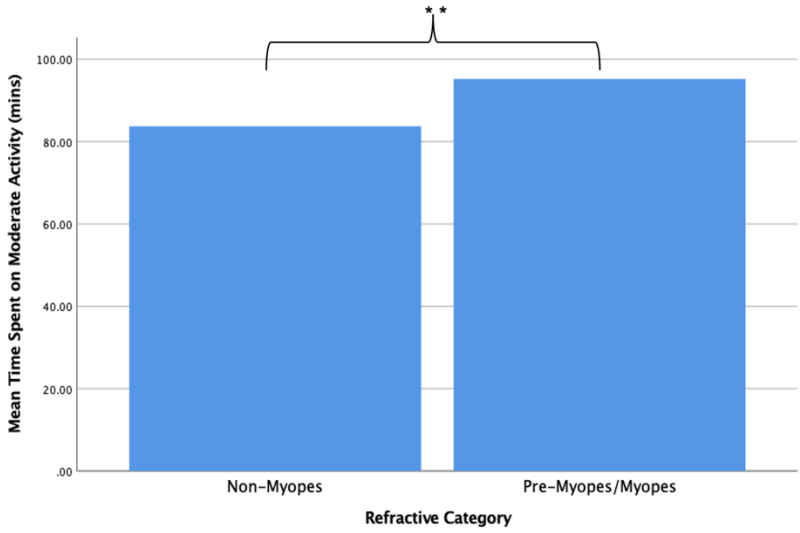


Figure 5.5.9. Bar chart showing the mean time spent on moderate activity between refractive groups with the brace and stars indicating the significant difference.

One-way ANOVAs between the three refractive groups showed no statistically significant differences for any of the physical activity parameters (all p>0.05).

Two-way ANOVAs found statistically significant differences between winter and summer for time spent sedentary (p=0.011) with participants spending significantly more time sedentary in winter than summer, but with no significant differences between refractive groups. Two-way ANOVAs also found statistically significant differences between winter and summer for PAQ-C Scores, with higher average PAQ-C scores in summer than winter (p=0.026), again with no significant differences between refractive groups.

5.5.5. Sleep Results (Actiwatch and PSQI)

The sleep parameters measured by the Actiwatch and PSQI, and their respective correlations with SER and AL are presented in Table 5.5.8.

Actiwatch Sleep Parameter	Average for all Participants	Correlation with SER	Correlation with AL
Bedtime (hh:mm:ss)	21:36:51	r=-0.068 p=0.504	r=0.015 p=0.883
Get Up Time (hh:mm:ss)	07:29:21	r=-0.066 p=0.517	r=-0.039 p=0.697
Total Time in Bed (hh:mm:ss)	09:52:08	r=0.032 p=0.754	r=-0.090 p=0.371
Total Hours of Sleep (hh:mm:ss)	08:27:45	r=-0.102 p=0.313	r=0.052 p=0.606
Sleep Onset (mins)	10.13	r=0.108 p=0.286	r=-0.120 p=0.233
Sleep Efficiency (%)	85.79	*r=-0.229* *p=0.022*	*r=0.232* *p=0.020*
Wake After Sleep Onset (WASO) (mins)	54.27	r=0.118 p=0.240	r=-0.140 p=-0.166
Number of Awakenings	41.83	r=-0.004 p=0.972	r=0.000 p=0.998
PSQI Sleep Parameter	**Average for all Participants**	**Correlation with SER**	**Correlation with AL**
Bedtime (hh:mm)	20:21	r=-0.084 p=0.376	r=0.091 p=0.337
Sleep Onset (mins)	24.97	r=-0.013 p=0.893	r=-0.015 p=0.873

Get Up Time (hh:mm)	07:14	r=0.038 p=0.690	r=0.083 p=0.380
Hours of Sleep (hours)	10.04	r=0.054 p=0.570	r=-0.030 p=0.755
PSQI Score	2.84	r=-0.73 p=0.441	r=0.008 p=0.934

Table 5.5.8. The average sleep parameters for all the participants combined and the Pearson's correlations between each sleep parameter with SER and AL.

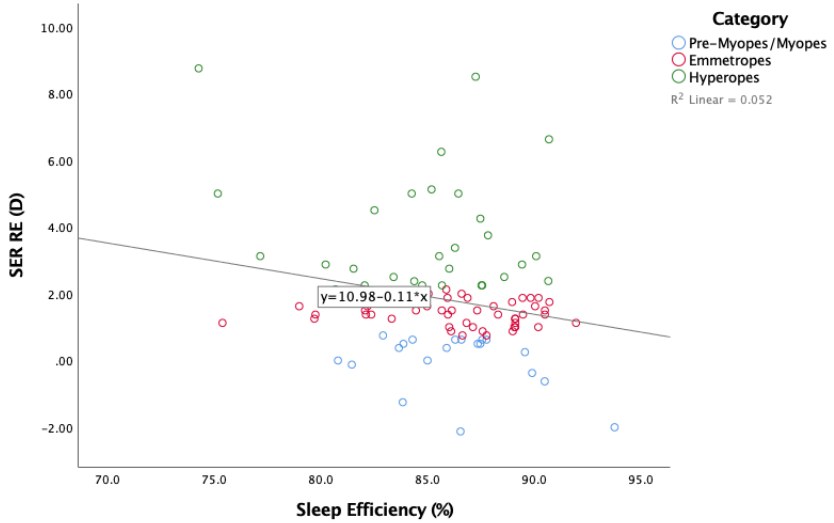


Figure 5.5.10. Scatterplot of sleep efficiency against SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.229, p=0.022).

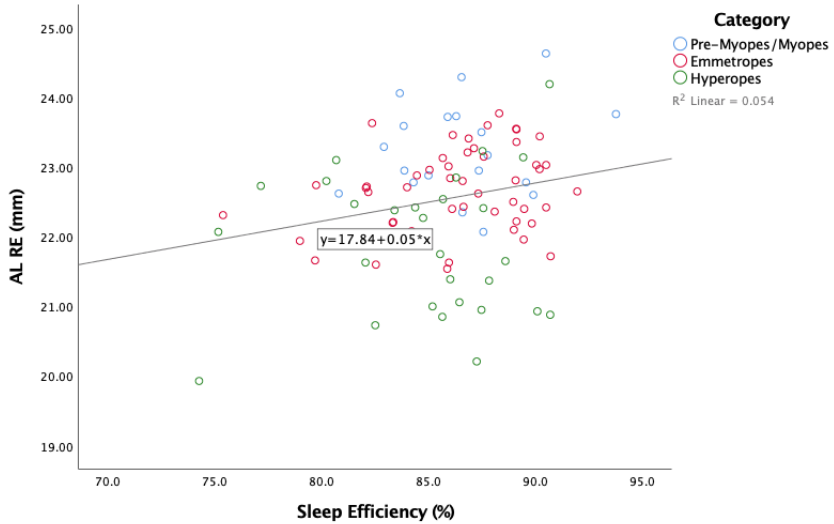


Figure 5.5.11. Scatterplot of sleep efficiency against AL (mm). Pearson's correlation shows a statistically significant positive correlation (r=0.232, p=0.02).

Hierarchical multiple regression analysis for AL found that sleep efficiency was independently associated with AL after controlling for age, gender, ethnicity, and parental myopia; with a higher percentage of sleep efficiency being associated with a longer AL. The whole model included all parameters with a significant association with AL and was statistically significant with the total variance explained by the model=35.9%, F (6, 69) =6.44, p<0.001. Sleep efficiency was statistically significant, beta=0.215, p=0.033.

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the sleep parameters are presented in Table 5.5.9.

Actiwatch Sleep Parameter	Pre-Myopes/Myopes Mean and (SD)	Non-Myopes Mean and (SD)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD)	Hyperopes Mean and (SD)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Bedtime (hh:mm:ss)	22:01:47 (1:24:41)	21:30:38 (0:58:09)	p=0.055	21:27:51 (0:54:09)	21:35:31 (1:05:19)	p=0.141	
Get Up Time (hh:mm:ss)	07:42:46 (1:23:42)	07:26:00 (0:41:27)	p=0.394	07:25:52 (0:40:33)	07:26:13 (0:43:42)	p=0.447	

Total Time in Bed (hh:mm:ss)	9:39:16 (0:36:18)	9:55:21 (0:36:34)	p=0.081	9:58:00 (0:35:11)	9:50:41 (0:39:04)	p=0.153	
Total Hours of Sleep (hh:mm:ss)	8:18:58 (0:31:40)	8:29:57 (0:38:40)	p=0.243	8:35:05 (0:33:31)	8:20:55 (0:45:36)	p=0.134	
Sleep Onset (mins)	11.00 (9.04)	9.92 (6.87)	p=0.556	8.99 (5.92)	11.55 (8.14)	p=0.272	
Sleep Efficiency (%)	86.26 (3.19)	85.68 (3.88)	p=0.540	86.19 (3.60)	84.77 (4.25)	p=0.220	
Wake After Sleep Onset (WASO) (mins)	53.57 (17.29)	54.45 (16.09)	p=0.831	52.59 (15.29)	57.71 (17.20)	p=0.395	
Number of Awakenings	40.99 (9.76)	42.04 (6.87)	p=0.654	42.10 (7.61)	41.94 (5.48)	p=0.854	
PSQI Sleep Parameter	**Pre-Myopes/Myopes Mean and (SD)**	**Non-Myopes Mean and (SD)**	**Independent t-test (Pre-Myopes/Myopes vs Non-Myopes**	**Emmetropes Mean and (SD)**	**Hyperopes Mean and (SD)**	**One-Way ANOVA**	**Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes**

							H=Hyperopes)
Bedtime (hh:mm)	20:30 (0:40)	20:19 (0:45)	p=0.275	20:14 (0:38)	20:29 (0:55)	p=0.177	
Sleep Onset (mins)	26.02 (21.48)	24.71 (24.49)	p=0.814	26.15 (28.99)	22.09 (12.86)	p=0.725	
Get Up Time (hh:mm)	07:11 (0:44)	07:15 (0:26)	p=0.507	7:12 (0:24)	7.22 (0:28)	p=0.275	
Hours of Sleep (hours)	9.74 (1.73)	10.12 (0.97)	p=0.167	10.12 (1.07)	10.11 (0.77)	p=0.391	
PSQI Score	3.65 (4.28)	2.63 (1.73)	p=0.263	2.83 (1.99)	2.28 (1.05)	p=0.129	

Table 5.5.9. The average sleep parameters for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories.

Independent samples t-tests were used to compare averages between the pre-myopes/myopes and non-myopes (emmetropes and hyperopes combined). There were no significant differences between the two refractive groups in any of the sleep parameters measured. On average, pre-myopes/myopes went to bed 31 minutes later than non-myopes (p=0.055) but this difference failed to reach significance at the 5% level.

There were no significant differences in the measures relating to sleep between the three refractive groups (all p>0.05, one-way ANOVA). Despite a downward trend for PSQI scores from pre-myopes/myopes (M=3.65, SD=4.28) to emmetropes (M=2.83, SD=1.99) and hyperopes (M=2.28, SD=1.05) (Figure 5.5.10.), ANOVA failed to reveal a statistically significant difference (p=0.129).

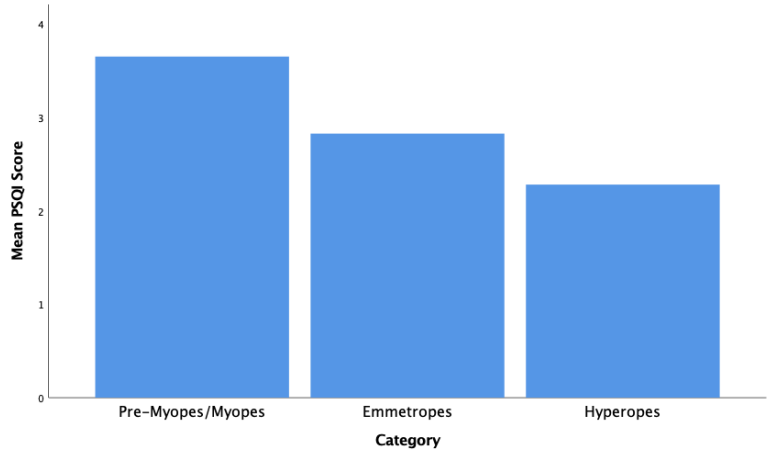


Figure 5.5.12. Bar chart depicting the downward trend in PSQI scores from pre-myopes/myopes to emmetropes to hyperopes.

Two-way ANOVAs found statistically significant differences between winter and summer for bedtimes (p=0.006) and time spent in bed (p=0.022), with participants going to bed significantly later and spending less time in bed in winter than summer. Two-way ANOVAs also found statistically significant differences between winter and summer for PSQI scores with statistically significantly higher PSQI scores in winter than summer (p=0.005). There were no significant differences between refractive groups for any of these parameters.

5.5.6. Near Activity Results (Clouclip)

The near activity parameters measured by the Clouclip, and their respective correlations with SER and AL are presented in Table 5.5.10.

Clouclip Near Activity Parameter	Average for all Participants	Correlation with SER	Correlation with AL
Average Viewing Distance (cm)	94.61	r=-0.116 p=0.384	r=0.062 p=0.646
Time Spent on Very Close Viewing (mins)	170.06	r=0.045 p=0.738	r=-0.002 p=0.987
Time Spent on Near Viewing (mins)	74.86	*r=-0.273* *p=0.038*	r=0.180 p=0.176
Time Spent on Intermediate Viewing (mins)	85.18	r=-0.233 p=0.078	r=0.161 p=0.227
Time Spent on Distance Viewing (mins)	235.03	r=-0.076 p=0.570	r=0.012 p=0.928
Average Duration of Near Work (mins)	125.39	r=-0.245 p=0.074	r=0.181 p=0.190
Maximum Duration of Near Work (mins)	30.04	r=-0.181 p=0.190	r=0.120 p=0.386
Average Near Work Distance (cm)	23.67	r=-0.141 p=0.308	r=0.039 p=0.781

Table 5.5.10. The average near activity parameters for all the participants and the Pearson's correlations between each near activity parameter with SER and AL.

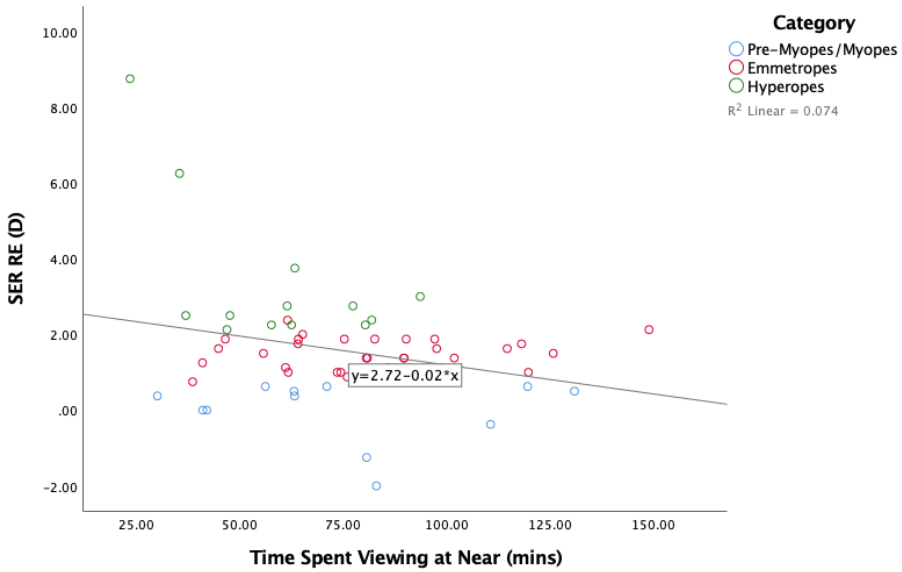


Figure 5.5.13. Scatterplot of time spent viewing at near against SER (D). Pearson's correlation showed a statistically significant negative correlation (r=-0.273, p=0.038).

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the near activity parameters are presented in Table 5.5.11.

Clouclip Near Activity Parameter	Mean and (SD) Pre-Myopes/Myopes	Mean and (SD) Non-Myopes	P-value results of independent t-test between pre-myopes/myopes and non-myopes	Mean and (SD) Emmetropes	Mean and (SD) Hyperopes	P-value from one way ANOVA P/M =Pre-myopes/Myopes E=Emmetropes H=Hyperopes	
Average Viewing Distance (cm)	89.56 (23.06)	95.92 (23.77)	p=0.411	96.24 (21.50)	95.12 (29.77)	p=0.708	
Time Spent on Very Close Viewing (mins)	172.22 (53.73)	169.49 (75.46)	p=0.907	172.77 (76.88)	161.17 (74.06)	p=0.881	
Time Spent on Near Viewing (mins)	74.33 (32.14)	75.00 (25.93)	p=0.941	81.23 (25.37)	59.16 (20.67)	*p=0.042*	p=0.712 P/M vs E p=0.318 P/M vs H *p=0.032 E vs H*

Time Spent on Intermediate Viewing (mins)	92.32 (59.63)	83.31 (29.91)	p=0.621	89.18 (29.76)	68.42 (25.66)	p=0.184	
Time Spent on Distance Viewing (mins)	217.11 (85.30)	239.70 (75.06)	p=0.370	245.33 (71.44)	225.41 (84.91)	p=0.494	
Average Duration of Near Work (mins)	136.58 (61.03)	122.19 (43.58)	p=0.362	125.24 (43.26)	115.38 (45.29)	p=0.549	
Maximum Duration of Near Work (mins)	21.92 (9.80)	24.17 (12.62)	p=0.572	26.10 (12.01)	19.85 (13.37)	p=0.255	
Average Near Work Distance (cm)	30.25 (4.12)	29.98 (3.73)	p=0.827	30.03 (3.66)	29.85 (4.02)	p=0.966	

Table 5.5.11. The average near activity parameters for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories.

Independent samples t-tests were used to compare averages between the pre-myopes/myopes and non-myopes (emmetropes and hyperopes combined). There were no statistically significant differences between groups in any of the near activity parameters recorded. The figure below (Figure 5.5.12.) presents the significant difference between groups for time spent on near viewing (p=0.042), with the emmetropes spending significantly more time on near viewing (M=81.23) than the hyperopes (M=59.16), p=0.032. There was no significant difference between the pre-myopes/myopes (M=74.33) and either the emmetropes or hyperopes, both p>0.05.

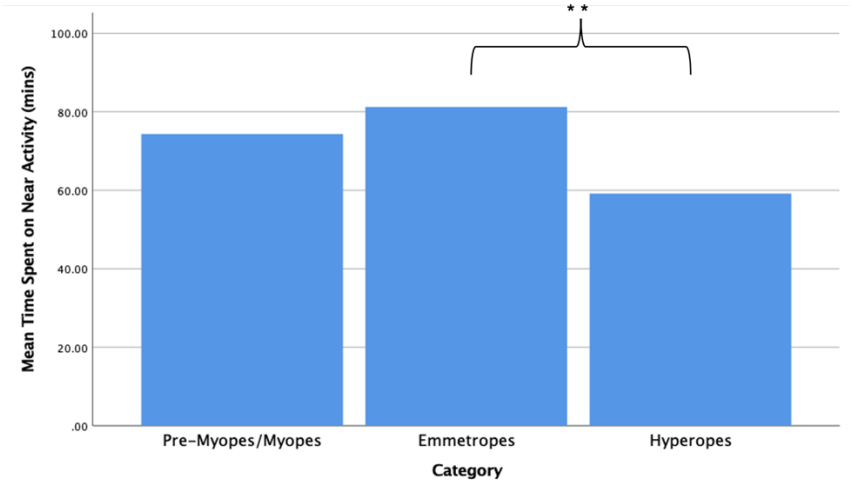


Figure 5.5.14. Bar chart showing the mean time spent on near activity between refractive groups, with the brace and stars indicating the significant difference.

Although there were no significant differences in the groups the pre-myopes/myopes tended to have a shorter average viewing distance (89.56 cm) throughout the week of Clouclip wear compared to both the emmetropes (96.24 cm) and the hyperopes (95.12 cm).

Two-way ANOVAs found no statistically significant differences between winter and summer for any near work parameters.

5.5.7. Screen-Time Results

The screen-time questionnaire was originally designed with questions about time spent watching TV/video games, on phone/tablets and on computer/laptops per day, with categories of; 0 hours, <1 hour, 1-2 hours, 2-3 hours, and 3+ hours for each. The categories were collapsed into <1 hour, 1-3 hours and 3 + hours to match categorisation by Harrington *et al.* (2019). The question about device use before sleep per night was

designed with categories of 0 mins, 1-30 mins, 30 mins-1 hour, 1-2 hours, and 2+ hours. The categories were collapsed into <30 mins, 30mins-1 hour, 1+ hours.

The screen-time data for the participants that had completed the parental reported screen time questionnaires are presented in graphical form in Figure 5.5.13.

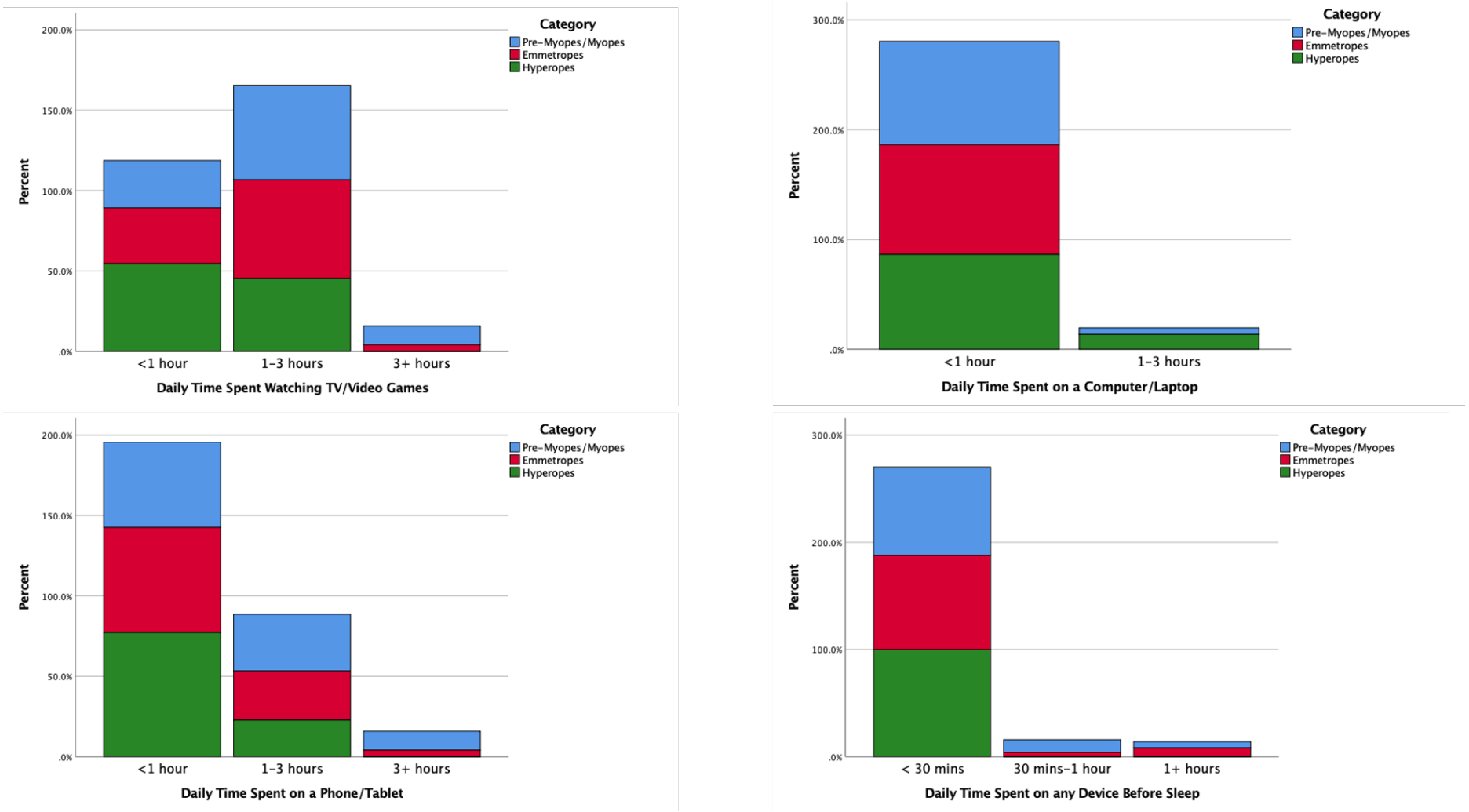


Figure 5.5.15. Bar charts showing the percentage of each refractive group for time spent on different screens per day from the parental-reported screen time questionnaire.

Chi-Squared tests for independence indicated no statistically significant associations hours spent on TV/video games, on a phone/tablet, on a computer/laptop or on device use before sleep and the classification as pre-myopic/myopic or non-myopic.

Logistic regression analysis found no statistically significant increased odds for classification as pre-myopic/myopia with any of the screen time parameters (all p>0.05).

5.5.8. Odds Ratios for Classification as Pre-Myopic/Myopic

All qualitative and quantitative measures were investigated for classification as pre-myopic/myopic using logistic regression analyses. The table below highlights the parameters where a significant result was identified on univariate logistic regression analysis for classification as pre-myopic/myopic rather than non-myopic. The significant parameters were then put into a multivariate analysis model.

Predictive Variables for Pre-Myopia/Myopia	Univariate ORs (95% CI) and Significance	Multivariate ORs (95% CI) and Significance
Age	*2.41 (1.02-5.68), p=0.045*	3.70 (0.94-14.51), p=0.061
Axial Length (RE)	*3.70 (1.80-7.62), p<0.001*	*4.43 (1.19-16.46), p=0.026*
Anterior Chamber Depth (RE)	*15.96 (1.99-127.88), p=0.009*	4.56 (0.08-271.19), p=0.466
Time Spent on Moderate Activity	*1.02 (1.00-1.05), p=0.046*	1.02 (0.99-1.05), p=0.237
Time Spent in Photopic Light night-time	*1.005 (1.001-1.009), p=0.027*	1.005 (0.999-1.01), p=0.131
Parental Myopia (0,1 or 2 myopic parents)	One myopic parent 2.33 (0.64-8.52), p=0.200 *Both Parents Myopic 8.75 (1.74-43.97), p=0.008*	One parent myopic 1.44 (0.23-9.22), p=0.700 Both Parents Myopic 5.17 (0.57-47.09), p=0.145

Table 5.5.12. Results of the univariate and multivariate analyses with the parameters that are significant underlined and in italics.

Univariate regression analysis identified a significant relationship between time spent in photopic light at night (p=0.027) and children being classified as pre-myopic/myopic; with increased time spent in photopic light at night being associated with increased odds of classification as pre-myopia/myopia (OR= 1.005; 95% CI, 1.001-1.009 per minute increase at night). The significance did not remain after multivariate analysis.

Univariate regression analysis identified a statistically significant relationship between refractive category and time spent on moderate activity; pre-myopic/myopic children spent more time undertaking moderate activity (p=0.046, OR 1.02, 95% CI, 1.00-1.05 per minute increase during the day) compared to children classified as emmetropic or hyperopic. This relationship was not sustained with multivariate analysis.

Univariate regression analysis found no significant relationships between refractive category and the sleep parameters (both Actiwatch measured and PQSI-reported), the near activity parameters (Clouclip measured), or the screen time (parental-reported Screen Time Questionnaire) (all $p>0.05$). However univariate regression analysis did find significant associations between older age, longer axial length, longer anterior chamber depth and having two myopic parents and increased odds of classification as pre-myopic/myopia (all $p<0.05$).

Having a longer axial length was the only significant univariate regression parameter to remain significant following multivariate regression analysis, p=0.026, OR 4.43, 95% CI's 1.19-16.46.

5.6. Discussion

This is the first study to quantify light exposure, physical activity, sleep, and near activity in young children in the UK and to explore relationships between children's refractive error/axial length and these objectively measured risk factors. The findings support the theory that disrupted circadian rhythm is associated with myopia and further evidence for time outdoors and near visual activities associations with myopia.

5.6.1. Light Exposure

When evaluated without considering the season during which measures were taken, there was no evidence for different light exposure profiles between children in different refractive groups at 6-7-years-old. In contrast to previous studies, children with pre-myopia and myopia did not spend less time exposed to light levels found outdoors. However, when season of data collection was considered, average winter daytime light exposure (measured by the Actiwatch) was statistically significantly higher for non-myopes compared to pre-myopes/myopes. This indicates that with limited hours of daylight available in winter, the non-myopes were exposed on average to higher levels of light than the pre-myopes/myopes. There was however no statistically significant difference in time spent outdoors in winter between refractive groups and during the summer months no statistically significant differences were found in light exposure or outdoor time between refractive groups. When considering the whole cohort (not separated by time of year) there were weak positive correlations between SER and average light exposure, time spent outdoors, illumination during near work, sunlight exposure duration and sunlight exposure frequency (all measured by the Clouclip) meaning that participants with more hyperopic SER's tended to have higher light exposures, but the correlations did not reach statistical significance.

Read *et al.* (2014) also used Actiwatches to monitor myopes and emmetropes aged 10-15 years old, and the authors reported that myopes spent significantly less time outdoors and had lower average light exposure than the emmetropes. Perhaps the associations between light exposure and time outdoors with refractive error do not appear until after the onset of myopia and as the majority of pre-myopic/myopic group in the present study were still pre-myopic, (>0.50DS and <+0.75DS in either eye) with only four of those already myopic (≤-0.50DS in either eye), the associations are not well established yet. It is possible that there is a threshold of time spent outdoors to gain adequate protection from myopia development (French *et al.*, 2013) and a lack of variation in time spent outdoors

in our cohort alongside a low prevalence of myopia prevented us from determining an association. There is also the potential that optometrists and parents now have an increased knowledge of the benefits of time outdoors in myopia prevention, and this could have influenced the behaviour of the children in the present study.

A notable finding from the present study was that was that pre-myopic/myopic children spent significantly more time in photopic light at night-time during sleep (M=90.68 mins, SD=161.82) compared to emmetropes (M=20.25 mins, SD=37.28). Although the pre-myopes/myopes also spent more time in photopic light during sleep than hyperopes (M=43.90 mins, SD=108.23) this difference did not reach statistical significance, p=0.22. Photopic light at night could be anything from a table lamp to full room lights on. Univariate analysis found that time spent in photopic light at night significantly increased the odds of classification as pre-myopic/myopic (OR=1.005 [95%CI 1.001-1.009] per minute increase at night, p=0.027). This translates that for every additional hour in photopic light at night during sleep, the child is 1.3 times more likely to be pre-myopic/myopic than non-myopic. These findings support those of Landis *et al*. (2018) where scotopic light is deemed protective against the onset of myopia. However, Landis *et al.* used light exposure data for waking hours only and noted the potential role of light exposure during sleep on the development and progression of myopia. Quinn *et al.* (1999) reported a dose dependant relationship between refraction and night-time light before the age of two years, with those children sleeping with a room light on having a higher prevalence of myopia and high myopia (>-5.00D) than those with a night-light, and higher again than those sleeping in darkness. Higher levels of light exposure during sleeping hours in the present study appears predictive of classification as pre-myopic/myopic in children aged 6-9 years and hence, increased risk of future myopia in this age group. This area requires further research in order to provide children, parents and eyecare professionals with advice regarding sleeping in the presence of light at night if it is a potential risk factor for myopia. The mechanism through which this occurs could be through the disruption of the circadian rhythm by decreasing melatonin (Gooley *et al.*, 2011; Chakraborty *et al.*, 2018; Leger *et al.*, 2019; Ostrin, 2019). Melatonin levels are known to rise in the evenings and to promote sleep onset and exposure to bright light at night strongly suppresses melatonin which therefore interferes with sleep timing and sleep quality (Gooley *et al.*, 2011; Bedrosian and Nelson, 2017).

Pre-myopes/myopes were experiencing an average of 27 times higher illumination (in lux) during sleep (M=4.86 lux) than emmetropes (M=0.18 lux), and 13.5 times more than hyperopes (M=0.36 lux). These differences were close to statistical significance (p=0.051). In Chapter 3 a photometer was used to estimate ambient light levels and the night-time assessment of a typical bedroom with room lights on ranged from 67.67-74.5 lux, while a room with only a night light ranged from 1.6-3 lux, ambient light from streetlights or hall lights into a room ranged from 0.4-0.78 lux. From these ambient light measures, we can conclude than on average the pre-myopes/myopes were sleeping with either a night-light/bedside light on or the room lights on for at least some of their sleep time, whereas the emmetropes and hyperopes were sleeping in near-dark conditions. This exposure to light at night is more likely to delay or suppress the synthesis of melatonin, and therefore reduce the total daily melatonin (Gooley *et al.*, 2011) leading to a disrupted circadian rhythm which is potentially a mechanism for myopic development (Chakraborty *et al.*, 2018).

Light exposure parameters were significantly different when collected in different seasons and hence analysis was conducted independently on groups whose data collection had occurred in winter or summer. These analyses revealed no statistically significant differences between environmental parameters measured in the different refractive groups during the summer months. This could have potentially been due to the smaller sample who had their objective measures taken in summer (n=25) compared to winter (n=75). Interestingly the differences between refractive groups light exposure are only present in those children who had their objective measures of risk factors taken in winter and the trends found in winter were not apparent in summer from the raw data. The winter measures that had statistically significant differences between refractive groups included: higher average daytime light exposure for non-myopes than pre-myopes/myopes, higher average daytime spent in photopic light (time spent in bright indoor lighting) in pre-myopes/myopes than non-myopes, more time spent in scotopic light (darkness) at night during sleep for non-myopes than pre-myopes/myopes and more time spent in photopic light at night during sleep for pre-myopes/myopes than emmetropes (all measured by the Actiwatch). The pre-myopes/myopes increased exposure to bright light during sleeping hours in winter, as opposed to scotopic light exposure is unlikely to be due to daylight streaming in the windows on lighter evenings, but rather an artificial light source such as a table lamp or full room lighting. During the winter months there are limited hours of daylight in the UK which is already known to disrupt the circadian rhythm due to differing

light/dark cycles (Lewy *et al.*, 2009). However, if we pair the lack of daylight hours with higher levels of light exposure during sleeping hours, this disruption to the circadian rhythm could be magnified and therefore lead to increased ocular growth. The pre-myopes/myopes also spent more time in photopic light during the daytime than non-myopes which could be a surrogate for increased time spent indoors in winter which is reducing their potential for more time outdoors or in higher levels of illumination which has been shown to be protective over myopia development (French *et al.*, 2013; Read, Collins and Vincent, 2014).

5.6.2. Sleep

The findings of the present study indicate that sleep efficiency (total sleep time/total time in bed x100) is significantly negatively correlated with SER and significantly positively correlated with AL showing that the more myopic participants and those with longer AL's tend be asleep for a greater proportion of their time in bed, compared with those less myopic or with smaller eyes. This is linked with the fact that pre-myopes/myopes tended to go to bed later (M=22:03 hrs) than non-myopes (M=21:51 hrs) which indicates that potentially those with more hyperopic refractive errors go to bed earlier and spend some time in bed awake prior to falling asleep, whereas the pre-myopes/myopes go to bed later and fall asleep quickly; hence increasing their sleep efficiency. A higher sleep efficiency can be found in those with a shorter night's sleep. In agreement with findings from other studies where shorter sleep durations were linked to increased prevalence of myopia (Zhou *et al.*, 2017; Xu *et al.*, 2017; Patel, Desai and Ramavat, 2019) the pre-myopes/myopes from the present study had a slightly shorter (but not statistically significant) sleep duration (8.32 hrs) than non-myopes (8.5 hrs). Sleep efficiency in the present study was found to be independently associated with AL after controlling for age, parental myopia, ethnicity, and gender, with a higher percentage sleep efficiency being significantly and independently associated with a longer AL. Ostrin *et al.* (2020) also reported that 10-15-year-old myopes had a higher sleep efficiency than non-myopes, but this only approached statistical significance (p=0.05).

Although the findings of differences in bedtime from the present study was only approaching statistical significance, p=0.055, it is similar to results by Ayaki *et al*. (2016) which identified later bedtimes amongst myopes compared with non-myopic children. While myopes and pre-myopes went to bed later and once in bed slept more, children with more hyperopic refractive errors took longer to get to sleep and woke more often

during the night. Ostrin *et al.*, (2020) found that myopes aged 10-15 years had a significantly faster sleep onset than non-myopes and reported that shorter sleep onsets can be associated with greater sleep debt and sleep deprivation. This could explain the finding of a downward trend for PSQI scores from pre-myopes/myopes (M=3.65, SD=4.28) to both the emmetropes (M=2.83, SD=1.99) and the hyperopes (M=2.28, SD=1.05), indicating a trend for poorer subjective sleep quality (parental-reported) in those with more myopic refractive error. The differences were not significant at this age, whereas by adulthood emmetropic participants were found to display significantly lower PSQI scores than myopes (Abbott, Queener and Ostrin, 2018) meaning the myopic adults had a poorer subjective sleep quality.

When separated into winter and summer participants were found to go to bed significantly later and spend less time in bed in winter than summer and additionally tended to have significantly higher PSQI scores in winter, indicating poorer sleep quality. These findings would support a role for reduced daylight hours in winter having a negative impact on children's sleep quality and patterns.

5.6.3. Near Activity

Many of the previous studies reporting the association between increased near work activity and increased risk of myopia among children were based on questionnaire data rather than objective measures which could lead to recall bias. The present study found a statistically significant negative correlation between SER and time spent on near viewing (r=-0.273, p=0.038), indicating that higher amounts of near viewing were found in those with less hyperopic SER. There were no statistically significant differences between refractive groups for any of the near activity parameters however, the pre-myopic/myopic group tended to have a shorter average viewing distance (89.56 cm) compared to both the emmetropes (96.24 cm) and the hyperopes (95.12 cm). The SER and viewing distance were also negatively correlated but this did not reach statistical significance. This indicates early signs of a viewing distance adjustment, but again this cross-sectional study design cannot confirm if the shorter viewing distance occurs before or after the onset of myopia. There were negative correlations that approached statistical significance between SER and time spent at intermediate viewing (r=-0.233, p=0.078) and average duration of near work (r=-0.245, p=0.074). These findings point towards some evidence for increased near work activity in those with less hyperopic SERs. This may be indicative of near

activity as a myopic risk factor or in contrast, may be task avoidance of near work among those with hyperopia (French *et al.*, 2009).

5.6.4. Screen Time

The participants in the present study were aged 6-9-years, and we discovered that most children this age did not own their own phone/tablet, therefore our initial plan to use objective measures of screen time using screen time monitoring apps could not be achieved as an individual's screen time could be overestimated by monitoring screen time on a shared device. To avoid this overestimation, we utilised a basic screen time questionnaire to estimate average time spent on phone/tablets as well as time spent on computers/tablets, TV/video games and on any of the respective devices prior to sleep. The results of the screen time questionnaire indicated that there were no notable associations between any of the respective versions of screen time and prevalence of pre-myopia/myopia. Harrington *et al.* (2019) found that screen use >3 hours per day had ORs of 3.7 (95% CI 2.1-6.3, $p<0.001$). Contrary to those findings, there was no statistically significant relationship between screen use and classification as pre-myopic/myopic in the present study, so differences in screen time between refractive groups might not be apparent in this age group prior to the onset of myopia. However the lack of findings of any relationship between screen time and refractive error in the present study could be limited by the sample size (n=87) whereas Harrington *et al.* (2019) had 1626 participants. Subjective parental reported screen time has potential for both recall bias and social desirability bias, it would be difficult to rule out screen time as a potential risk factor for myopia without more robust evaluation using objective measures in the future. The use of a screen time monitoring app would be a good option for a slightly older cohort as in 2021 Ofcom Communications Market Report (2021) found 14% of children aged 5-7-years have their own smartphone and 57% have their own tablet, whereas 91% of children aged 12-15-years have their own smartphone and 59% have their own tablet. A more robust evaluation exploring associations between myopia and the use of handheld electronic devices (along with other near vision tasks) would provide much-needed information to support public health advice for parents, children, and eye care professionals.

5.6.5. Physical Activity

Contrary to the findings from Northern Ireland Childhood Errors of Refraction (NICER) 1.0 our objective measures of physical activity did not show any association between

higher levels of PA (>3hr/week) and a lower prevalence of myopia. Albeit, their findings were from a 12-13-year old sample (O'Donoghue *et al.*, 2015). Harrington, Stack and O'Dywer (2019) from the Ireland Eye Study (IES) also found that within their 6-7-year-old cohort, 8.1% of those with sedentary lifestyles were myopic, dropping to just 3.1% for those with a more active profile and in their 12-13-years-old cohort 35.2% of participants with sedentary lifestyles were myopic, decreasing to 14.4% among participants with a more active profile. The effect seems to begin at the younger age but is more pronounced in the older cohort and possibly the associations between sedentary behaviour and myopia would also develop in the cohort from the present study with increasing age. However, the physical activity data from the NICER 1.0 study and the IES were collected via questionnaires which would be subject to recall bias. Interestingly, time spent on moderate activity in the present study was found to be associated with refractive error, with those more myopic/less hyperopic children spending slightly more time on moderate activity. Univariate regression analysis found a significant relationship between refractive category and increased time on moderate activity; those with higher levels of moderate activity were more likely to be classified as pre-myopic/myopic (OR= 1.02; 95% CI, 1.00-1.05 per minute increase per day, p=0.046). This translates that every additional hour performing moderate physical activity per day increased the likelihood of a pre-myopia/myopia classification by 2.2 times. Flanagan *et al.* (2020) found that more time spent on moderate activity was related to higher levels of morning serum melatonin, which in turn was associated with more myopic SER in a population of young adults. The time spent in moderate activity had a unique significant contribution to morning serum melatonin levels. These findings again support a role of circadian rhythm in ocular growth control mechanisms as both physical activity and light exposure provide temporal cues to the circadian system (Flanagan *et al.*, 2020). Moderate activity is classified as 3-5.9 metabolic equivalent of task (METs) (Trost *et al.*, 2001) and includes activities such as brisk walking, bike riding, or dancing. In the present study, time spent sedentary or on light or vigorous activity did not significantly increase or decrease the odds for pre-myopia/myopia classification.

Participants spent more time sedentary and demonstrated lower PAQ-C scores in winter than summer indicating a tendency to have reduced PA levels in the winter months, coinciding with reduced daylight hours.

5.6.6. Parental History of Myopia

Parental history of myopia is well known to be associated with childhood myopia, and the findings of our study support this with OR of 8.75 (95% CI 1.74-43.97, p=0.008) for being classified as pre-myopic/myopic at 6-9-years old with two myopic parents. Having one myopic parent had OR of classification as pre-myopic/myopic of 2.33 (95% CI 0.64-8.52, p=0.200), but the result was not statistically significant. Perhaps any association between having one myopic parent and classification as pre-myopic/myopic is not apparent until an older age, whereas those with two myopic parents are more likely to develop myopia earlier. These results are in strong agreement with those from the NICER 1.0 study where they presented ORs of 2.91 and 7.79 for myopia classification for 12-13-year-olds with one and two myopic parents respectively (O'Donoghue *et al.*, 2015). But of note here is the inclusion of pre-myopes as well as myopes to calculate these odds ratios as we were examining a mainly white, younger cohort of children, where the prevalence of myopia is relatively low. However, these children are expected to become myopic in the future based of their current low hyperopic refraction at baseline (French *et al.*, 2013; Flitcroft *et al.*, 2019; McCullough *et al.*, 2020).

5.6.7. Comparison of Objectively and Subjectively Measured Risk Factors

A comparison of between objectively and subjectively measured sleep and physical activity parameters demonstrated a very strong correlation between parental reported and objectively measured bedtime and get-up times using the PSQI and Actiwatch 2 devices. This strong relationship between objective measures and subjective report did not extend to all sleep parameters, notably in relation to sleep onset metrics. Parental reported sleep onset times were not significantly associated with objectively measured sleep onset, indicating a limitation of the PSQI for this parameter. Comparison of physical activity profiles derived from the Actiwatch, and subjective parental report indicate that the latter provides moderately comparable data to objectively measures.

5.6.8. Strengths and Limitations

The present study has many strengths, namely the focus on young children aged 6-9-years-old, a cohort which researchers (Landis *et al.*, 2018) recommended would be useful to determine risk factors which precede the development of myopia. Many studies which present significant differences in risk factors for myopia are from older cohorts aged 10-15-years (Read, Collins and Vincent, 2014; O'Donoghue *et al.*, 2015; Ostrin *et al.*, 2020) therefore making it difficult to determine if the differences were a cause or simply an effect of myopia. Additionally, this study is the first of its kind in the UK and Ireland

where objective measures of the potential risk factors for myopia were taken alongside a robust evaluation of refractive error using cycloplegic autorefraction. Another benefit is the inclusion of pre-myopic as well as myopic children at this age, enabling us to determine if there are differences in behaviours between those children with high risk of future myopia compared to those at low or no risk of future myopia based on their refractive error in early childhood.

However, there are a number of limitations to the present study. Firstly, there is the loss of data from Clouclip, this was attributed predominantly to the poor battery life of the Clouclip (40 hrs) and challenged for participants/parents in remembering to charge it at night. Secondly, the data collection was limited by failed compliance with device wear where 19/119 children failed to meet the required wearing times of the Actiwatch as noted in the exclusion criteria. Another limitation was the sample size and uneven number of participants in each refractive group; 20 pre-myopes/myopes, 51 emmetropes and 29 hyperopes. This refractive group profile made it difficult to solidify trends in behavioural patterns between refractive groups. However, the numbers for each group were reflective of the proportion of refractive errors in the general population at this age. Thirdly, the light exposure data is limited by collection of data year-round rather than during seasons where the day length was similar. Our study did not pair up the myopic (or pre-myopic/myopic kids in our case) and non-myopic participants as done by Read *et al.* (2014) in order to control for the differing light levels available to the participants and therefore had more participants tested during winter than summer months. Our initial plan was to collect the same data on 12-13-year-olds, to determine if there were differences in behavioural patterns between myopes and non-myopes at this age, however this age group proved to be non-compliant with the wearable devices. This was likely due to increased image awareness or self-consciousness meaning they did not want to wear the spectacles with the Clouclip attached. Within the first cohort of 12-13-year-olds, 29 participants were recruited, 18 agreed to take part but only eight of those wore the devices continuously over the one-week period. The decision was made to cease data collection on this cohort and concentrate on the younger cohort to determine differences in behaviours prior to the onset of myopia.

5.7. Conclusion

To conclude, this study of device measured environmental and behavioural risk factors associated with pre-myopia/myopia further supports the theory that disrupted circadian rhythm is associated with myopia. The data captured identifies differences in light exposure during sleep as well as differences in bedtimes and sleep efficiency associated with refractive error in early childhood. Time spent outdoors is a well-established and evidenced environmental risk factor, conferring benefit for delaying onset of myopia. In the present study, winter light exposure profiles of pre-myopic/myopic children indicated less time spent outdoors than non-myopes and suggest that public health messages need to be reinforced to encourage these children to spend more time outdoors. Children with less hyperopic refractive errors also spent more time in near vision activities. While the evidence for a strong association between increased near vision activity and myopia onset and progression is less convincing in the literature, it may be helpful to encourage a better mix of visual activities to promote long-term visual health. Evaluation of these environmental and behavioural metrics and their association with short-term eye growth will be evaluated in Chapter 7.

Chapter 6: Light Exposure, Near Work and Physical Activity at Different Periods of the Day and Relationship with Refractive Error

Chapter 6: Light Exposure, Near Work and Physical Activity at Different Periods of the Day and Relationship with Refractive Error

6.1. Introduction

Landis *et al.* (2018) reported a protective effect of time spent in scotopic light as well as time spent outdoors on myopia development among children aged 10-15-years. However, the authors recommended that further research into the light exposure profile experienced by younger cohorts would provide useful insight. In particular further work is required into the type of light exposure experienced and therefore retinal signalling potentially via rod photoreceptors (Park *et al.*, 2014), that might precede myopia development. The authors suggested that rod photoreceptors might be a critical part of retinal signalling with a role in circadian rhythms, and therefore refractive development (Park *et al.*, 2014).

Previous studies have noted a relationship between time spent sedentary and increased prevalence of myopia (O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019). Similarly, there is a notable relationship between increased near activity and myopia prevalence in children (Mutti *et al.*, 2002; Saw *et al.*, 2002; Ip *et al.*, 2008; Deng, Gwiazda and Thorn, 2010; French *et al.*, 2013; Saxena *et al.*, 2015; Li *et al.*, 2015; Guo *et al.*, 2016; Hsu *et al.*, 2016; Williams *et al.*, 2018; Singh *et al.*, 2019; Han *et al.*, 2019; Harrington, Stack and O'Dwyer, 2019), in addition to short working distances (<30 cm) being linked to increased myopic progression. However, it is currently not known whether the time of physical inactivity or near activities take place within the day have any impact on myopia development.

Dopamine and melatonin are mutually inhibitory hormones that oscillate in antiphase throughout the day with dopamine peaking during the day and melatonin peaking at night. However, the levels of dopamine or melatonin can be changed by altering the light exposure patterns, which can encourage or suppress the secretion of both hormones earlier or later in the 24-hour circadian cycle (Duffy, Kronauer and Czeisler, 1996). Dopamine has been shown to act as a stop signal in refractive eye growth (X. Zhou *et al.*, 2017), whereas myopes were found to have up to three times higher melatonin concentrations in the mornings than non-myopes (Kearney *et al.*, 2017; Chakraborty *et al.*, 2018). Phillips, Backhouse and Collins (2012) reported that night-

time light disrupts the circadian rhythm, rapidly decreasing melatonin and increasing dopamine, therefore potentially upsetting the normal balance in ocular growth. The authors noted that bright light in the middle of the day does not affect the timing of the circadian rhythm, so bright light at dawn and dusk are more likely to be problematic.

It is generally well accepted that spending time outdoors has an influence on ocular growth, protecting against the onset of myopia (Dirani *et al.*, 2009; Wu *et al.*, 2010; Sherwin *et al.*, 2012; French *et al.*, 2013; Lin *et al.*, 2014; Read, Collins and Vincent, 2014; He *et al.*, 2015; Landis *et al.*, 2018), but recent evidence suggests that the profile of low light level exposure may also have a role in eye growth regulation and hence the onset and progression of myopia (Landis *et al.*, 2018). Using objectively measured light exposure, Landis *et al.* (2018) presented evidence that myopic children received significantly less scotopic light (e.g. room with no lights on) during weekends than non-myopic children, with exposure during evening hours showing the largest differences (approximately 3 hours before falling asleep). On weekends, myopic children generally spent significantly more time in mesopic light (e.g., bedside/night light only) than non-myopic children and both groups spent more time in indoor photopic light (e.g., full room lights) on weekdays than weekends. Outdoor photopic light was most often experienced in the middle of the day for both refractive groups, corresponding with breaks in the school day and non-myopic children spent more time in outdoor light than myopes on weekends.

Also using objective measures of light exposure, Li *et al.* (2021) found no significant association between the timing of outdoor light exposures and spherical equivalent refraction (SER), axial length (AL) or risk of myopia in children aged 9-years-old, but did determine that greater objectively measured time spent outdoors was associated with lower odds of myopia (OR=0.82, 95% CI 0.70-0.95/daily hour increase, p=0.009).

Williams *et al.* (2019) reported adult participants, regardless of refractive error type, spent more time on near and intermediate viewing on weekdays than weekends and myopes spent more time on near and intermediate viewing than non-myopes but this difference was not statistically significant. Williams *et al.* did not discriminate between the times at which near viewing was occurring during weekdays and weekends. Wen *et al.* (2019) used the Clouclip to compare children's light exposure and near activity parameters on the weekday and weekend, with the weekdays split into the school period and after-school

period. However, the aim of Wen *et al.*'s study was to compare behaviour between urban and rural participants rather than their refractive error classification. The study found urban children spent significantly less time exposed to bright light (>1000 lux) than rural children and that urban children spent significantly more time on near work and continuous near work than rural children in the after-school period and demonstrated a shorter average viewing distance in this after-school period.

Read *et al.* (2014) reported that the mean physical activity undertaken by all participants (aged 10-15-years-old) in the Role of Outdoor Activity in Myopia (ROAM) study was significantly greater than that measured at weekends, but there was no significant difference in the mean physical activity between myopes and emmetropes, or on time spent on moderate to vigorous physical activity between the refractive groups. There was also no significant difference between the timing of physical activity and either refractive group. There are limited studies evaluating the duration, timing, and frequency of light exposure, near activity, and physical activity and their relationship with refractive status in children. This chapter was designed to examine the parameters from Chapter 5 in more detail to investigate relationships between the timing of near vision activity, physical activity and light exposure and determine if any patterns of activity throughout the course of the day, both weekday and weekend, were associated with refractive status.

6.1.1. Aims

The present study was designed to answer the following questions:

- What is the general pattern of light exposures, physical activity levels and near viewing behaviours across the day on weekdays and weekends for 6-9-year-old children?
- Is there a difference in the timing and duration of exposure to different light levels, engagement in different levels of physical activity and near work intensity between children at high and low risk of myopia?

6.2. Methods

6.2.1. Data Acquisition

The same categorisation of light exposure levels (Rosenfield and Logan, 2009; SolarLight, 2014; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020, and using the

validation cut-offs), viewing distances (Bilton, 2010; Long *et al.*, 2017) and physical activity levels (Read, Collins and Vincent, 2014; Ekblom *et al.*, 2016) as used in Chapter 5 were used for data analysis within this chapter. The data were divided to separate data collected on weekdays from that collected at weekends and then further categorised into morning, afternoon, and evening data.

The methods for recruitment and data collection are previously described in Chapter 5.2 and 5.3 and objective data from the Actiwatch 2 and Clouclip, for physical activity, light exposure and near activity will be used in this chapter.

6.2.2. Exclusion Criteria

Participants were excluded from the study if they had >1.50 D anisometropia between right and left eyes, to avoid misclassification of refractive grouping. Data from each device were only included if there were at least four days of data (including at least one weekend day), and Clouclip data were only used if at least eight hours of wearing time was available.

6.2.3. Data Extraction and Categorisation

Physical activity and light exposure data were downloaded from the Actiwatch 2 using Actiware software and the raw data were exported to Excel (Microsoft, www.microsoft.com) for categorising the parameters as described below. The Clouclip data on light exposure and near working distance were downloaded via the Clouclip Medical app and exported to Excel for categorising the parameters. The time spent under different lighting conditions, at different working distances or varying physical activity levels throughout the different periods of the day were calculated.

Compliance (i.e., wear) with Clouclip is indicated by the accelerometer output. This allows the researcher to determine the number of hours which the Clouclip has been worn during the study period. Actiwatch data were initially screened to remove any invalid data, i.e., where it was evident that the watch was removed for more than 15 minutes, or the light sensor was covered by clothing.

The data were organised into weekdays and weekends and then further coded into three time periods of each day, morning, afternoon, and evening. These three time points were classified as follows in Table 6.2.1. The time spent in different light levels, undertaking

different levels of physical activity, and spent viewing at different distances were averaged for each participant for each of the three periods on both weekdays and weekends.

Period	Time
Morning	Wake to 12pm
Afternoon	12pm to 4pm
Evening	4pm to Bedtime

Table 6.2.1. Cut-offs for morning, afternoon, and evening time periods, based on the approach utilised by Li et al. (2021).

Li *et al.* (2021) defined morning, midday and evening periods for participants wearing a FitSight wrist worn watch for recording light exposure between 7am-7pm. However, as the participants in the present study were wearing the Actiwatches 24 hours per day, the time periods in the present study were adjusted to capture behaviours from waking to bedtime and examine any potential impact on circadian rhythm.

The average time for getting up and going to bed in this cohort of 6-9-year-olds was approximately 7:30am and 9:30pm. The average school day for this age group is between 9am to 2pm.

The participants were classified as high risk of future myopia or low/no risk of future myopia as before in Chapter 5:

a) Pre-Myopes/Myopes (Children at high risk of developing myopia or already myopic): SER <+0.75DS in **EITHER** eye.

b) Emmetropes: (Children at low risk of developing myopia): SER ≥+0.75-<+2.00DS.

c) Hyperopes (Hyperopic children with no risk of developing myopia): SER ≥+2.00DS.

6.2.4. Ethical Approval

The study was in compliance with the Declaration of Helsinki and was approved by the Ulster University's Research and Ethics Committee on 30th January 2019, application number: REC/18/0102.

6.3. Statistical Analysis

Data were entered into SPSS Version 25 which was used for statistical analysis. Descriptive statistics were used to describe data for each devices' parameters over the course of the 7-day data collection period and the data were presented in tabular form. Scatterplots of SER and AL vs. each of the potential risk factors for future myopia over the different periods of the day on weekdays (W/D) and weekends (W/E) were constructed, and Pearson's correlations were used to describe these relationships. Parametric testing was used throughout due to the large sample size (Frost, 2015). Multiple regression analyses were performed to identify variables with a unique significant contribution to SER or AL. Univariate and multivariate logistic regression analyses were used to calculate odds ratios for the risk factors associated with pre-myopia/myopia. Independent samples t-tests were used to evaluate statistically significant differences between pre-myopes/myopes and non-myopes (emmetropes and hyperopes combined) and one-way between groups ANOVA were used to evaluate statistically significant differences in exposure to environmental risk factors between the three refractive groups (pre-myopes/myopes, emmetropes and hyperopes), with post hoc analyses to determine where any statistically significant differences lay. Bar charts with 95% confidence intervals were plotted demonstrating the mean for each parameter on weekdays and weekends across the different periods of the day for pre-myopes/myopes, emmetropes and hyperopes. Paired t-tests were used to compare all the parameters between weekdays and weekends.

6.4. Results

The descriptive data for this set of participants are described in detail in Chapter 5 (Section 5.5.1) but Table 6.4.1. below briefly summarises the number of participants with data for this timings chapter. The results henceforth will focus on the timings of light exposure, physical activity and near activity on weekdays and weekends.

	Number	Number (%) of Participants Successfully Completing Data Collection	
		Actiwatch	Clouclip
All participants	119	100 (84.9%)	58 (48.7%)
Pre-myopes/Myopes	24	20 (83.3%)	12 (50%)
Emmetropes	62	51 (82.3%)	33 (53.2%)
Hyperopes	33	29 (87.9%)	13 (39.4%)

Table 6.4.1. Table describes the success rate for participation and successful completion of the week of data collection with each wearable device, along with the numbers in each refractive group.

6.4.1. Timing of Light Exposure

The duration of different light exposures measured by the Actiwatch and Clouclip on weekdays (W/D) and weekends (W/E) across the different time periods, and their respective correlations with SER and AL are presented in Table 6.4.2.

Actiwatch Light Exposure Parameter	Average for all Participants (mins)	Correlation with SER	Correlation with AL
W/D Morning Time Spent in Scotopic Light	19.55	r=-0.013 p=0.899	r=0.029 p=0.776
W/D Morning Time Spent in Mesopic Light	23.60	r=-0.063 p=0.530	r=0.025 p=0.804
W/D Morning Time Spent in Photopic Light	227.99	r=0.041 p=0.683	r=-0.003 p=0.975
W/D Morning Time Spent Outdoors	13.08	r=0.013 p=0.901	r=0.074 p=0.463
W/D Afternoon Time Spent in Scotopic Light	6.02	r=-0.022 p=0.827	r=0.014 p=0.890
W/D Afternoon Time Spent in Mesopic Light	14.45	r=0.006 p=0.954	r=-0.020 p=0.843
W/D Afternoon Time Spent in Photopic Light	194.71	r=0.012 p=0.903	r=-0.082 p=0.417
W/D Afternoon Time Spent Outdoors	27.66	r=0.021 p=0.835	r=0.086 p=0.395
W/D Evening Time Spent in Scotopic Light	37.89	r=-0.002 p=0.987	r=-0.031 p=0.762
W/D Evening Time Spent in Mesopic Light	48.40	r=0.051 p=0.615	r=-0.078 p=0.441

W/D Evening Time Spent in Photopic Light	226.39	r=-0.103 p=0.308	r=0.059 p=0.557
W/D Evening Time Spent Outdoors	9.99	r=0.051 p=0.617	r=0.064 p=0.529
W/E Morning Time Spent in Scotopic Light	23.22	r=-0.060 p=0.557	r=0.070 p=0.489
W/E Morning Time Spent in Mesopic Light	26.91	r=-0.054 p=0.593	r=0.053 p=0.605
W/E Morning Time Spent in Photopic Light	180.48	r=0.157 p=0.121	r=-0.074 p=0.469
W/E Morning Time Spent Outdoors	14.02	r=0.013 p=0.897	r=0.101 p=0.321
W/E Afternoon Time Spent in Scotopic Light	7.58	r=0.134 p=0.186	r=-0.100 p=0.324
W/E Afternoon Time Spent in Mesopic Light	16.97	r=-0.005 p=0.963	r=0.002 p=0.981
W/E Afternoon Time Spent in Photopic Light	188.04	r=-0.196 p=0.052	r=0.133 p=0.190
W/E Afternoon Time Spent Outdoors	26.35	r=-0.033 p=0.749	r=0.044 p=0.665
W/E Evening Time Spent in Scotopic Light	52.33	r=-0.056 p=0.580	r=-0.017 p=0.870

W/E Evening Time Spent in Mesopic Light	60.71	r=0.052 p=0.611	r=-0.109 p=0.281
W/E Evening Time Spent in Photopic Light	220.10	r=-0.083 p=0.416	r=0.059 p=0.563
W/E Evening Time Spent Outdoors	14.02	r=0.049 p=0.628	r=0.022 p=0.826
Clouclip Parameter	**Average for all Participants (mins)**	**Correlation with SER**	**Correlation with AL**
W/D Morning Time Spent in Mesopic Light	4.68	r=-0.060 p=0.655	r=0.211 p=0.113
W/D Morning Time Spent in Photopic Light	202.32	r=-0.218 p=0.101	r=0.195 p=0.141
W/D Morning Time Spent Outdoors	15.66	r=0.114 p=0.396	r=-0.075 p=0.575
W/D Afternoon Time Spent in Mesopic Light	2.55	r=-0.057 p=0.672	r=0.036 p=0.789
W/D Afternoon Time Spent in Photopic Light	163.96	r=0.002 p=0.986	r=-0.144 p=0.280
W/D Afternoon Time Spent Outdoors	24.84	r=0.166 p=0.213	r=-0.022 p=0.868
W/D Evening Time Spent in Mesopic Light	11.77	r=-0.186 p=0.162	r=0.060 p=0.653

W/D Evening Time Spent in Photopic Light	174.51	r=-0.055 p=0.682	r=-0.021 p=0.877
W/D Evening Time Spent Outdoors	10.32	r=0.189 p=0.156	r=-0.058 p=0.666
W/E Morning Time Spent in Mesopic Light	2.89	r=-0.012 p=0.933	r=0.136 p=0.316
W/E Morning Time Spent in Photopic Light	118.29	r=-0.069 p=0.615	r=0.153 p=0.261
W/E Morning Time Spent Outdoors	9.49	r=0.000 p=0.998	r=0.187 p=0.168
W/E Afternoon Time Spent in Mesopic Light	4.55	r=-0.113 p=0.405	r=0.064 p=0.637
W/E Afternoon Time Spent in Photopic Light	159.11	r=0.001 p=0.995	r=-0.003 p=0.982
W/E Afternoon Time Spent Outdoors	15.41	r=0.210 p=0.121	r=-0.074 p=0.589
W/E Evening Time Spent in Mesopic Light (mins)	15.18	r=0.005 p=0.970	r=0.022 p=0.872
W/E Evening Time Spent in Photopic Light (mins)	158.08	r=0.108 p=0.429	r=-0.136 p=0.319
W/E Evening Time Spent Outdoors (mins)	11.53	r=0.170 p=0.211	r=-0.004 p=0.979

Table 6.4.2. The average light exposure parameters for all the participants combined and the correlations between each light exposure parameter with SER and AL. Light exposure was analysed in two ways; using the original cut-offs to define the category, and using the new cut-offs determined by the validation study of the devices (Chapter 3), with the latter being presented in the table. There were no notable differences between the outputs using the original and new cut-offs hence only the adjusted cut-offs were used for all further analysis.

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the duration of light exposures across the different time periods are presented in Table (6.4.3.)

Actiwatch Light Exposure Parameter	Pre-Myopes/Myopes Mean and (SD) (mins)	Non-Myopes Mean and (SD) (mins)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD) (mins)	Hyperopes Mean and (SD) (mins)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Weekday Morning Scotopic	18.44 (14.26)	19.83 (16.85)	p=0.735	19.98 (16.14)	19.55 (18.32)	p=0.939	
Weekday Morning Mesopic	23.82 (18.98)	23.55 (15.08)	p=0.944	24.15 (16.08)	22.49 (13.32)	p=0.902	
Weekday Morning Photopic	222.91 (65.98)	229.26 (44.43)	p=0.608	231.24 (36.52)	225.79 (56.29)	p=0.785	

Weekday Morning Outdoors	14.92 (21.69)	12.62 (14.93)	p=0.577	11.39 (14.36)	14.78 (15.91)	p=0.580	
Weekday Afternoon Scotopic	5.78 (5.40)	6.09 (9.07)	p=0.885	5.03 (5.77)	7.94 (12.93)	p=0.332	
Weekday Afternoon Mesopic	16.08 (12.14)	14.04 (11.54)	p=0.486	13.53 (10.13)	14.94 (13.84)	p=0.687	
Weekday Afternoon Photopic	191.14 (38.10)	195.60 (31.47)	p=0.588	196.29 (29.83)	194.39 (34.68)	p=0.838	
Weekday Afternoon Outdoors	30.09 (30.08)	27.05 (26.83)	p=0.660	25.62 (26.45)	29.57 (27.77)	p=0.751	
Weekday Evening Scotopic	34.45 (33.83)	38.74 (23.29)	p=0.505	37.45 (22.72)	41.02 (24.50)	p=0.671	
Weekday Evening Mesopic	47.02 (32.92)	48.74 (29.22)	p=0.818	47.69 (28.22)	50.59 (31.32)	p=0.894	

Weekday Evening Photopic	250.09 (107.30)	220.47 (44.93)	p=0.241	219.86 (43.90)	221.55 (47.44)	p=0.170	
Weekday Evening Outdoors	13.50 (25.14)	9.11 (20.61)	p=0.418	7.34 (16.93)	12.24 (25.90)	p=0.449	
Weekend Morning Scotopic	23.27 (24.13)	23.21 (22.28)	p=0.991	23.64 (22.24)	22.41 (22.73)	p=0.974	
Weekend Morning Mesopic	25.88 (25.06)	27.17 (19.97)	p=0.807	27.56 (19.61)	26.46 (20.96)	p=0.947	
Weekend Morning Photopic	165.55 (83.17)	184.26 (52.25)	p=0.347	180.97 (49.44)	190.26 (57.49)	p=0.371	
Weekend Morning Outdoors	16.37 (27.04)	13.42 (20.98)	p=0.598	11.81 (21.20)	16.36 (20.63)	p=0.600	
Weekend Afternoon Scotopic	5.92 (8.88)	8.00 (12.63)	p=0.489	6.79 (10.38)	10.20 (15.93)	p=0.381	

Weekend Afternoon Mesopic	18.47 (23.20)	16.59 (20.82)	p=0.725	15.93 (18.14)	17.80 (25.31)	p=0.878	
Weekend Afternoon Photopic	201.20 (73.81)	184.71 (55.16)	p=0.269	191.89 (55.97)	171.63 (52.10)	p=0.189	
Weekend Afternoon Outdoors	31.06 (36.36)	25.16 (36.20)	p=0.517	21.59 (34.75)	31.66 (38.50)	p=0.405	
Weekend Evening Scotopic	70.72 (120.30)	47.68 (41.75)	p=0.409	49.97 (43.31)	43.50 (7.40)	p=0.344	
Weekend Evening Mesopic	63.60 (69.29)	59.97 (39.54)	p=0.824	60.97 (41.67)	58.16 (35.98)	p=0.924	
Weekend Evening Photopic	228.68 (79.32)	217.93 (78.03)	p=0.585	222.44 (80.00)	209.71 (75.03)	p=0.680	
Weekend Evening Outdoors	17.59 (30.68)	13.12 (30.69)	p=0.562	8.23 (24.29)	22.02 (38.74)	p=0.134	

Clouclip Light Exposure Parameter	**Pre-Myopes/Myopes Mean and (SD)** (mins)	**Non-Myopes Mean and (SD)** (mins)	**Independent t-test (Pre-Myopes/Myopes vs Non-Myopes**	**Emmetropes Mean and (SD)** (mins)	**Hyperopes Mean and (SD)** (mins)	**One-Way ANOVA**	**Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)**
Weekday Morning Mesopic CC	3.94 (2.90	4.88 (5.85)	p=0.595	5.21 (5.72)	4.04 (6.33)	p=0.702	
Weekday Morning Photopic CC	197.50 (34.93)	203.57 (39.91)	p=0.633	215.09 (35.43)	174.35 (36.56)	*p=0.004*	P/M vs E p=0.315 P/M vs H p=0.244 *E vs H p=0.003*
Weekday Morning Outdoor CC	22.38 (23.63)	13.91 (13.93)	p=0.256	12.16 (12.89)	18.36 (15.97)	p=0.149	
Weekday Afternoon Mesopic CC	2.69 (3.16)	2.51 (3.21)	p=0.863	2.93 (3.59)	1.45 (1.59)	p=0.365	
Weekday Afternoon Photopic CC	153.84 (52.80)	166.60 (44.34)	p=0.397	170.97 (48.26)	155.52 (31.24)	p=0.417	

Weekday Afternoon Outdoor CC	30.74 (27.84)	23.30 (20.67)	p=0.307	19.03 (18.41)	34.14 (22.82)	p=0.066	
Weekday Evening Mesopic CC	9.87 (10.75)	12.27 (10.28)	p=0.480	14.47 (10.37)	6.67 (7.90)	p=0.051	
Weekday Evening Photopic CC	170.11 (51.15)	175.66 (66.28)	p=0.789	183.14 (71.45)	156.67 (48.14)	p=0.431	
Weekday Evening Outdoor CC	16.94 (25.47)	8.59 (15.54)	p=0.298	5.03 (8.41)	17.62 (24.36)	*p=0.035*	P/M vs E p=0.113 P/M vs H p=0.995 E vs H p=0.077
Weekend Morning Mesopic CC	1.68 (2.29)	3.21 (4.45)	p=0.256	3.58 (3.89)	2.35 (5.67)	p=0.352	
Weekend Morning Photopic CC	129.38 (97.92)	115.27 (71.66)	p=0.648	124.62 (75.49)	92.96 (58.18)	p=0.403	
Weekend Morning Outdoor CC	15.58 (22.51)	7.83 (12.04)	p=0.272	5.76 (10.37)	12.76 (14.59)	p=0.104	

Weekend Afternoon Mesopic CC	2.38 (4.48)	5.15 (6.94)	p=0.198	6.37 (7.66)	2.23 (3.58)	p=0.067	
Weekend Afternoon Photopic CC	158.61 (63.59)	159.24 (66.80)	p=0.977	168.85 (69.99)	136.34 (54.19)	p=0.330	
Weekend Afternoon Outdoor CC	19.74 (25.36)	14.23 (19.84)	p=0.426	7.54 (10.29)	30.19 (27.45)	*p=0.002*	P/M vs E p=0.154 P/M vs H p=0.364 *E vs H p=0.002*
Weekend Evening Mesopic CC	12.05 (12.50)	16.03 (13.17)	p=0.352	16.30 (12.47)	15.39 (15.23)	p=0.637	
Weekend Evening Photopic CC	155.03 (57.67)	158.92 (71.76)	p=0.864	150.03 (64.94)	180.10 (84.98)	p=0.415	
Weekend Evening Outdoor CC	15.09 (27.31)	10.56 (25.88)	p=0.598	5.90 (21.59)	21.68 (32.33)	p=0.162	

Table 6.4.3. The average duration of light exposure for the Actiwatch and Clouclip for each of the refractive categories across the time periods, and the results of independent t-tests and one-way ANOVAs between these categories.

The figures below present the duration of light exposure over the different time periods on weekdays and weekends for the refractive groups. The lines and triple stars indicate statistically significant differences between the duration of light exposure during the different time periods

using one-way analyses of variance (ANOVAs). The braces and single stars indicate statistically significant different between refractive groups for duration of light exposure during a particular period of the day using one-way ANOVAs.

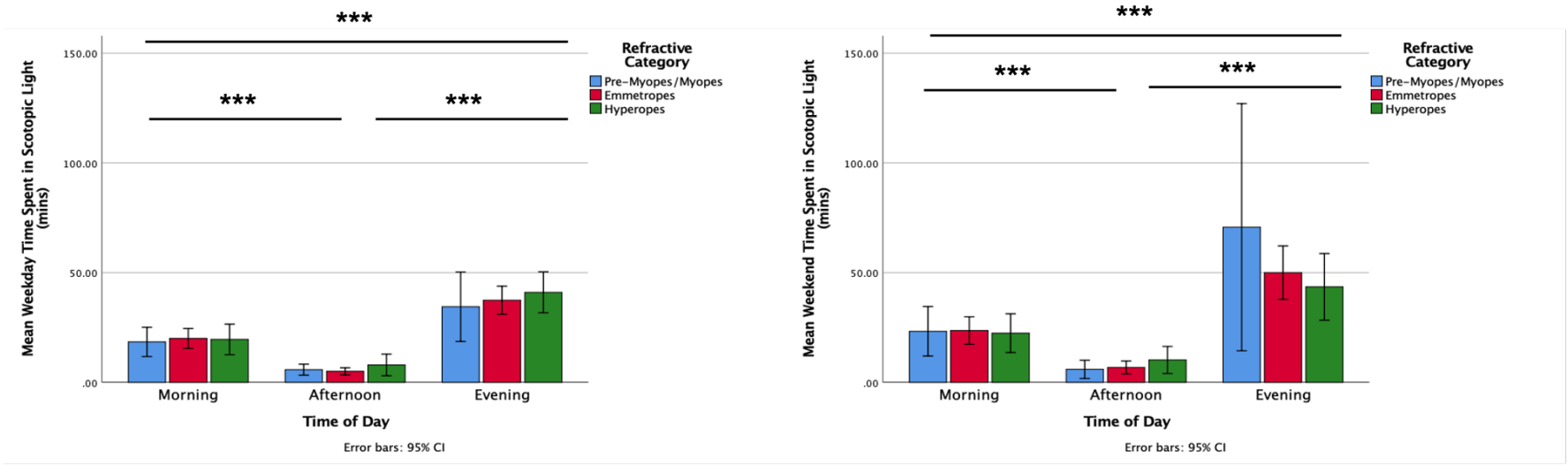


Figure 6.4.1. Bar charts showing the mean duration of time spent in scotopic light (measured by the Actiwatch) between refractive groups with the line and triple stars indicating significant differences in time spent in scotopic light across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.1. shows that all participants spent statistically significantly less time in scotopic light (measured by Actiwatch) in the afternoons compared to both mornings and evenings, on weekdays and weekends, and participants also spent statistically significantly more time in scotopic light in the evenings than the mornings.

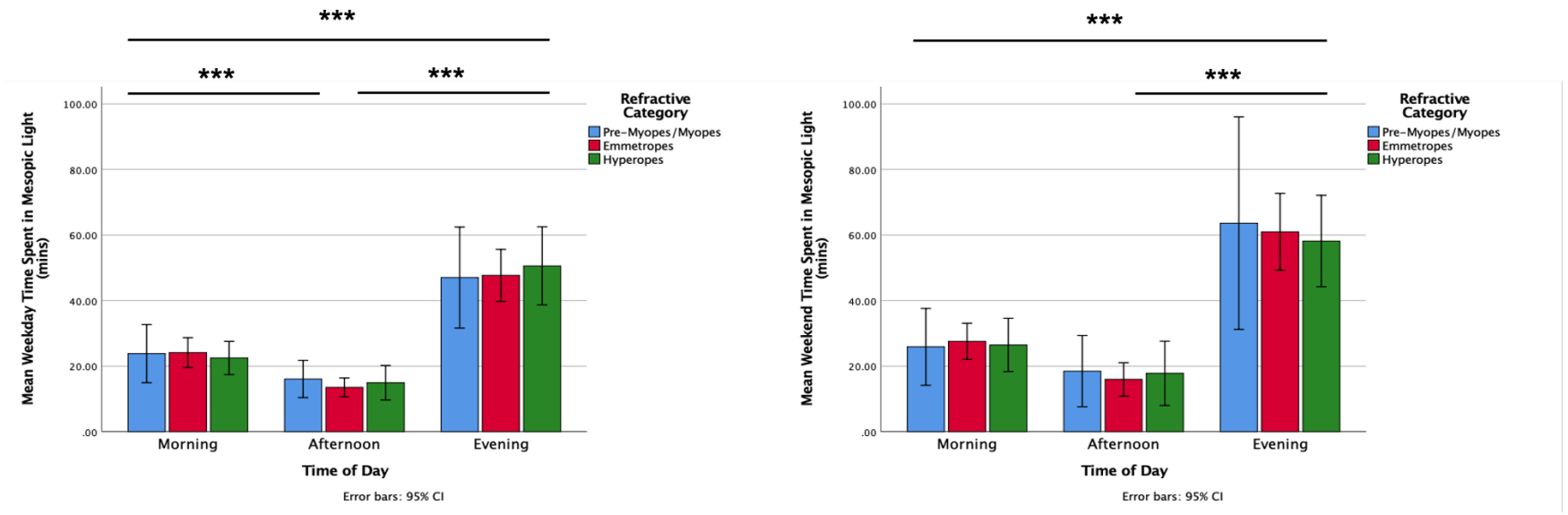


Figure 6.4.2. Bar charts showing the mean duration of time spent in mesopic light (measured by the Actiwatch) between refractive groups with the line and triple stars indicating significant differences in time spent in mesopic light across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.2. shows that all participants spent statistically significantly less time in mesopic light (measured by Actiwatch) in the afternoons compared to both mornings and evenings, on weekdays, and significantly more time in mesopic light on weekday evenings than mornings. On the weekend participants spent statistically significantly more time in mesopic light in the evenings than both the morning and afternoons.

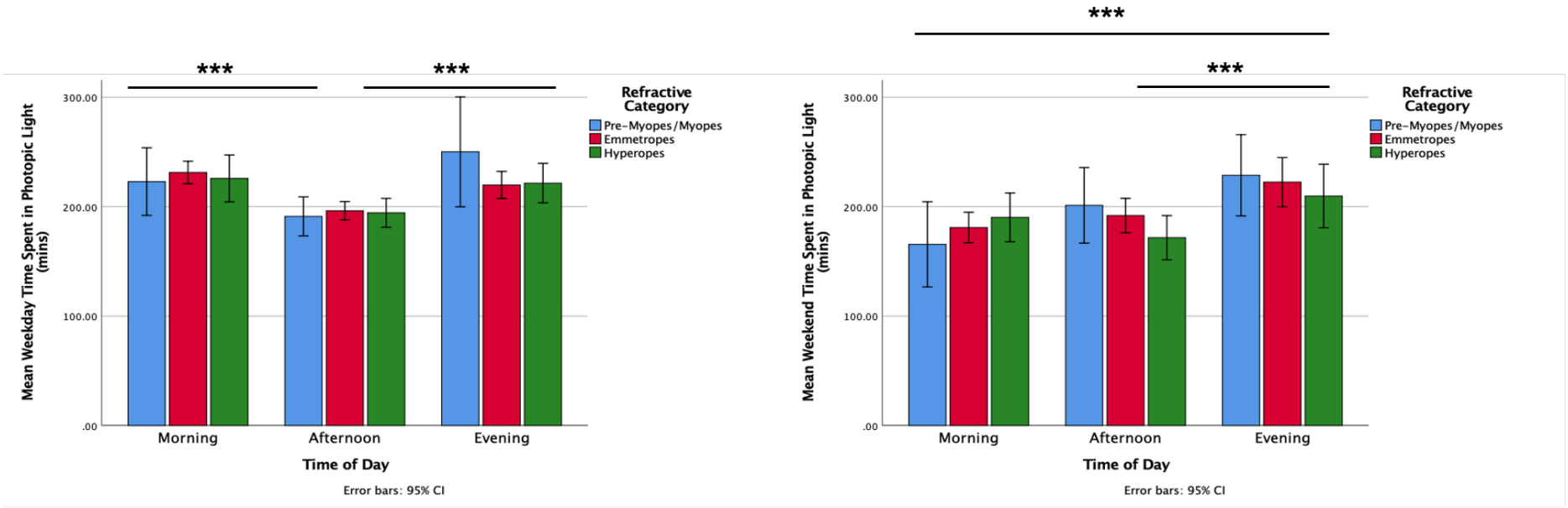


Figure 6.4.3. Bar charts showing the mean duration of time spent in photopic light (measured by the Actiwatch) between refractive groups with the line and triple stars indicating significant differences in time spent in photopic light across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.3. shows that all participants spent statistically significantly less time in photopic light (measured by Actiwatch) in the afternoons compared to both mornings and evenings on weekdays and significantly more time in photopic light on weekend evenings than both morning and afternoons.

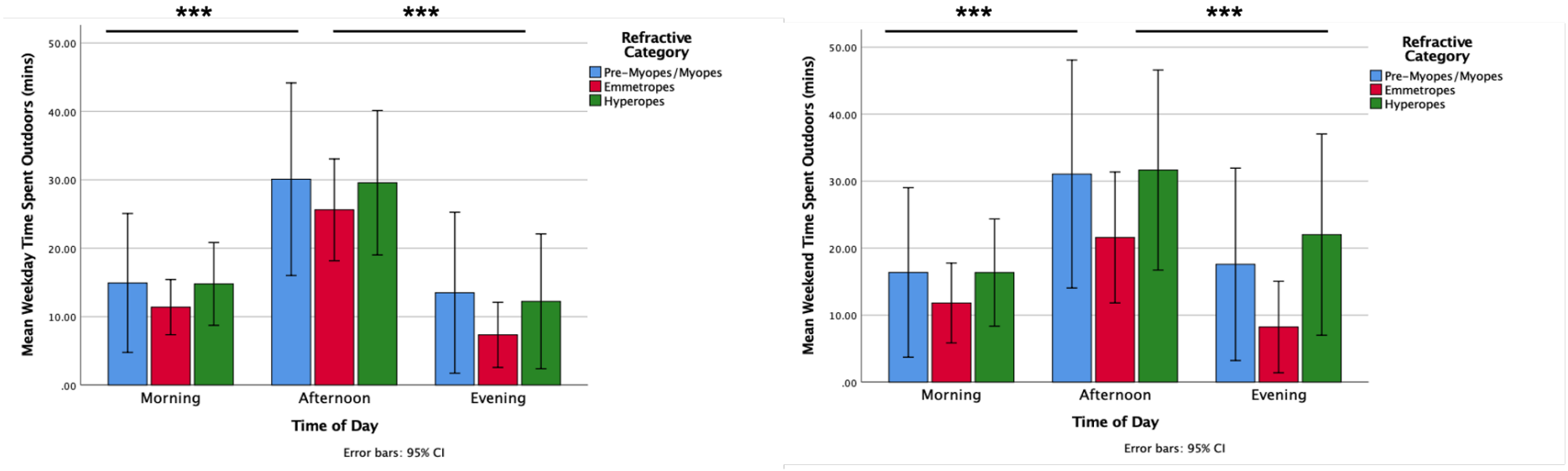


Figure 6.4.4. Bar charts showing the mean duration of time spent outdoors (measured by the Actiwatch) between refractive groups with the line and triple stars indicating significant differences in time spent outdoors across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.4. shows that all participants spent statistically significantly more time outdoors (measured by Actiwatch) in the afternoons compared to both mornings and evenings, on weekdays and weekends.

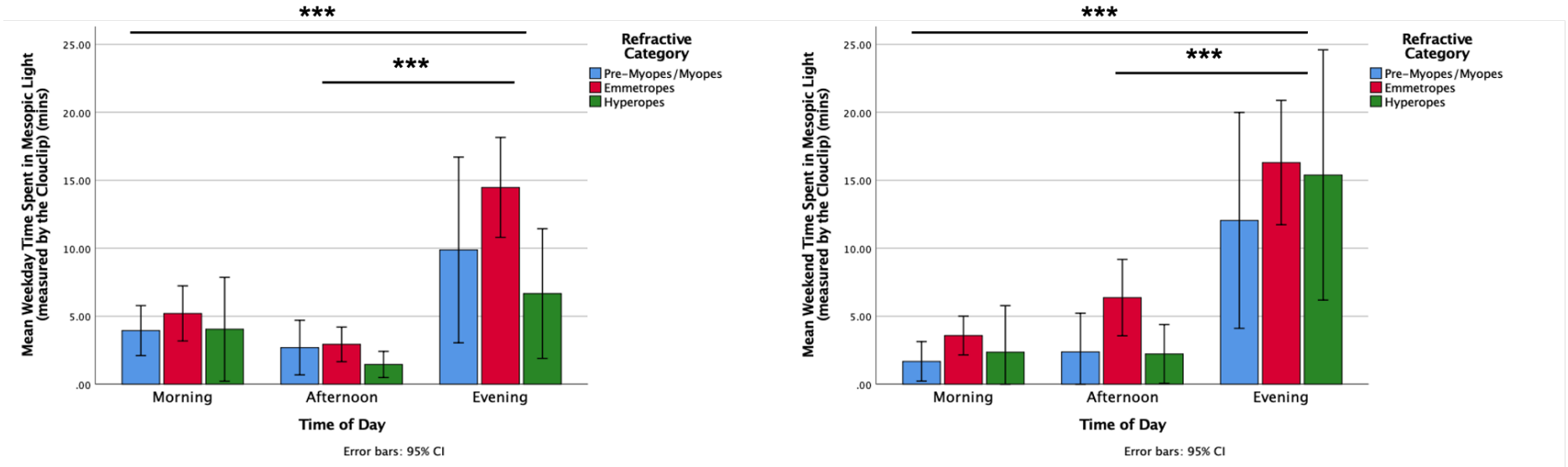


Figure 6.4.5. Bar charts showing the mean duration of time spent in mesopic light (measured by the Clouclip) between refractive groups with the line and triple stars indicating significant differences in time spent in mesopic light across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.5. shows that all participants spent statistically significantly more time in mesopic light (measured by Clouclip) in the evenings compared to both mornings and afternoons, on weekdays and weekends

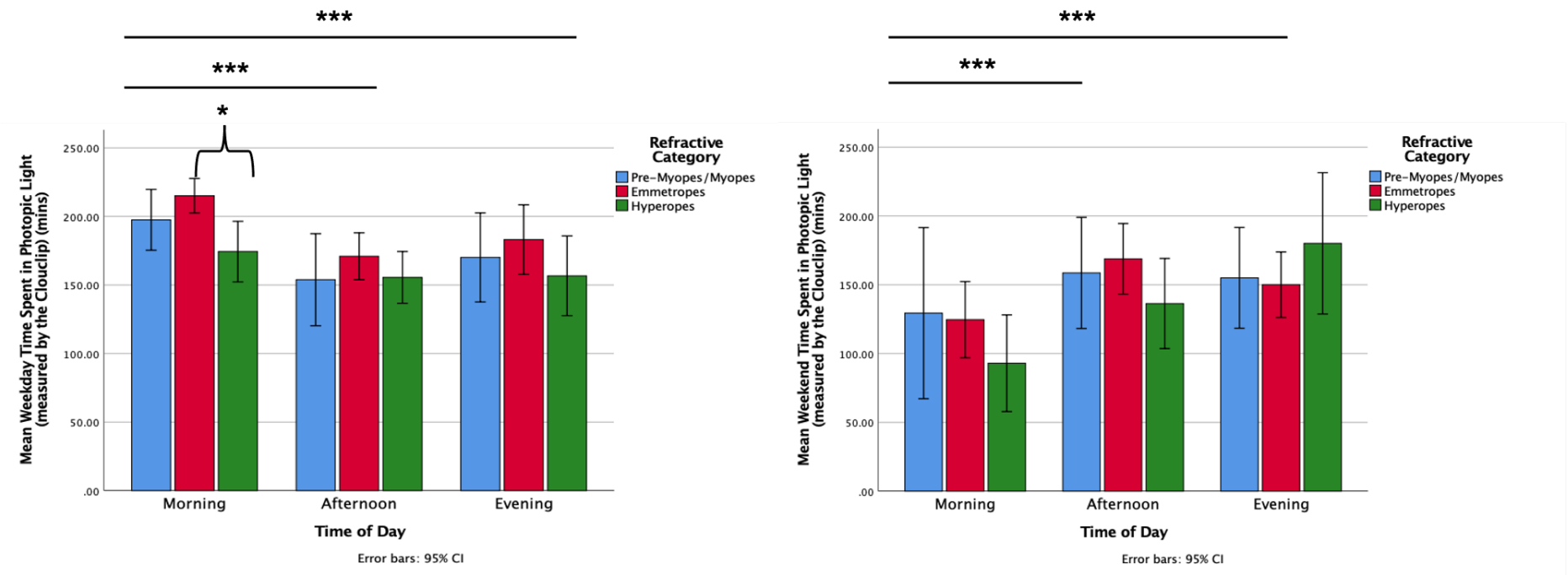


Figure 6.4.6. Bar charts showing the mean duration of time spent in photopic light (measured by the Clouclip) between refractive groups with the brace and single star indicating a difference between emmetropes and hyperopes and with the line and triple stars indicating significant differences in time spent in photopic light across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.6. shows that all participants spent statistically significantly more time in photopic light (measured by Clouclip) on weekday mornings compared to both afternoons and evenings and significantly less time in photopic light on weekend mornings than both afternoons and evenings. There was also a significance between refractive groups for weekday morning time spent in photopic light measured by the Clouclip, $p=0.004$. The emmetropes spent significantly more time in photopic light on weekday mornings ($M=215.09$) than the hyperopes ($M=174.35$), $p=0.003$. There were no significant differences between the pre-myopes/myopes ($M=197.50$) and either the emmetropes or hyperopes (both $p>0.05$).

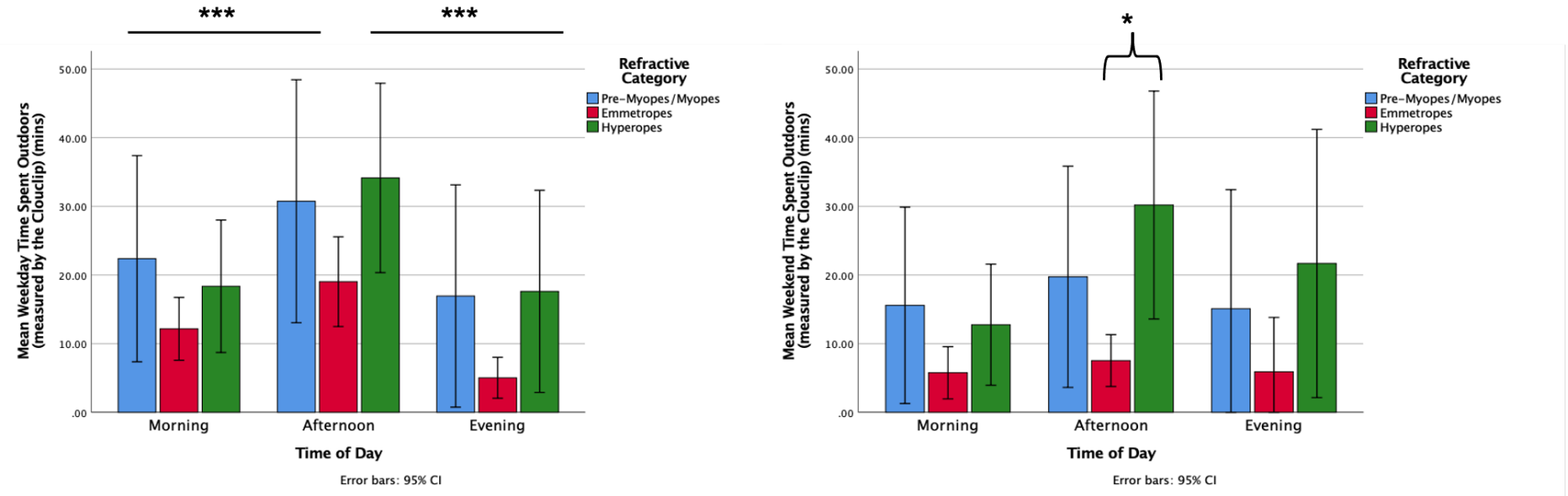


Figure 6.4.7. Bar charts showing the mean duration of time spent outdoors (measured by the Clouclip) between refractive groups with the brace and single star indicating a difference between emmetropes and hyperopes and with the line and triple stars indicating significant differences in time spent outdoors across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.7. shows that all participants spent statistically significantly more time outdoors (measured by Clouclip) on weekday afternoons compared to both mornings and evenings, but there were no significant differences in time spent outdoors for the whole cohort during the different time periods on weekends. However, there was a significant difference between refractive groups for weekend afternoon time spent outdoors measured by the Clouclip, $p=0.002$. The hyperopes spent significantly more time outdoors on weekend afternoons ($M=30.19$) than the emmetropes ($M=7.54$). The time spent outdoors on weekend afternoons by pre-myopes/myopes ($M=19.74$) was not significantly different to either the emmetropes or hyperopes (both $p>0.05$).

6.4.2. Timing of Physical Activity

The duration of different physical activity levels measured by the Actiwatch on weekdays (W/D) and weekends (W/E) across the different time periods, and their respective correlations with SER and AL are presented in Table 6.4.4.

Actiwatch Physical Activity Parameter	Average for all Participants (mins)	Correlation with SER	Correlation with AL
Weekday Morning Time Spent Sedentary	116.46	r=0.024 p=0.815	r=-0.043 p=0.674
Weekday Morning Time Spent on Light Activity	128.97	r=0.013 p=0.901	r=0.041 p=0.682
Weekday Morning Time Spent on Moderate Activity	25.12	r=-0.017 p=0.869	r=0.093 p=0.357
Weekday Morning Time Spent on Vigorous Activity	16.71	r=0.052 p=0.606	r=0.093 p=0.355
Weekday Afternoon Time Spent Sedentary	78.21	r=0.035 p=0727	r=-0.104 p=0.303
Weekday Afternoon Time Spent on Light Activity	108.97	r=0.040 p=0.693	r=-0.055 p=0.588
Weekday Afternoon Time Spent on Moderate Activity	29.31	r=-0.036 p=0.722	r=0.049 p=0.625
Weekday Afternoon Time Spent on Vigorous Activity	26.35	r=-0.022 p=0.827	r=0.165 p=0.100
Weekday Evening Time Spent Sedentary	143.65	r=-0.046	r=-0.007

		p=0.648	p=0.941
Weekday Evening Time Spent on Light Activity	122.38	r=-0.034 p=0.739	r=0.023 p=0.823
Weekday Evening Time Spent on Moderate Activity	31.83	r=-0.050 p=0.624	r=0.048 p=0.632
Weekday Evening Time Spent on Vigorous Activity	24.72	r=0.001 p=0.989	r=0.070 p=0.492
Weekend Morning Time Spent Sedentary	112.35	*r=0.205* *p=0.042*	r=-0.096 p=0.342
Weekend Morning Time Spent on Light Activity	95.10	r=0.053 p=0.602	r=0.006 p=0.956
Weekend Morning Time Spent on Moderate Activity	21.82	r=-0.140 p=0.167	r=0.169 p=0.094
Weekend Morning Time Spent on Vigorous Activity	15.34	r=-0.112 p=0.270	r=0.143 p=0.157
Weekend Afternoon Time Spent Sedentary	89.91	r=0.072 p=0.482	r=-0.063 p=0.538
Weekend Afternoon Time Spent on Light Activity	99.58	*r=-0.207* *p=0.040*	r=0.154 p=0.129
Weekend Afternoon Time Spent on Moderate Activity	27.21	*r=-0.299* *p=0.003*	r=0.194 p=0.055

Weekend Afternoon Time Spent on Vigorous Activity	22.21	*r=-0.237* *p=0.018*	*r=0.210* *p=0.037*
Weekend Evening Time Spent Sedentary	148.86	r=0.078 p=0.443	r=-0.069 p=0.499
Weekend Evening Time Spent on Light Activity	132.82	r=-0.079 p=0.440	r=0.005 p=0.961
Weekend Evening Time Spent on Moderate Activity	35.60	*r=-0.197* *p=0.050*	r=0.107 p=0.293
Weekend Evening Time Spent on Vigorous Activity	28.78	r=-0.175 p=0.083	r=0.113 p=0.266

Table 6.4.4. The average physical activity parameters for all the participants combined and the correlations between each physical activity parameter with SER and AL.

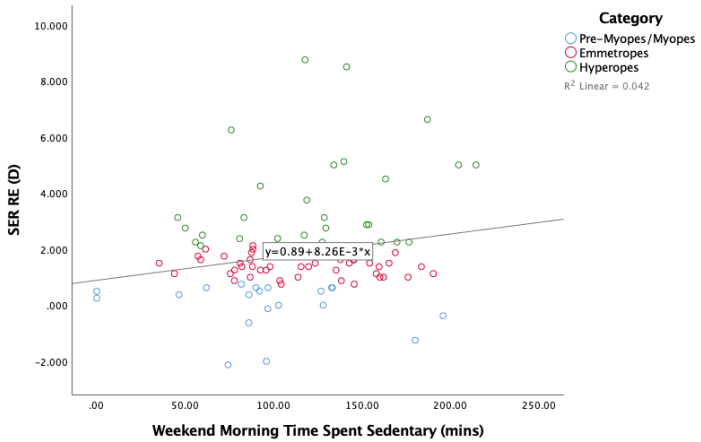


Figure 6.4.8. Scatterplot demonstrating a statistically significant positive correlation between SER and weekend morning time spent sedentary (r=0.205, p=0.042).

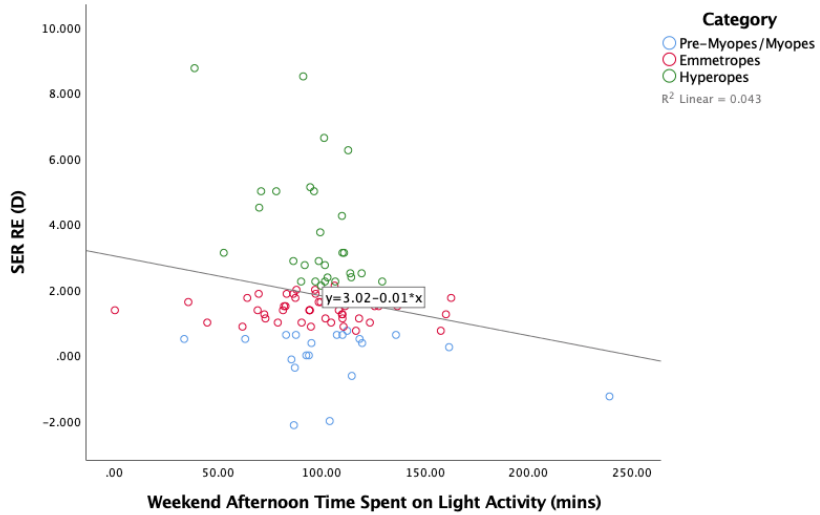


Figure 6.4.9. Scatterplot demonstrating a statistically significant negative correlation between SER and weekend afternoon time spent on light activity (r=-0.207, p=0.040).

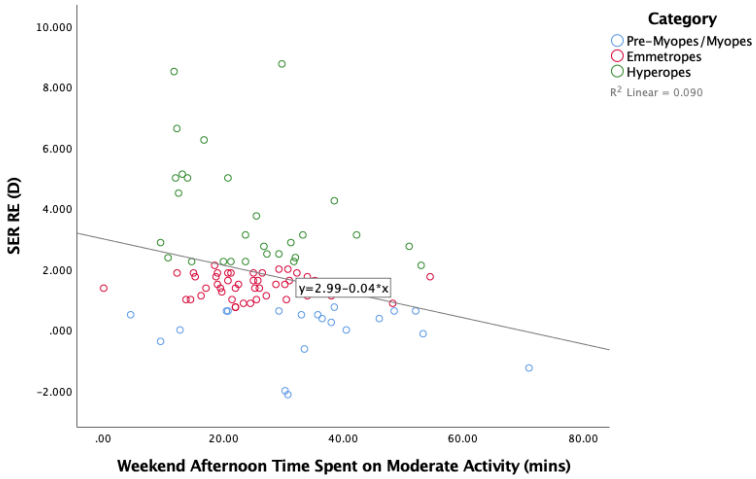


Figure 6.4.10. Scatterplot demonstrating a statistically significant negative correlation between SER and weekend afternoon time spent on moderate activity (r=-0.299, p=0.003).

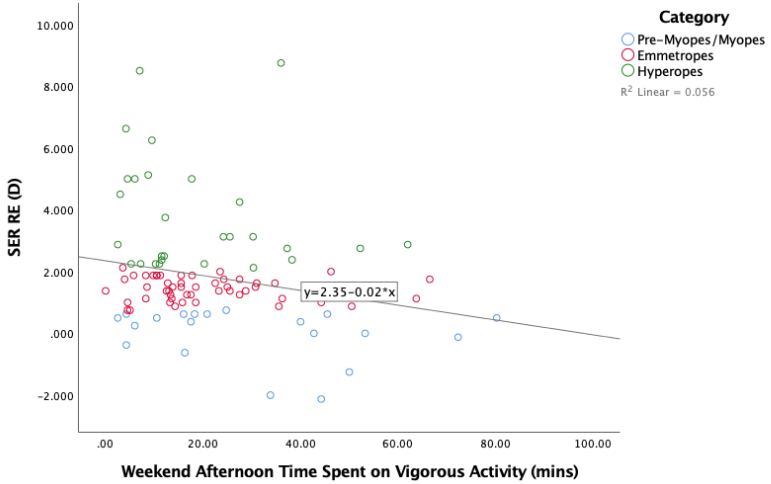


Figure 6.4.11. Scatterplot demonstrating a statistically significant negative correlation between SER and weekend afternoon time spent on vigorous activity (r=-0.237, p=0.018).

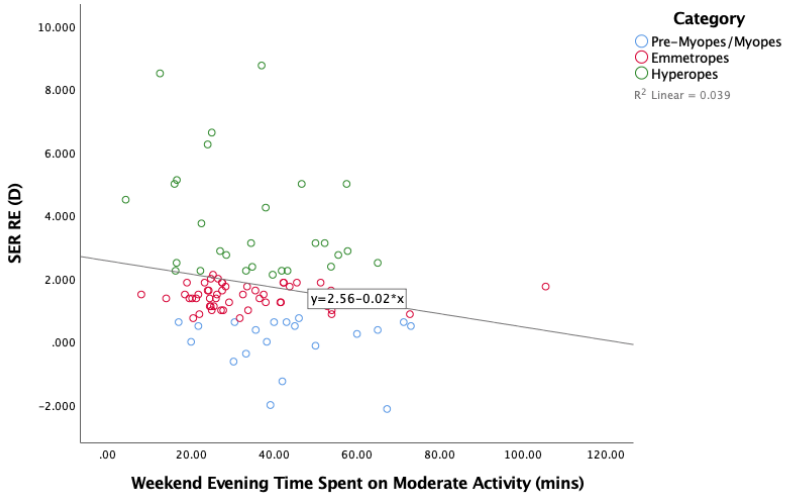


Figure 6.4.12. Scatterplot demonstrating a statistically significant negative correlation between SER and weekend evening time spent on moderate activity (r=-0.197, p=0.050).

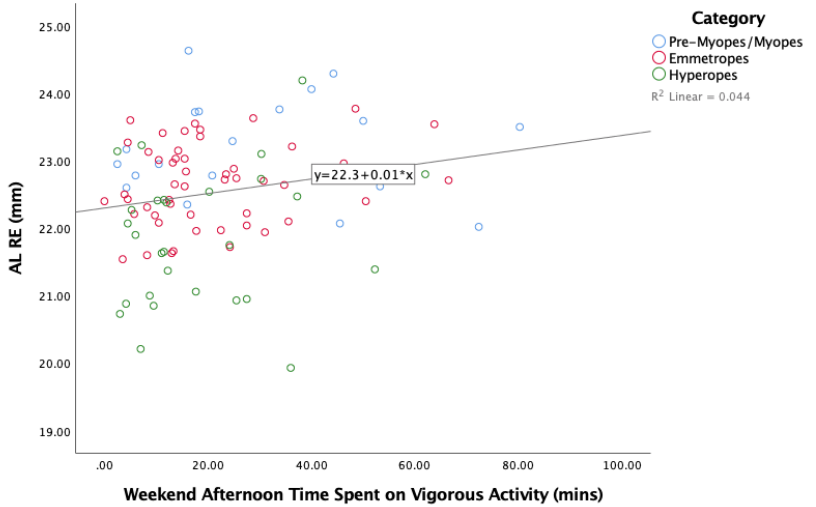


Figure 6.4.13. Scatterplot demonstrating a statistically significant positive correlation between AL and weekend afternoon time spent on vigorous activity (r=0.210, p=0.037).

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the duration of physical activity levels across the different time periods are presented in Table (6.4.5.).

Actiwatch Physical Activity Parameter	Pre-Myopes/Myopes Mean and (SD) (mins)	Non-Myopes Mean and (SD) (mins)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD) (mins)	Hyperopes Mean and (SD) (mins)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Weekday Morning Sedentary	113.28 (41.02)	117.25 (32.87)	p=0.647	118.90 (34.43)	114.35 (30.29)	p=0.769	
Weekday Morning Light	119.10 (45.60)	131.43 (26.08)	p=0.257	131.65 (27.01)	131.06 (24.83)	p=0.285	
Weekday Morning Moderate	26.00 (11.94)	24.90 (9.15)	p=0.654	24.71 (8.79)	25.25 (9.89)	p=0.879	
Weekday Morning Vigorous	16.72 (9.27)	16.70 (12.89)	p=0.996	15.43 (8.29)	18.94 (18.38)	p=0.470	
Weekday Afternoon Sedentary	80.42 (31.43)	77.66 (19.66)	p=0.711	78.44 (19.77)	76.30 (19.75)	p=0.816	

Weekday Afternoon Light	103.96 (24.24)	110.22 (15.67)	p=0.284	109.47 (15.22)	111.53 (16.62)	P=0.330	
Weekday Afternoon Moderate	29.67 (10.17)	29.22 (8.36)	p=0.838	28.64 (7.55)	30.23 (9.68)	p=0.721	
Weekday Afternoon Vigorous	29.03 (15.03)	25.68 (14.52)	p=0.362	23.92 (9.35)	28.79 (20.56)	p=0.238	
Weekday Evening Sedentary	154.27 (64.68)	147.81 (78.65)	p=0.735	150.43 (87.79)	143.22 (60.46)	p=0.870	
Weekday Evening Light	125.43 (38.74)	121.87 (20.22)	p=0.658	119.74 (27.66)	125.62 (34.46)	p=0.667	
Weekday Evening Moderate	35.93 (10.55)	30.91 (11.10)	p=0.071	30.56 (10.16)	31.54 (12.76)	p=0.183	
Weekday Evening Vigorous	29.42 (22.47)	23.88 (16.59)	p=0.218	23.40 (15.30)	24.72 (18.91)	p=0.447	

Weekend Morning Sedentary	95.35 (48.52)	116.65 (41.36)	*p=0.050*	113.23 (37.67)	122.90 (47.44)	p=0.093	
Weekend Morning Light	90.88 (46.22)	96.17 (32.85)	p=0.557	95.56 (33.24)	97.27 (32.70)	p=0.825	
Weekend Morning Moderate	24.76 (15.79)	21.08 (10.75)	p=0.334	21.69 (10.57)	19.95 (11.18)	p=0.390	
Weekend Morning Vigorous	20.09 (24.28)	14.14 (15.15)	p=0.307	13.46 (10.18)	15.38 (21.66)	p=0.357	
Weekend Afternoon Sedentary	85.80 (36.42)	90.95 (36.55)	p=0.574	90.50 (35.96)	91.77 (38.25)	p=0.846	
Weekend Afternoon Light	106.44 (40.87)	97.84 (26.46)	p=0.253	98.88 (29.66)	95.95 (19.69)	p=0.478	
Weekend Afternoon Moderate	34.25 (15.96)	25.43 (10.35)	*p=0.028*	25.90 (9.52)	24.58 (11.85)	*p=0.012*	*P/M vs E p=0.022* *P/M vs H p=0.016* E vs H p=0.880

Weekend Afternoon Vigorous	30.16 (22.72)	20.19 (15.17)	p=0.075	20.93 (15.09)	18.85 (15.50)	p=0.061	
Weekend Evening Sedentary	149.07 (109.20)	148.81 (59.17)	p=0.989	151.05 (53.88)	144.73 (68.63)	p=0.933	
Weekend Evening Light	146.96 (73.08)	129.24 (44.27)	p=0.170	130.02 (45.76)	127.82 (42.22)	p=0.385	
Weekend Evening Moderate	43.41 (16.69)	33.62 (15.97)	*p=0.017*	33.03 (16.03)	34.71 (16.10)	p=0.054	
Weekend Evening Vigorous	40.72 (37.08)	25.75 (21.63)	*p=0.021*	25.56 (21.51)	26.10 (22.23)	p=0.069	

Table 6.4.5. The average duration of physical activity parameters for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories, across the different time periods.

The figures below present the duration of physical activity levels over the different time periods on weekdays and weekends for the refractive groups. The lines and triple stars indicate statistically significant differences between the duration of physical activity levels during the different time periods using one-way analyses of variance (ANOVAs). The braces and single stars indicate statistically significant different between refractive groups for duration of physical activity levels during a particular period of the day using one-way ANOVAs.

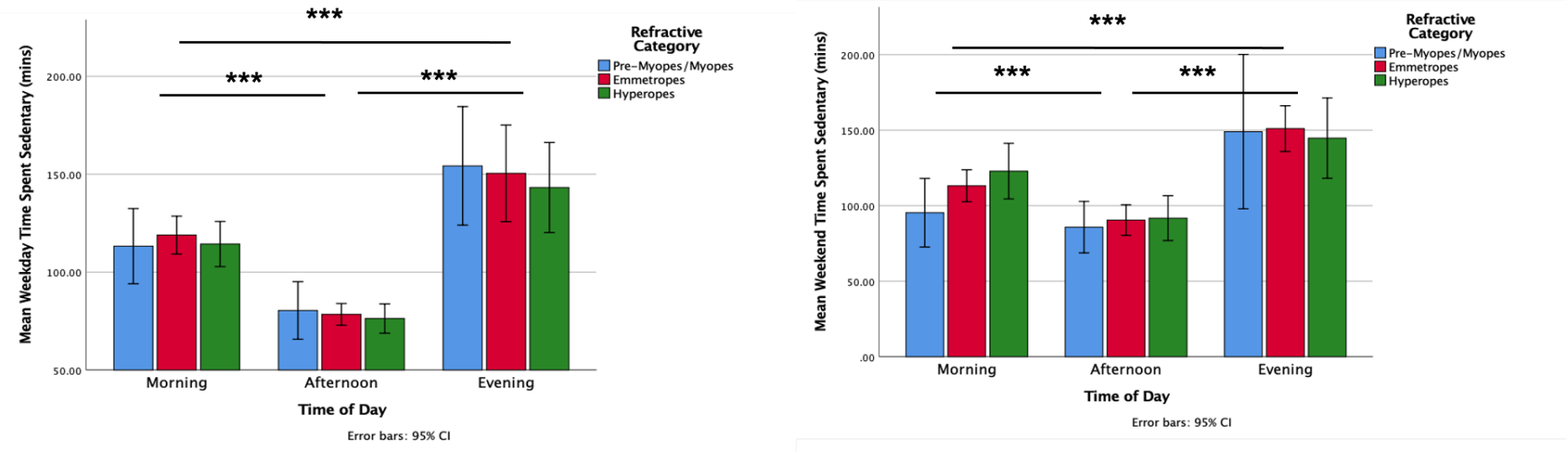


Figure 6.4.14. Bar charts showing the mean duration of time spent sedentary between refractive groups with the line and triple stars indicating significant differences in time spent sedentary across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.14. shows that all participants spent statistically significantly less time sedentary in afternoons compared to both mornings and evenings, on weekdays and weekends and participants spent significantly more time sedentary on both weekday and weekend evenings than the mornings.

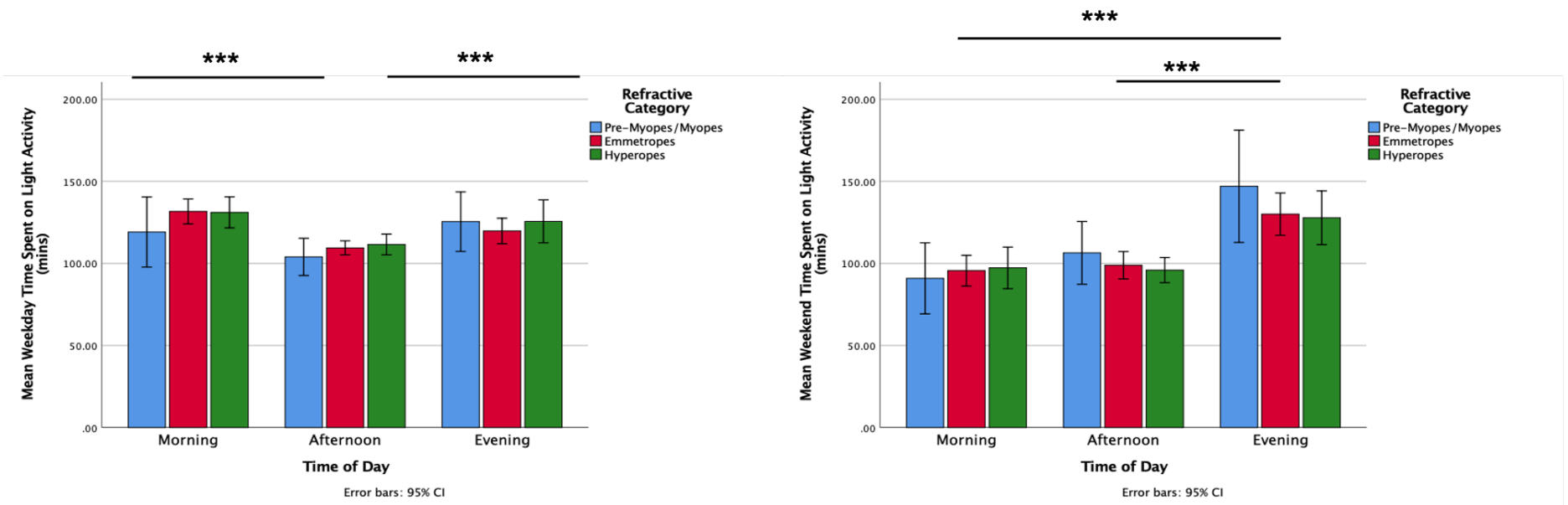


Figure 6.4.15. Bar charts showing the mean duration of time spent on light activity between refractive groups with the line and triple stars indicating significant differences in time spent on light activity across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.15. shows that all participants spent statistically significantly less time on light activity on weekday afternoons compared to both mornings and evenings and significantly more time on light activity on weekend evenings compared to both morning and afternoons.

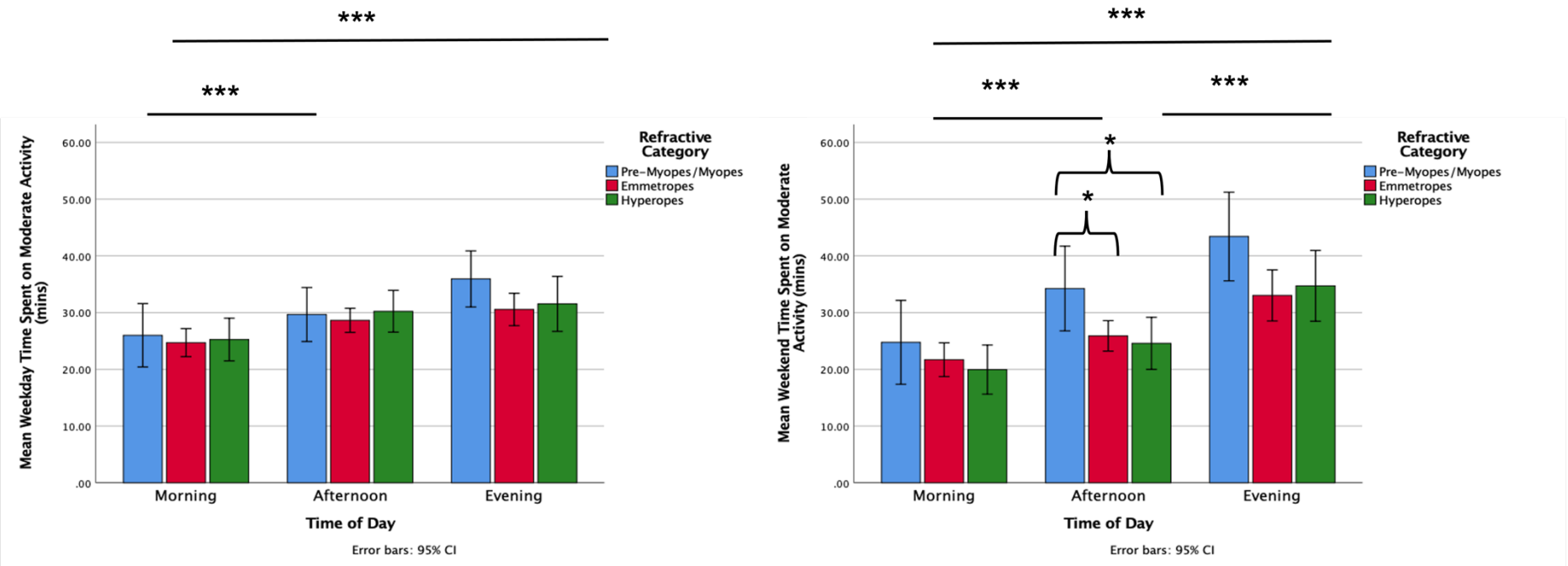


Figure 6.4.16. Bar charts showing the mean duration of time spent on moderate activity between refractive groups with the brace and single star indicating a difference between pre-myopes/myopes and emmetropes and hyperopes, and with the line and triple stars indicating significant differences in time spent on moderate activity across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.16. shows that all participants spent statistically significantly less time on moderate activity on weekday and weekend mornings compared to both afternoons and evenings. On weekends participants also spent significantly more time on moderate activity in the evenings compared to the afternoons. Pre-myopes/myopes spent significantly more time on moderate activity on weekend afternoons than both emmetropes and hyperopes.

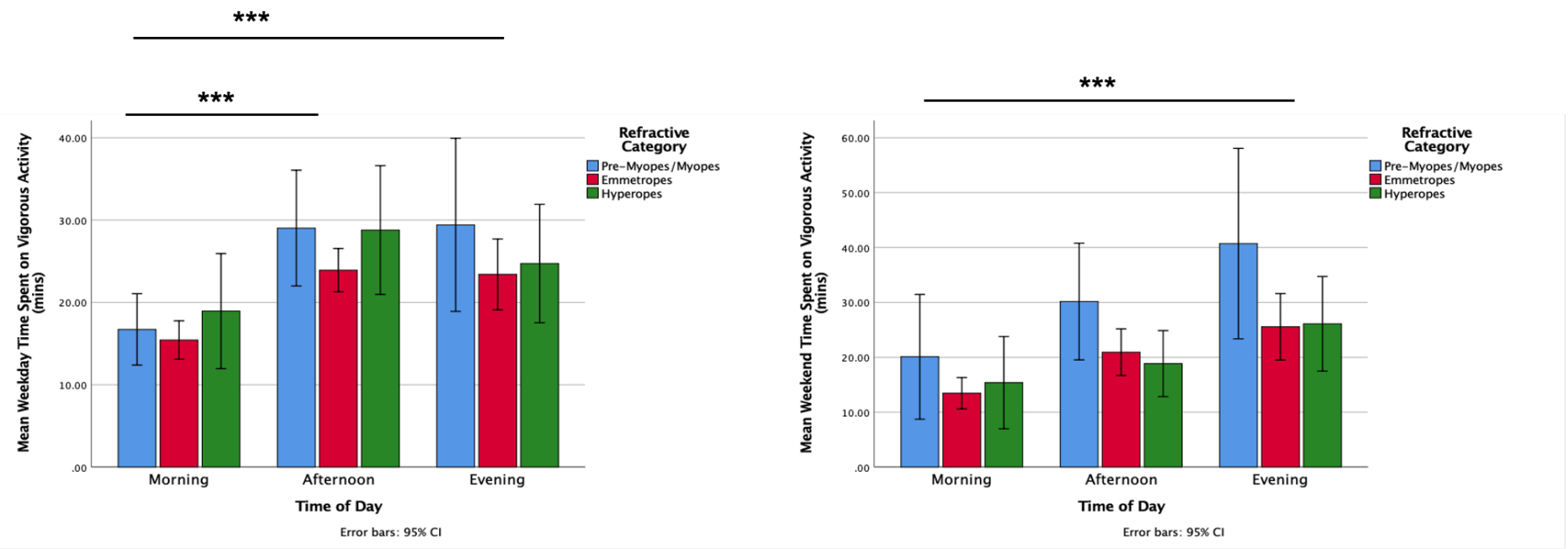


Figure 6.4.17. Bar charts showing the mean duration of time spent on vigorous activity between refractive groups with the line and triple stars indicating significant differences in time spent on vigorous activity across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.17. shows that all participants spent statistically significantly less time on vigorous activity on weekday mornings compared to both afternoons and evenings. On weekends participants spent significantly more time on vigorous activity in the evenings compared to the mornings.

6.4.3. Timing of Near Activity

The duration of near activities measured by the Clouclip on weekdays (W/D) and weekends (W/E), across the different time periods and their respective correlations with SER and AL are presented in Table 6.4.6.

Clouclip Near Activity Parameter	Average for all Participants (mins)	Correlation with SER	Correlation with AL
W/D Morning Time Spent on Very Close Viewing	58.72	r=-0.140 p=0.295	r=0.175 p=0.189
W/D Morning Time Spent on Near Viewing	31.29	*r=-0.291* *p=0.027*	r=0.192 p=0.148
W/D Morning Time Spent on Intermediate Viewing	33.97	r=-0.244 p=0.065	r=0.132 p=0.322
W/D Morning Time Spent on Distance Viewing	89.24	r=-0.127 p=0.341	r=0.147 p=0.271
W/D Afternoon Time Spent on Very Close Viewing	49.12	r=0.052 p=0.697	r=-0.077 p=0.565
W/D Afternoon Time Spent on Near Viewing	24.72	r=-0.125 p=0.350	r=0.067 p=0.617
W/D Afternoon Time Spent on Intermediate Viewing	28.31	r=-0.084 p=0.529	r=-0.034 p=0.798
W/D Afternoon Time Spent on Distance Viewing	78.75	r=0.006 p=0.967	r=-0.095 p=0.476

W/D Evening Time Spent on Very Close Viewing	66.42	r=0.046 p=0.732	r=-0.101 p=0.449
W/D Evening Time Spent on Near Viewing	25.86	r=-0.134 p=0.316	r=0.034 p=0.802
W/D Evening Time Spent on Intermediate Viewing	30.16	r=-0.113 p=0.400	r=0.095 p=0.480
W/D Evening Time Spent on Distance Viewing	81.37	r=0.118 p=0.376	r=-0.128 p=0.337
W/E Morning Time Spent on Very Close Viewing	37.97	r=0.017 p=0.898	r=0.107 p=0.433
W/E Morning Time Spent on Near Viewing	15.13	r=-0.162 p=0.233	*r=0.275* *p=0.040*
W/E Morning Time Spent on Intermediate Viewing	17.15	r=-0.172 p=0.206	r=0.222 p=0.099
W/E Morning Time Spent on Distance Viewing	47.69	r=-0.151 p=0.268	r=0.202 p=0.136
W/E Afternoon Time Spent on Very Close Viewing	55.85	r=-0.117 p=0.392	r=0.209 p=0.122
W/E Afternoon Time Spent on Near Viewing	20.16	r=-0.200 p=0.139	r=0.154 p=0.257
W/E Afternoon Time Spent on Intermediate Viewing	24.77	r=-0.168 p=0.217	r=0.149 p=0.273

W/E Afternoon Time Spent on Distance Viewing	67.29	r=0.085 p=0.536	r=-0.117 p=0.392
W/E Evening Time Spent on Very Close Viewing	70.35	*r=0.368* *p=0.005*	r=-0.210 p=0.121
W/E Evening Time Spent on Near Viewing	19.99	r=-0.209 p=0.123	r=0.028 p=0.835
W/E Evening Time Spent on Intermediate Viewing	24.75	*r=-0.277* *p=0.039*	r=0.156 p=0.251
W/E Evening Time Spent on Distance Viewing	80.07	r=-0.021 p=0.877	r=-0.034 p=0.805

Table 6.4.6. The average near activity parameters for all the participants combined and the correlations between each near activity parameter with SER and AL.

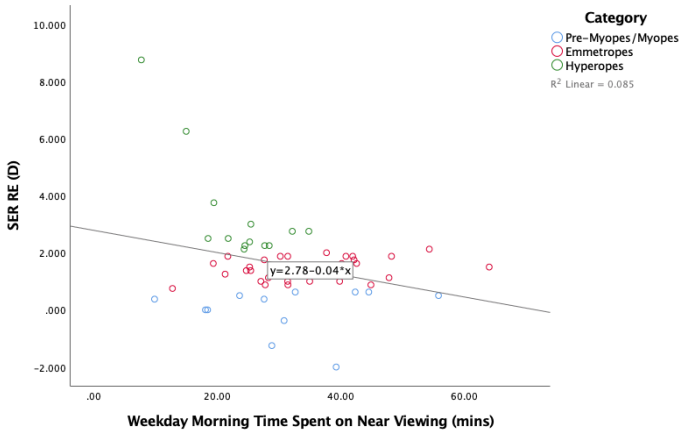


Figure 6.4.18. Scatterplot demonstrating a statistically significant negative correlation between SER and weekday morning time spent on near viewing (r=-0.291, p=0.027).

Figure 6.4.19. Scatterplot demonstrating a statistically significant positive correlation between SER and weekend evening time spent on very close viewing (r=0.368, p=0.005).

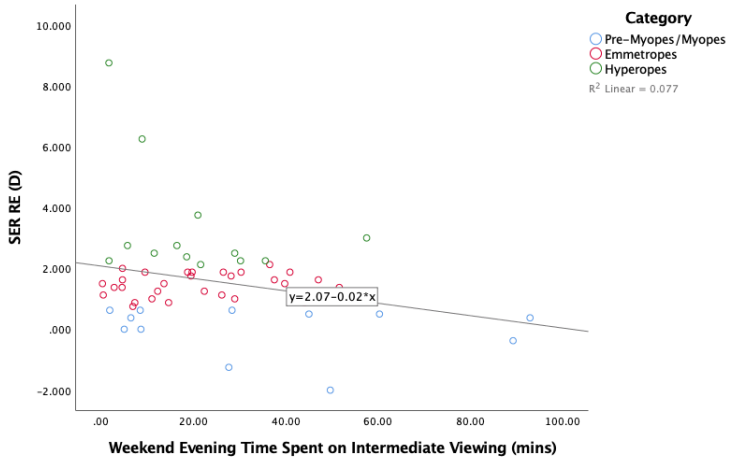


Figure 6.4.20. Scatterplot demonstrating a statistically significant negative correlation between SER and weekend evening time spent on intermediate viewing (r=-0.277, p=0.039).

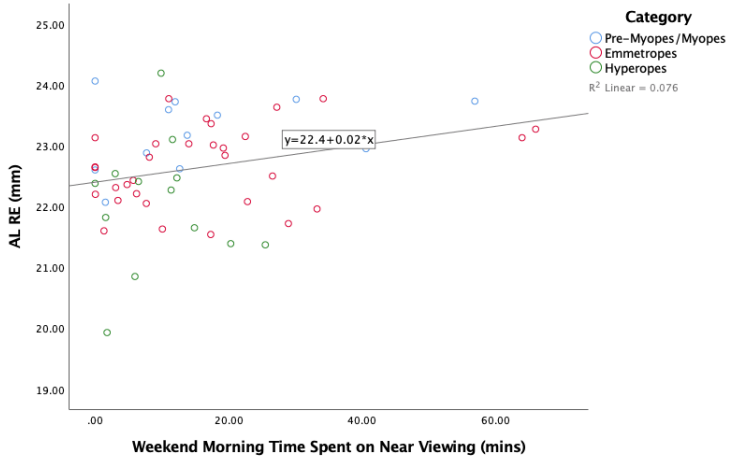


Figure 6.4.21. Scatterplot demonstrating a statistically significant positive correlation between AL and weekend morning time spent on near viewing (r=0.275, p=0.040).

Hierarchical multiple regression analysis for SER with all parameters that had a statistically significant correlation with SER using Pearson's, found that time spent viewing at near on weekday mornings was independently associated with SER after controlling for age, gender, ethnicity, and parental myopia; with more time viewing at near on weekday mornings being associated with a more myopic refractive error. The whole model included all parameters with a significant association with SER and approached statistical significance with the total variance explained by the model=48.7%, F (12, 26) =2.05, p=0.061. Only time spent viewing at near on weekday mornings was statistically significant, beta=-0.43, p=0.018.

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the duration of near activity over the different time periods are presented in Table (6.4.7.).

Clouclip Near Activity Parameter	Pre-Myopes/Myopes Mean and (SD) (mins)	Non-Myopes Mean and (SD) (mins)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD) (mins)	Hyperopes Mean and (SD) (mins)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Weekday Morning V Close	65.44 (25.22)	56.96 (29.91)	p=0.372	59.59 (30.48)	50.31 (28.49)	p=0.421	
Weekday Morning Near	30.93 (12.95)	31.38 (10.97)	p=0.904	34.53 (10.67)	23.40 (7.19)	*p=0.009*	P/M vs E p=0.573 P/M vs H p=0.184 *E vs H p=0.006*
Weekday Morning Intermediate	33.58 (15.98)	34.08 (12.47)	p=0.908	36.63 (12.29)	27.59 (10.82)	p=0.107	
Weekday Morning Distance	83.16 (26.42)	90.83 (29.46)	p=0.416	95.20 (28.24)	79.75 (30.70)	p=0.188	
Weekday Afternoon V Close	54.36 (25.74)	47.76 (25.81)	p=0.433	48.24 (25.59)	46.53 (27.38)	p=0.723	

Weekday Afternoon Near	25.21 (11.30)	24.59 (9.18)	p=0.845	25.21 (9.08)	23.04 (9.63)	p=0.778	
Weekday Afternoon Intermediate	26.94 (13.73)	28.66 (10.79)	p=0.643	29.74 (11.44)	25.93 (8.72)	p=0.537	
Weekday Afternoon Distance	73.24 (31.17)	80.19 (28.06)	p=0.458	79.77 (28.21)	81.25 (28.79)	p=0.752	
Weekday Evening V Close	66.00 (32.89)	66.52 (44.58)	p=0.970	68.48 (49.36)	61.56 (30.31)	p=0.885	
Weekday Evening Near	23.35 (11.36)	26.52 (13.74)	p=0.466	29.17 (14.64)	19.79 (8.29)	p=0.072	
Weekday Evening Intermediate	35.91 (40.77)	28.66 (14.97)	p=0.556	30.68 (15.60)	23.52 (12.31)	p=0.387	
Weekday Evening Distance	72.39 (45.88)	83.72 (46.47)	p=0.454	83.64 (37.97)	83.89 (65.22)	p=0.758	
Weekend Morning V Close	42.10 (36.14)	36.85 (27.94)	p=0.591	38.21 (26.99)	33.60 (31.00)	p=0.778	

Weekend Morning Near	17.05 (17.36)	14.60 (14.65)	p=0.624	16.70 (16.40)	9.59 (7.60)	p=0.327	
Weekend Morning Intermediate	20.25 (20.79)	16.31 (16.36)	p=0.489	18.70 (17.91)	10.59 (10.33)	p=0.290	
Weekend Morning Distance	56.49 (48.01)	45.29 (37.95)	p=0.396	48.75 (38.40)	37.01 (37.00)	p=0.476	
Weekend Afternoon V Close	54.53 (31.32)	56.21 (39.64)	p=0.893	59.60 (42.59)	48.14 (31.53)	p=0.658	
Weekend Afternoon Near	22.33 (15.38)	19.57 (14.82)	p=0.573	22.12 (16.11)	13.47 (9.02)	p=0.181	
Weekend Afternoon Intermediate	29.91 (23.73)	23.36 (17.81)	p=0.299	25.55 (19.02)	18.15 (13.80)	p=0.297	
Weekend Afternoon Distance	60.01 (37.89)	69.28 (44.40)	p=0.512	68.59 (45.34)	70.92 (43.81)	p=0.798	
Weekend Evening V Close	53.28 (42.66)	75.00 (56.42)	p=0.221	66.07 (49.99)	96.30 (66.80)	p=0.112	

Weekend Evening Near	23.16 (17.41)	19.12 (13.94)	p=0.403	19.56 (13.85)	18.08 (14.68)	p=0.676	
Weekend Evening Intermediate	35.27 (32.44)	21.88 (15.82)	p=0.190	22.71 (16.09)	19.90 (15.62)	p=0.133	
Weekend Evening Distance	77.78 (54.78)	80.69 (54.64)	p=0.871	75.00 (48.33)	94.28 (67.65)	p=0.561	

Table 6.4.7. The average duration of the near activity parameters for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories across the different time periods.

The figures below present the duration of near activities over the different time periods on weekdays and weekends for the refractive groups. The lines and triple stars indicate statistically significant differences between the duration of near activities during the different time periods using one-way analyses of variance (ANOVAs). The braces and single stars indicate statistically significant different between refractive groups for duration of near activities during a particular period of the day using one-way ANOVAs.

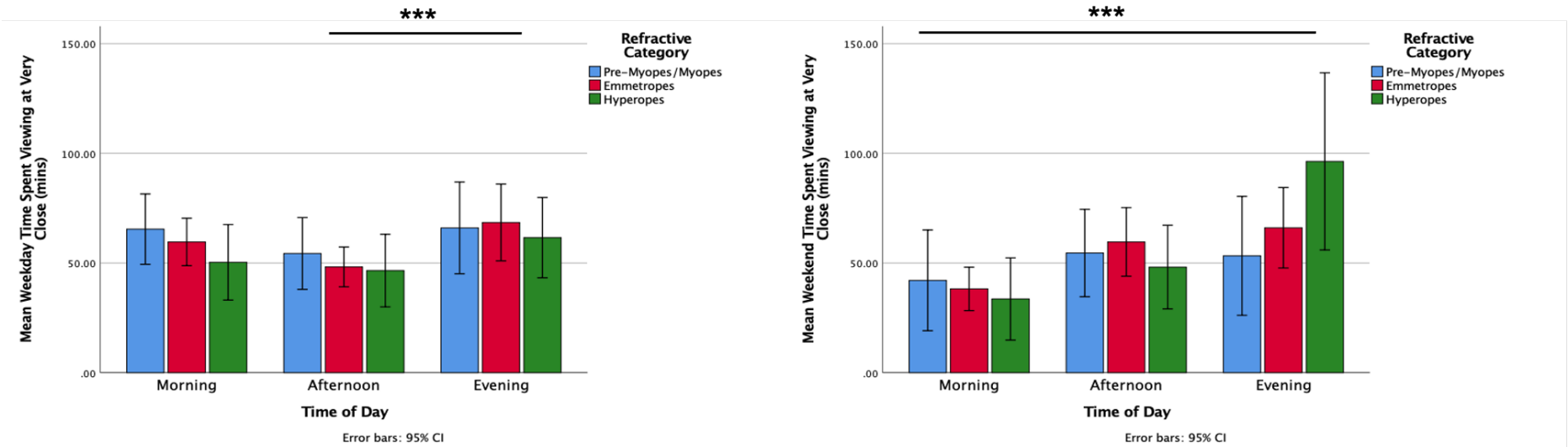


Figure 6.4.22. Bar charts showing the mean duration of time spent viewing at very close between refractive groups with the line and triple stars indicating significant differences in time spent viewing at very close across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.22. shows that all participants spent statistically significantly more time viewing at very close on weekday evenings than afternoons and on weekend evenings than mornings.

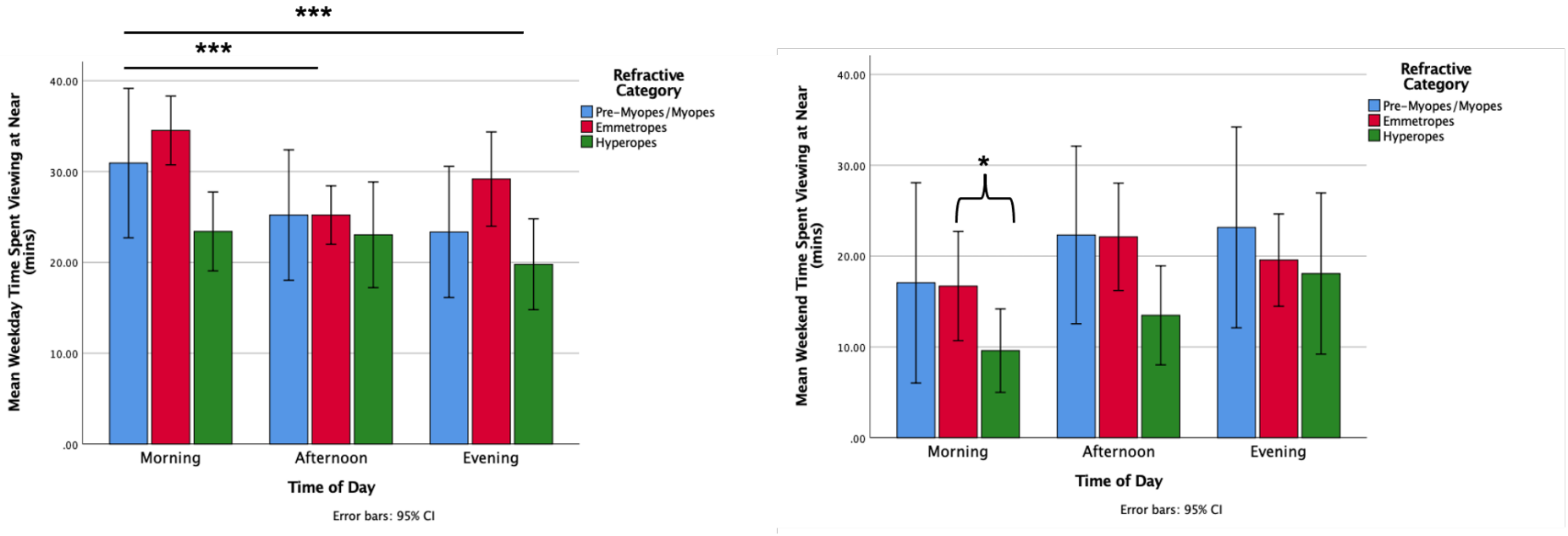


Figure 6.4.23. Bar charts showing the mean duration of time spent viewing at near between refractive groups with the brace and single star indicating a difference between emmetropes and hyperopes, and with the line and triple stars indicating significant differences in time spent viewing at near across the different periods of the day for both weekdays and weekends for all participants

Figure 6.4.23. shows that all participants spent statistically significantly more time viewing at near on weekday mornings than both afternoons and evenings. There were no statistically significant differences in time spent viewing at near for the difference periods of the day on weekends. However, emmetropes spent statistically significantly more time viewing at near on weekend mornings than hyperopes.

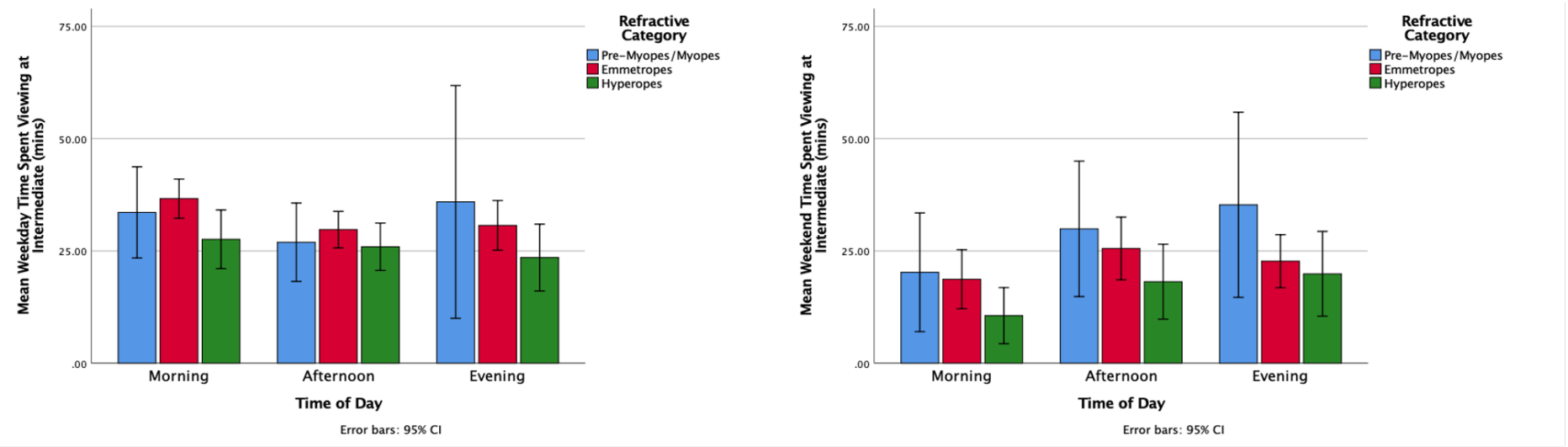


Figure 6.4.24. Bar charts showing the mean duration of time spent viewing at intermediate between refractive groups across the different periods of the day for both weekdays and weekends for all participants. There were no significant differences between refractive groups for each period of the day or between time spent viewing at intermediate across the different periods of the day for the whole cohort.

Figure 6.4.24. shows that there were no statistically significant differences in time spent viewing at intermediate for the difference periods of the day on weekdays or weekends.

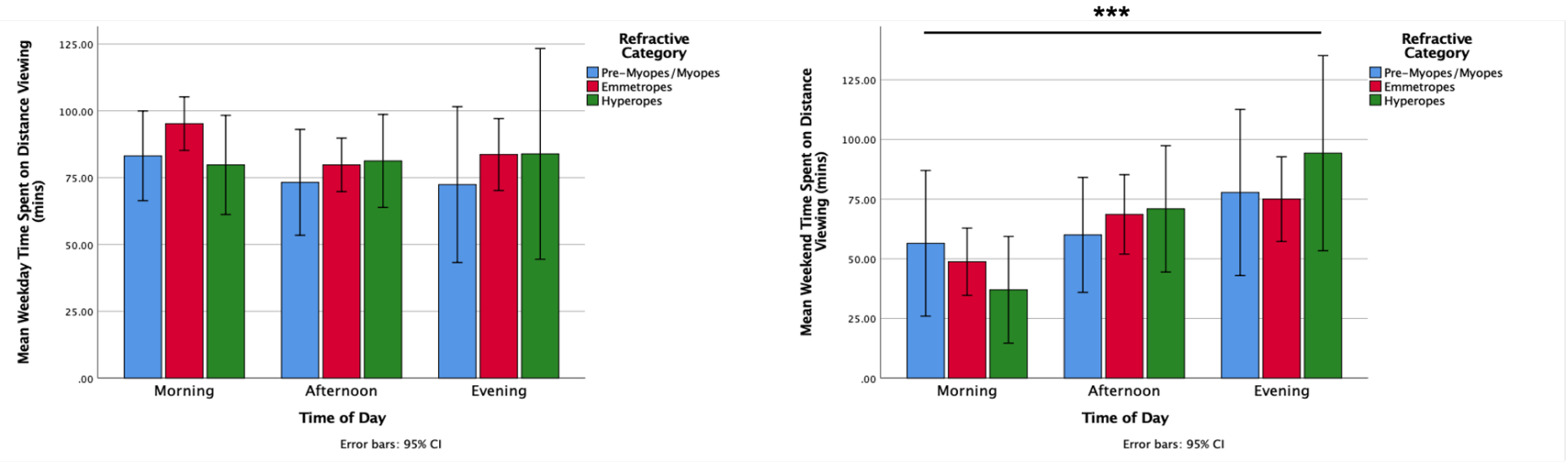


Figure 6.4.25. Bar charts showing the mean duration of time spent on distance viewing between refractive groups with the line and triple stars indicating significant differences in time spent on distance viewing across the different periods of the day for both weekdays and weekends for all participants.

Figure 6.4.25. shows that all participants spent statistically significantly more time viewing at distance on weekend evenings than mornings. There were no statistically significant differences in time spent viewing at distance for the difference periods of the day on weekdays.

6.4.4. Odds Ratios for Classification as Pre-Myopic/Myopic

Logistic regression analyses used to explore the association between the risk factors under investigation and the classification of pre-myopic/myopic (compared with a classification of non-myopic [emmetropic or hyperopic]). The table below highlights the parameters where a significant association was identified and presents the odds ratios derived. These parameters were then included in a multivariate analysis model.

Predictive Variables for Pre-Myopia/Myopia	Univariate ORs (95% CI) and Significance	Multivariate ORs (95% CI) and Significance
Weekend Afternoon Moderate Physical Activity	*1.061 (1.017-1.107), p=0.007*	1.039 (0.983-1.098), p=0.177
Weekend Afternoon Vigorous Physical Activity	*1.031 (1.003-1.059), p=0.027*	1.007 (0.961-1.055), p=0.770
Weekend Evening Moderate Physical Activity	*1.034 (1.004-1.065), p=0.025*	1.017 (0.978-1.058), p=0.402
Weekend Evening Vigorous Physical Activity	*1.019 (1.001-1.037), p=0.039*	1.055 (0.977-1.033), p=0.755

Table 6.4.8. Results of the univariate and multivariate analyses with the parameters that are significant underlined and in italics.

Univariate regression analysis identified a significant relationship between pre-myopia/myopia categorisation and more time spent on both moderate and vigorous activity on weekend afternoons with OR and 95% CIs of 1.061 (1.017-1.107) and 1.031 (1.003-1.059), and significance of p=0.007 and 0.027, respectively. Univariate regression analysis also identified a significant relationship between pre-myopia/myopia categorisation and more time spent on both moderate and vigorous activity on weekend evenings with OR and 95% CIs of 1.034 (1.004-1.065) and 1.019 (1.001-1.037), and significance of p=0.025 and 0.039, respectively. None of these remained significant after multivariate analysis.

Univariate regression analysis found no significant trend between any light exposure or near activity parameters and odds for pre-myopia/myopia (all p>0.05).

6.4.5. Comparison of Weekday to Weekend

The results of paired samples t-tests between weekdays and weekends for each of the parameters are presented in Table 6.4.9.

Parameter	Weekday Mean (mins)	Weekend Mean (mins)	Paired Samples T-Test Results
Sedentary	112.77	117.04	p=0.097
Light	120.10	109.17	*p<0.001*
Moderate	28.75	28.21	p=0.408
Vigorous	22.59	22.11	p=0.566
AW Scotopic	21.00	27.71	*p=0.001*
AW Mesopic	28.60	34.86	*p<0.001*
AW Photopic	216.52	196.21	*p<0.001*
AW Outdoor	17.04	18.13	p=0.354
Very Close	58.87	54.72	p=0.207
Near	27.07	18.13	*p<0.001*
Intermediate	30.63	22.22	*p<0.001*
Distance	83.13	65.02	*p<0.001*
CC Mesopic	6.31	7.54	*p=0.040*
CC Photopic	180.60	145.16	*p<0.001*
CC Outdoor	17.23	12.15	*p<0.001*

Table 6.4.9. Results of paired samples t-tests between weekdays and weekends for the total time spent in each parameter for all participants combined. There were significant differences between weekday and weekend for all participants for most parameters. Only time spent sedentary, on moderate and on vigorous activity, time spent outdoors (AW), and time spent viewing at very close, were not significantly different between the weekdays and weekends.

The results of paired samples t-tests between weekdays and weekends for each of the parameters at morning, afternoon and evening are presented in Table 6.4.10.

Parameter	Weekday Mean (mins)	Weekend Mean (mins)	Paired Samples T-Test Results
Morning Sedentary	116.35	112.35	p=0.336
Afternoon Sedentary	78.18	89.91	*p=0.001*
Evening Sedentary	143.65	148.86	p=0.335
Morning Light	129.37	95.10	*p<0.001*
Afternoon Light	109.02	99.58	*p=0.006*
Evening Light	122.38	132.82	*p=0.013*
Morning Moderate	25.26	21.82	*p=0.002*
Afternoon Moderate	29.36	27.21	p=0.086
Evening Moderate	31.83	35.60	*p=0.004*
Morning Vigorous	16.79	15.34	p=0.247
Afternoon Vigorous	26.42	22.21	*p=0.012*
Evening Vigorous	24.72	28.78	*p=0.036*
Morning Scotopic AW	19.49	23.22	p=0.062
Afternoon Scotopic AW	5.96	7.58	p=0.212
Evening Scotopic AW	37.56	52.33	*p=0.009*
Morning Mesopic AW	23.45	26.91	p=0.095
Afternoon Mesopic AW	14.15	16.97	p=0.165

Evening Mesopic AW	48.19	60.71	*p<0.001*
Morning Photopic AW	228.65	180.48	*p<0.001*
Afternoon Photopic AW	194.98	188.04	p=0.295
Evening Photopic AW	225.93	220.10	p=0.413
Morning Outdoor AW	13.13	14.02	p=0.605
Afternoon Outdoor AW	27.90	26.35	p=0.537
Evening Outdoor AW	10.09	14.02	*p=0.028*
Morning Very Close	59.11	37.97	*p<0.001*
Afternoon Very Close	50.24	55.85	p=0.316
Evening Very Close	67.26	70.35	p=0.613
Morning Near	31.01	15.13	*p<0.001*
Afternoon Near	24.96	20.16	*p=0.004*
Evening Near	25.25	19.99	*p=0.011*
Morning Intermediate	33.60	17.15	*p<0.001*
Afternoon Intermediate	28.62	24.77	p=0.080
Evening Intermediate	29.68	24.75	p=0.061
Morning Distance	88.90	47.69	*p<0.001*
Afternoon Distance	79.84	67.29	*p=0.019*
Evening Distance	80.66	80.07	p=0.933
Morning Mesopic CC	4.50	2.89	*p=0.033*
Afternoon Mesopic CC	2.59	4.55	*p=0.024*
Evening Mesopic CC	11.86	15.18	*p=0.013*

Morning Photopic CC	202.16	118.29	*p<0.001*
Afternoon Photopic CC	166.33	159.11	p=0.429
Evening Photopic CC	173.32	158.08	p=0.126
Morning Outdoor CC	15.98	9.49	*p<0.001*
Afternoon Outdoor CC	25.46	15.41	*p<0.001*
Evening Outdoor CC	10.24	11.53	p=0.617

Table 6.4.10. Results of paired samples t-tests between weekdays and weekends for the total time spent in each parameter in the different periods of the day, for all participants combined. Those parameters that were statistically significantly different on weekdays vs weekends are underlined and in italics.

6.5. Discussion

This is the first study to objectively quantify the timing and duration of light exposure, physical activity, and near activity in young children in the UK and to explore relationships between children's refractive error/axial length and these objectively measured risk factors. Given the fact that very few of pre-myopic/myopic group were already myopic (n=4), this chapter is primarily useful for examining a UK cohort prior to the onset of myopia.

The Myopia Profile website (https://www.mykidsvision.org/en-us) recommends at least 90 minutes per day spent outdoors to delay the onset of myopia (Xiong *et al.*, 2017). On average the participants spent only 51 and 54 minutes outdoors on weekdays and weekends respectively. This is comparable to children living in Singapore where they demonstrated an average of 61 minutes outdoors per day, while Australian children experienced significantly longer time outdoors (105 minutes) (Read *et al.*, 2018). Children aged 5-18 years old are recommended at least 1 hour of moderate to vigorous physical activity per day (Davies *et al.*, 2019) and the participants in the present study were spending an average of 1.3 hours per day on moderate-vigorous physical activity.

When comparing weekdays and weekends, the participants were found to spend statistically significantly more time in scotopic and mesopic light on weekends than weekdays, but statistically significantly less time in indoor photopic light on weekends than weekdays and more time in scotopic, mesopic, and outdoor light on weekend evenings than weekday evenings. This could be due to participants having more freedom of choice of their activities without schoolwork/homework or other organised after-school activities. They also spent more time in indoor photopic light on weekday mornings than weekend mornings, which could be possibly attributed to later get-up times on weekends than weekdays. The 6-9-year-old children in the present study tended to spend more time in darkness and dimmer light first thing in the morning and last thing in the evening, a finding similar to that reported by Landis *et al*. (2018). Also in agreement with Landis *et al*. (2018) and Li *et al.* (2021), the participants in the present study were found to spend most time outdoors during the middle of the day and more time exposed to indoor photopic light in the mornings and evenings on both weekdays and weekends. More time outdoors in the afternoons corresponds with lunch break and time directly after school (children in this age group finish school between 2-3pm).

The 6-9-year-old children in the present study spent less time sedentary during the afternoons (both on weekdays and weekends) and more time sedentary in the evenings than mornings. The participants spent most time on moderate and vigorous physical activity in the afternoons and evenings of weekdays and weekends. Participants spent significantly more time on light activity on weekdays than weekends, specifically on weekday mornings and afternoons than weekends. They also spent more time sedentary on the weekend afternoons than weekdays which could be due to lunch break on school days encouraging more active participation in games with their peers. More time was spent on moderate and vigorous activity on weekend evenings than weekday evenings indicating an increase in higher intensity exercise in the evenings where they have more freedom to choose how they spend their time, as opposed to school nights where homework may take priority. Read *et al.* (2014) reported higher levels of physical activity at weekends in participants aged 10-15 years old, which is in agreement with our findings that time spent on light, moderate and vigorous activity was higher on weekdays than weekends.

Participants in the present study spent more time on very close, near and intermediate viewing on weekdays compared to weekends in agreement with Williams *et al.* (2019) who reported a similar finding for adult participants. In our cohort this finding is likely due to a focus on schoolwork and homework during the week. Participants also spent more time in near viewing activities (across all four categories) on weekday mornings compared with weekend mornings; this can probably be attributed to earlier rising during the school week and near viewing activities in school. The 6-9-year-old children in the present study spent more time in very close ($\leq$30 cm) near viewing activities on weekday evenings than afternoons and on weekend evenings than mornings, indicating such very close near vision activity was more prevalent outside of school hours. This finding may be attributed to the use of screens (tablets/smart phones) as they tend to be held at closer viewing distances than traditional printed material due to increased attention and concentration (Bao *et al.*, 2015). Furthermore, users tend to take fewer breaks when using electronic devices compared to when they are viewing printed material (Bhandari and Ostrin, 2020). By contrast, during weekday (school) mornings, participants in the present study spent more time viewing at near (31-49 cm) than they did in the afternoon and evening. Participants spent more time viewing at distance (>120cm) on weekend evenings than mornings, possibly indicating different activities such as physical activity or TV viewing during this time.

6.5.1. Duration of Light Exposure During Different Periods of the Day and Pre-Myopia/Myopia

The Actiwatch data failed to reveal any significant differences between refractive groups in terms of the duration, timing, and intensity of light exposure. This finding aligns with those of Li *et al.* (2021) who found no significant associations between the timing of light exposures and SER, AL, or risk of myopia in children aged 9-years-old in Singapore. The Clouclip data revealed that emmetropes spent statistically significantly more time in photopic light on weekday mornings (M=215.09 mins) than hyperopes (M=174.35 mins) and that hyperopes spent significantly more time outdoors on weekend afternoons (M=30.19 mins) than emmetropes (M=7.54 mins). The reason for differences between the Actiwatch and Clouclip light exposures may be attributed to the number of children wearing the devices. More children wore the Actiwatch devices for the required time frame so the results from their light exposure data are likely more robust.

The present study found no difference between the time pre-myopes/myopes and non-myopes spent in scotopic light during weekends, with both groups spending similar time in scotopic light overall, but with more time in scotopic light on weekends than weekdays. By contrast, Landis *et al.* (2018) found myopic children received significantly less scotopic light during weekends than non-myopic children, with a difference of up to three hours between groups in the evenings. A potential reason for this difference in findings could be the unconventional and extended definition of scotopic (<1-1 lux) and mesopic light (1-30 lux) used by Landis *et al.* In the present study both groups spent significantly less time in mesopic light on weekdays compared to weekends, but Landis *et al.* (2018) reported that non-myopic children spent less time in mesopic light on weekdays than on weekends. The present study found more time spent in indoor photopic light for both refractive groups on weekdays compared to weekends which concurs with Landis *et al.* (2018) findings and could be attributed to the more rigid indoor-based routine on weekdays due to school. There were no significant differences in the amount of time spent outdoors (as indicated by the time spent in outdoor photopic light) between pre-myopes/myopes and non-myopes in the present study, whereas Landis *et al.* (2018) found that the slightly older non-myopic children in the Role of Outdoor Activity in Myopia (ROAM) study were exposed to more outdoor light on weekends than myopic children.

This could indicate that the trend for less time outdoors follows myopia onset rather than precedes it.

6.5.2. Duration of Physical Activity Levels During Different Periods of the Day and Pre-Myopia/Myopia

Hyperopia in the present study was associated with more sedentary behaviour, particularly on the weekends. Non-myopes spent significantly more time sedentary on weekend mornings than pre-myopes/myopes. Pre-myopes/myopes spent significantly more time on moderate activity on weekend afternoons and evenings, and on vigorous activity on weekend evenings than non-myopes. This contrasts with other reports from the literature. O'Donoghue *et al.* (2015) and Harrington *et al.* (2019) report that myopes aged 12-13-years-old tend to have more sedentary lifestyles and Guggenheim *et al.* (2012) reported that non-myopes spent more time on moderate-vigorous physical activity than myopes aged 11-years-old. The difference in the ages of the children studied may account for this difference and increased time spent sedentary could be a side effect of myopia rather than casual, and with limited children in the present study classified as "already myopic" (<-0.50DS), the relationship between established myopia and physical activity could not be explored robustly. It is possible that the participants in the present study have been advised by eye health professionals that they are at risk of future myopia based on their current refractive error, and parents might be encouraging outdoor activity to avoid the onset/progression of myopia.

Read *et al.* (2014) report no significant differences in the amount of time 10-15-year-old myopes or emmetropes spent on moderate to vigorous physical activity, and no significant differences between refractive groups in relation to the time of day of physical activity occurred. The age difference between the present cohort and that investigated by Read *et al.* may explain this discrepancy, and as it has been reported that the amount of time spent sedentary tends to increase with age (Jago *et al.*, 2017). Furthermore, the difference could be due to the classifications of refractive error, the pre-myopic/myopic group in the present study contained low hyperopes (<+0.75 DS) which Read *et al.* classified as emmetropes.

Univariate logistic regression analysis identified a significant relationship between pre-myopia/myopia classification and more time spent on both moderate and vigorous activity on weekend afternoons with ORs indicating a mild inflation of risk associated

with the refractive category pre-myopia/myopia (OR 1.061 and 1.031 per minute increase of activity in that time period, respectively). There was also a significant relationship between pre-myopia/myopia classification and more time spent on both moderate and vigorous activity on weekend evenings with ORs of 1.034 and 1.019 per minute increase of activity in that time period, respectively. These ORs indicate a very small increased risk (between 2%-6%) of pre-myopia/myopia classification and none remained significant after multivariate analysis. Exercise, just like light exposure is a strong entrainment signal for the circadian clock (Tahara, Aoyama and Shibata, 2017), through regulation of blood pressure, heart rate, body temperature and hormone levels (Hower, Harper and Buford, 2018). Shibata *et al.* (2011) found higher levels of melatonin at bedtime amongst children with higher total daily physical activity recorded using an accelerometer. By contrast, Yamanaka *et al.* (2006) reported that physical activity later in the day leads to a phase delay in the circadian rhythm in plasma melatonin, delaying the onset of secretion usually seen in the early evening. Rubio-Sastre *et al.* (2014) report that evening physical activity in young women impairs the circadian rhythms and might not be as beneficial to healthy sleep/wake rhythm as morning physical activity. Therefore, there is the potential that those individuals in the present study with higher physical activity levels later in the day are disrupting their circadian rhythms, which could be to be promoting myopia development. Longitudinal studies would be required to explore this hypothesis.

6.5.3. Duration of Near Activities During Different Periods of the Day and Pre-Myopia/Myopia

Those individuals with less hyperopic refractive errors in the present study were found to spend more time viewing at near on weekday mornings and viewing at intermediate on weekend evenings. This agrees with findings of Li *et al.* (2015) where continuous reading (>45 minutes) was significantly associated with myopia. On schooldays those less hyperopic individuals are more likely to be doing more viewing at near than their more hyperopic peers. Emmetropes spent statistically significantly more time on near viewing on weekday mornings than the hyperopes. Longer axial lengths were associated with more time spent on near viewing on weekend mornings, highlighting that the those with longer eyes were more likely to perform near work even on non-school days. These findings may be indicative of near activity as a myopic risk factor and/or may indicate near work task avoidance associated with hyperopia as previously described in the Sydney Myopia Study (French *et al.*, 2009).

6.5.4. Strengths and Limitations

This study provides novel insight into the behaviours and visual environments of young children at an age where myopia has not yet become manifest in the majority of children in the UK. The study also used a robust evaluation of refractive error alongside device measured environmental and behavioural risk factors. Children were all tested during the school term ensuring that inter-group behaviours were more comparable than if some data were collected during school holiday periods. This potential for disparity is illustrated by the differences seen in weekend versus weekday behaviour and environment profiles. Additionally, categorising the periods of the day and weekdays and weekends helps solidify any patterns of behaviour which may lead to increased risk of future myopia in this young cohort. The limitations of the present investigation have been outlined in Chapter 5. Pertinent to this study, these include the loss of data from the Clouclip due to its battery life and the uneven sample sizes representing the different refractive groups. None-the-less, the numbers of participants in each refractive group reflected the underlying distribution of refractive in the UK population at this age. It would have been ideal to collect data at a single time during the year, rather than in different seasons, to limit the impact of the different day lengths on participant behaviour as detailed in Chapter 5. However, the author was restricted by the limited number of measuring devices available, and the time taken to collect data.

6.6. Conclusion

To conclude, this study examining the timing of exposure to environmental and behavioural risk factors using objective measurements supports some of the trends in behaviour in children for light exposure, near activity and physical activity found in other studies. The main finding of this study is that more time spent on moderate and vigorous activity on weekend afternoons and evenings is associated with an increased likelihood of being classed as pre-myopic/myopic. There were differences in near work parameters between refractive groups with evidence of those with more hyperopic errors spending less time on near viewing activities. It may be appropriate for clinicians to recommend that to promote visual health, children undertake a mix of visual activities and consider reducing the time spent on moderate-vigorous physical activity later in the evening. Further investigation into these behaviours and their effect on short-term eye growth will be evaluated in Chapter 7.

Chapter 7: Profile of Environmental Risk Factors (Qualitative and Quantitive Data) for Myopia Progression and Axial Growth in Northern Irish School Children

Chapter 7: Profile of Environmental Risk Factors (Qualitative and Quantitive Data) for Myopia Progression and Axial Growth in Northern Irish School Children

7.1. Introduction

Following the cross-sectional examination of objective risk factors (physical activity, light exposure, sleep quality, and near viewing behaviours) for pre-myopia/myopia in Chapter 5 and 6, a longitudinal follow-up was designed to elicit which potentially modifiable risk factors were related to myopic shift and axial elongation in this young UK based cohort.

The main findings from the cross-sectional chapter (Chapter 5) were that non-myopes had significantly higher average light exposure than pre-myopes/myopes during winter and, pre-myopes/myopes spent significantly more time in photopic light during sleeping hours than non-myopes and less time in scotopic light during sleeping hours also during winter. Pre-myopes/myopes spent significantly more time on moderate activity than non-myopes. Those with more myopic spherical equivalent refraction (SER) and longer axial lengths (AL) had higher sleep efficiency (higher percentage of time asleep/time in bed), and pre-myopes/myopes tended to have later bedtimes and poorer subjective sleep quality than non-myopes. Those with less hyperopic SERs spent significantly more time on near viewing and pre-myopes/myopes tended to have shorter viewing distances than non-myopes. There were increased odds for classification as pre-myopic/myopic for those older at baseline, with longer AL, deeper anterior chambers, more time spent on moderate activity, more time spent in photopic light at night, and having two myopic parents on univariate analysis. On multivariate analysis only longer AL at baseline remained statistically significant.

The main findings from the timings of exposure to environmental and behavioural risk factors chapter (Chapter 6) were that hyperopia was associated with more sedentary behaviour particularly on the weekends. Pre-myopes/myopes spent significantly more time on moderate activity than both emmetropes and hyperopes on weekend afternoons. Increased time spent on moderate and vigorous activity on weekend afternoons and evenings were all related to increased odd ratios for classification as pre-myopic/myopic on univariate analysis. None of these parameters remained statistically significant on

multivariate analysis. Those individuals with more myopic refractive errors in the present study were found to spend more time viewing at near on weekday mornings and viewing at intermediate on weekend evenings. Longer ALs were associated with more time spent on near viewing on weekend mornings. However, on weekend evenings, those with more hyperopic refractive errors spent more time viewing at very close. There were no associations between the duration of light exposures throughout the different periods of the day with either SER or AL.

To date there is evidence that individuals who habitually adopt close working distances (≤30 cm) have an increased risk of myopia progression over a 6 month period when compared to individuals with longer working distances (>30 cm) (Huang *et al.*, 2019).

There are several published studies which have found that myopia progresses faster in winter and slower in summer. This is likely due to increased time spent outdoors, which has been found to be protective against myopia progression by other studies, but could also be a result of reduced near work and reduced educational pressures when children are on their summer holidays from school (Fulk, Cyert and Parker, 2002; Donovan *et al.*, 2012; Cui, Trier and Munk Ribel-Madsen, 2013; Gwiazda *et al.*, 2014).

A longitudinal study in Houston, Texas using objective measurements of light exposure, demonstrated that children were exposed to higher levels of light and spent more time outdoors during the summer break compared with during school terms, whereas activity and sleep were similar across the year (Ostrin, Sajjadi and Benoit, 2018). This suggests that differing light exposure and time spent outdoors are the main reasons for varying trends of myopic eye growth throughout the year.

An intervention study in Taiwan also identified an association between light exposure and myopia progression. The authors report an increased recess outdoors by 80 minutes per day for a year resulted in significantly lower levels of myopia onset in the intervention group compared with the control group (8.41% vs. 17.65%), and significantly slower progression of myopia (−0.25 D/year vs. −0.38 D/year) (Wu *et al.*, 2013).

Northern Ireland has a larger variation in daylight hours between winter and summer (7-8 hours in winter vs 16-17 hours in summer) *(www.timeanddate.com*) than experienced in many parts of the world. The winter daylight hours coincide almost entirely with the

school/workday hence the amount of free time during which children can experience outdoor light (>1000 lux) is much more limited in winter than in summer. This may have had significant impact on the findings recorded in Chapter 5, as any associations between light exposure/time outdoors and myopia may have been masked by variations in the season during which data collection took place. Statistically significant differences were found between participants' average light exposure and time spent outdoors between those whose data were collected in winter compared to summer (Chapter 5 Section 5.5.3.), regardless of refractive classification. When the data were analysed for summer and winter separately there were some interesting differences in light exposure between pre-myopes/myopes and non-myopes during winter only. Non-myopes had significantly higher average light exposure than pre-myopes/myopes. Pre-myopes/myopes spent significantly more daytime in photopic light than non-myopes. Non-myopes spent significantly more time in scotopic light during sleeping hours than pre-myopes/myopes and pre-myopes/myopes spent significantly more time in photopic light during sleeping hours than non-myopes.

A literature review and meta-analysis by Ho, Wu and Liou (2019) concluded that 10 h/week, or 120 min/day of outdoors time for children aged 4-14-years-old can reduce the incidence of myopia by 63.7% as well as reducing myopic progression by 0.16 D/year. However, the intervention studies included in the review have only been conducted on Asian children meaning the results may not be generalizable to all ethnic groups. Northern Irish children are more likely to achieve these 'anti-myopia' outdoor exposure goals during the summer months rather than the winter months when the school day directly coincides with the extent of daylight hours.

There are limited studies which compare each of the objectively measurable environmental risk factors to the progression of SER and axial length to explore longitudinal associations between environment and refractive development. If associations between lifestyle choices and the development and progression of myopia can be determined, these data can be used to provide evidence-based information to both the patients and their parents and allow clinicians to better target myopia management services.

7.1.1. Aims

The aims of the study were to determine:

- If 12-month ocular growth differs in children whose refractive error at baseline (aged 6-9-years old) puts them at high vs low risk of future myopia.
- If any of the previously measured environmental risk factors are associated with myopic shift in refraction or axial elongation.

7.2. Methods

7.2.1. Recruitment and Data Acquisition

Children (aged 6-9-years) who had participated in NICER Study 2.0 (Ethics application number: REC/18/0102) and the study described in Chapter 5 were invited for a follow up visit 12 months (+/-3 months) after baseline measurements. Following informed parental consent, data collection occurred on the school premises, during the school day or on the Ulster University campus. Participants provided written assent prior to testing.

The measures pertinent to the present study were taken as follows:

- Cycloplegia was obtained following one drop of 0.5% Proxymetacaine Hydrochloride and instillation of 1% Cyclopentolate Hydrochloride within 5 minutes of applying the anesthetic.
- Refractive error was assessed 20 minutes later by cycloplegic autorefraction using an open-field autorefractor and distance fixation (Shin-Nippon SRW-5000).
- Ocular biometry, including corneal curvature, anterior chamber depth, lens thickness and axial length was measured on the Zeiss IOL Master 700.

Refractive error for each eye was defined using Spherical Equivalent Refraction (SER, sphere + cylinder/2). Baseline refractive error and biometry measures were subtracted from the one-year follow-up measures to provide the change over one year for each metric.

Based on eye growth data in a young UK cohort aged 6-7-years old followed up three years later, the 90th centile of axial elongation is 0.77 mm, translating as 0.26 mm of axial elongation/year*. Axial elongation more than 0.26mm over a 12-month period indicates a growth profile only demonstrated by the fastest growing eyes in a population-based cohort of comparable age. Using these data, in the present study those children showing growth >0.26 mm/year were determined to have ‘accelerated’ eye growth and those demonstrating less axial growth during the follow-up period were classed as exhibiting

* derived from analysis of NICER 1.0 data

'normal' eye growth. These classifications were used to evaluate associations between normal and accelerated eye growth and the myopia risk factors measured and described in Chapters 5 and 6.

7.2.2. Exclusion Criteria

Children were not invited to take part in the 12-month follow-up if they did not previously complete both parts of the original NICER 2.0 study or if they had an adverse reaction to cyclopentolate/proxymetacaine during the baseline assessment.

7.2.3. Data Extraction and Categorisation

In addition, to data detailing the 12-month change in SER and axial length, the objectively measured environmental risk factors (Chapter 5) and duration and timing of environmental risk factors (Chapter 6) for myopia at baseline were compared with the refractive error progression and axial elongation data to associations between the risk factors and refractive error and axial change.

7.2.4. Ethical Approval

The study protocols complied with the Declaration of Helsinki and was approved by the Ulster University's Research and Ethics Committee on 11th October 2019, application number: REC/19/0078.

7.3. Statistical Analysis

Data were entered into SPSS Version 25 which was used for statistical analysis. Descriptive statistics were used to describe the change in refractive error and ocular biometry over the 12-month period and the data were presented in tabular form. Differences between participants and non-participants for the follow-up were investigated using independent samples t-test (SER, AL & age), and chi-squared analysis (gender, refraction category & parental myopia). Paired t-tests were used to evaluate the change in ocular measures between baseline and follow-up. Independent samples t-tests were used to compare the change in refractive error and ocular biometry for those children with accelerated vs normal eye growth as defined using the 90th centile of axial growth over a 12-month period derived from analysis of NICER 1.0 data. Scatterplots of the change in SER and change in AL vs. each of the potential risk factors for future myopia were constructed and Pearson's correlations were used to describe these relationships.

Parametric testing was used due to the sample size (Norman, 2010). Hierarchical multiple regression analyses were performed to identify variables with a unique significant contribution to SER or AL change after controlling for additional variables (age, gender, parental myopia, time of year tested and baseline SER). Univariate and multivariate logistic regression analysis was used to calculate odds ratios for the risk factors associated with accelerated eye growth. Independent samples t-tests were used to evaluate statistically significant differences between pre-myopes/myopes and non-myopes (emmetropes and hyperopes combined) refractive and ocular biometry change. One-way between groups ANOVAs were used to evaluate statistically significant differences in refractive and ocular biometry change between the three refractive groups (pre-myopes/myopes, emmetropes and hyperopes), with post hoc analysis to find out where the statistically significant differences lay. One-way between groups ANOVAs were used to evaluate differences in SER and AL change compared to categorical variables including parental myopia and time spent on screens (TV/Video games, phone/tablet, computer/laptop, and time spent on devices before sleep).

7.4. Results

7.4.1. Descriptive Data

73 white children were invited to participate in the 12-month follow-up visit of which 42 (57.53%) agreed to take part. There was a mean of 358 days between visits (range 269-405 days) and data collection took place between March 2020 and March 2021.

There were no statistically significant differences between participants and non-participants in the follow-up in terms of age (t=1.49, *p*=0.098), SER (t=-1.51, p=0.133), AL (t=0.43, p=0.670), gender (X^2=3.49, *p*=0.062), refractive category (X^2=1.18, *p*=0.553), and parental myopia (X^2=0.47, *p*=0.790).

Table 7.4.1 describes the demographic of participants at baseline and follow-up and the success rates for each metric under investigation.

	Number	Age at Follow-Up (Range)	Gender	Number (%) of Participants Successfully Completing Data Collection				
				Actiwatch	Clouclip	Physical Activity Questionnaire for Children	Pittsburgh Sleep Quality Index	Screen Time Questionnaire
All participants	42	8.0 (7.3-8.6)	12 Male 30 Female	37 (88.1%)	23 (54.76%)	41 (97.62%)	41 (97.62%)	31 (73.81%)
Pre-myopes/Myopes	7	8.0 (7.3-8.6)	5 Male 2 Female	7 (100%)	6 (85.7%)	7 (100%)	7 (100%)	6 (85.7%)
Emmetropes	21	7.9 (7.3-8.5)	4 Male 17 Female	18 (85.7%)	9 (42.9%)	20 (95.2%)	20 (95.2%)	15 (71.4%)
Hyperopes	14	8.1 (7.6-8.6)	3 Male 11 Female	12 (85.7%)	8 (57.1%)	14 (100%)	14 (100%)	10 (71.4%)

Table 7.4.1. Table describes the success rate for participation and successful completion of the week of data collection with wearable devices and questionnaires. The table also presents the demographics of the participating children.

The 12-month change in ocular biometry and refractive error between baseline and follow-up is presented in Table 7.4.2.

	Change in Spherical Equivalent Refraction (SER) RE (D)	Change in Spherical Equivalent Refraction (SER) LE (D)	Change in Axial Length (AL) RE (mm)	Change in Axial Length (AL) LE (mm)	Change in Anterior Chamber Depth (ACD) RE (mm)	Change in Anterior Chamber Depth (ACD) LE (mm)	Change in Lens Thickness (LT) RE (mm)	Change in Lens Thickness (LT) LE (mm)
Average (Range) for All Participants	-0.21 (-1.13-0.88)	-0.21 (-1.50-0.63)	0.23 (0.04-0.71)	0.22 (-0.04-0.51)	0.05 (-0.07-0.16)	0.05 (-0.08-0.17)	-0.04 (-0.11-0.03)	-0.04 (-0.12-0.00)
Average (Range) for Pre-Myopes/Myopes	-0.41 (-1.13-0.38)	-0.41 (-1.50-0.00)	0.34 (0.14-0.71)	0.30 (0.14-0.51)	0.08 (0.04-0.16)	0.09 (0.06-0.17)	-0.06 (-0.11--0.03)	-0.07 (-0.12--0.05)
Average (Range) for Emmetropes	-0.15 (-0.75-0.50)	-0.15 (-0.63-0.63)	0.23 (0.12-0.38)	0.23 (0.12-0.36)	0.04 (-0.05-0.12)	0.04 (-0.05-0.12)	-0.04 (-0.07-0.00)	-0.04 (-0.09-0.00)

Average (Range) for Hyperopes	-0.20 (-0.88-0.88)	-0.21 (-0.75-0.25)	0.18 (0.04-0.45)	0.17 (-0.04-0.35)	0.04 (-0.07-0.09)	0.04 (-0.08-0.09)	-0.03 (-0.05-0.03)	-0.05 (-0.08--0.02)

Table 7.4.2. Table describing the average SER change and biometric change for the group as a whole and for each refractive grouping for right and left eyes. There was a strong positive correlation between right and left eyes for change in SER (r=0.649), change in AL (r=0.914), change in ACD (r=0.861), and change in LT (r=0.571), all p<0.001.

As the right and left eyes were strongly correlated for all change in biometry parameters and change in SER, the right eye only was used for all further analyses. Therefore, when SER or ocular biometry parameters are reported henceforth it is the SER or ocular biometric measures of the right eye.

Over the 12-months between visits, the mean SER became significantly less hyperopic (2.11 vs 1.90 D, $p=0.002$), The mean axial length (22.53 vs 22.76 mm, $p<0.001$) and ACD (3.64 vs 3.68 mm, $p<0.001$) both became significantly longer. The mean lens thickness also reduced significantly (3.42 vs 3.38 mm, $p<0.001$).

The results of independent samples t-test between pre-myopes/myopes and non-myopes, and one-way ANOVAs between all three refractive groups for the follow-up parameters are presented in Table 7.4.3.

Parameter	Pre-Myopes/Myopes Mean and (SD)	Non-Myopes Mean and (SD)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes)	Emmetropes Mean and (SD)	Hyperopes Mean and (SD)	One-Way ANOVA	Between Groups: P/M =Pre-myopes/Myopes E=Emmetropes H=Hyperopes
Age at Follow-Up (years)	7.95 (0.45)	7.99 (0.35)	p=0.809	7.92 (0.33)	8.09 (0.35)	p=0.412	
Change in SER RE (D)	-0.41 (0.55)	-0.17 (0.38)	p=0.167	-0.15 (0.32)	-0.20 (0.47)	p=0.372	
Change in AL RE (mm)	0.34 (0.18)	0.21 (0.09)	p=0.126	0.23 (0.06)	0.18 (0.11)	*p=0.008*	P/M vs E p=0.061 *P/M vs H p=0.006* E vs H p=0.327
Change in ACD RE (mm)	0.08 (0.05)	0.04 (0.04)	*p=0.011*	0.04 (0.04)	0.04 (0.04)	*p=0.038*	P/M vs E p=0.051 *P/M vs H p=0.044* E vs H p=0.959
Change in LT RE (mm)	-0.06 (0.03)	-0.03 (0.02)	*p=0.007*	-0.04 (0.02)	-0.03 (0.02)	*p=0.016*	P/M vs E p=0.062 *P/M vs H p=0.012* E vs H p=0.523

Table 7.4.3. The average age, refractive change, and ocular biometry change for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories.

	Accelerated Eye Growth (n=12)	Normal Eye Growth (n=30)
Mean Change in SER (D) (SD)	-0.44 (0.44)	-0.12 (0.37)
Mean Change in AL (mm) (SD)	0.37 (0.13)	0.18 (0.06)
Mean Change in ACD (mm) (SD)	0.07 (0.05)	0.03 (0.04)
Mean Change in LT (mm) (SD)	-0.05 (0.02)	-0.03 (0.02)

Table 7.4.4. The change in SER and biometry measures between those with normal and accelerated eye growth. The average change in all four parameters were significantly different between those with normal vs accelerated eye growth (independent samples t-tests, $p<0.005$).

The figures below (Figures 7.4.1.-7.4.3.) present the ocular biometry change parameters with significant differences between refractive groups using one-way analyses of variance (ANOVAs).

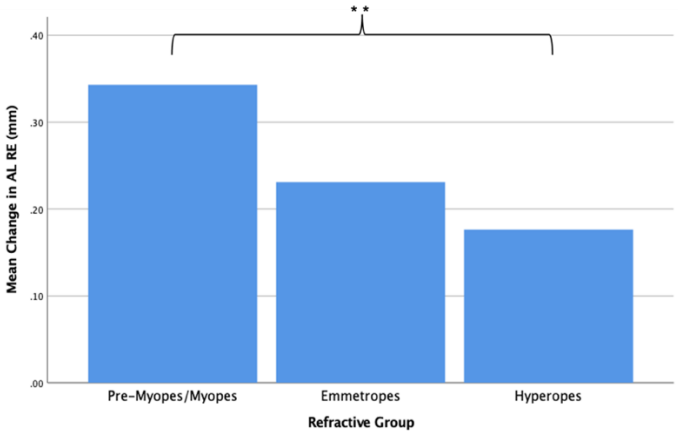


Figure 7.4.1. Bar chart showing the mean change in AL between refractive groups, with the brace and stars indicating where the significant difference is.

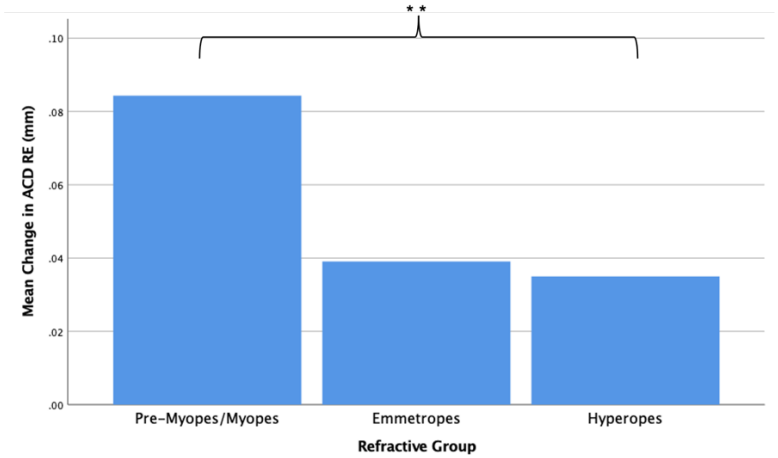


Figure 7.4.2. Bar chart showing the mean change in ACD between refractive groups, with the brace and stars indicating where the significant difference is.

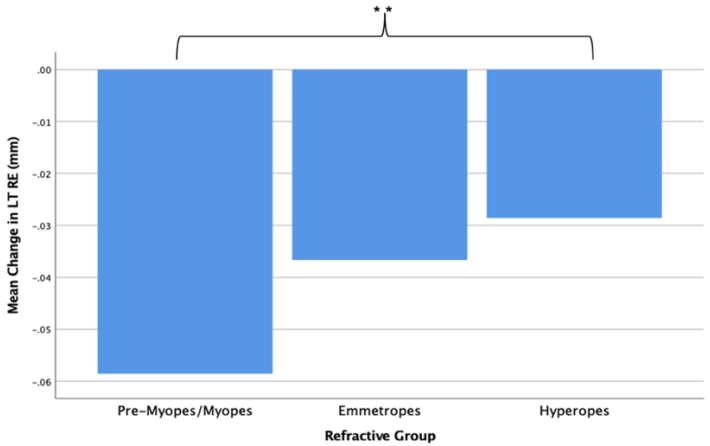


Figure 7.4.3. Bar chart showing the mean change in LT between refractive groups, with the brace and stars indicating where the significant difference is.

One-way ANOVAs identified that the number of myopic parents did not influence the magnitude of change in SER or AL measured in the 12-month period ($p>0.05$ for one or two myopic parents). However, those with one myopic parent had on average -0.41 D of myopic shift compared to a mean of -0.15 D amongst those with no myopic parents. The mean axial elongation measured was 0.22, 0.26, and 0.25 mm for children with none, one and two myopic parents, respectively.

7.4.2. Light Exposure and Change in SER and AL (Actiwatch and Clouclip)

The light exposure parameters and the duration of the light exposure during different periods of the day, and their respective correlations with SER and AL change are presented in Table 7.4.5.

Actiwatch Light Exposure Parameter	Average for all Participants	Correlation with SER Change	Correlation with AL Change
Light Exposure Daytime (lux)	654.23	r=-0.081 p=0.636	r=0.132 p=0.437
Time Spent in Scotopic Light Daytime (mins)	71.90	r=0.198 p=0.241	r=-0.159 p=0.348
Time Spent in Mesopic Light Daytime (mins)	79.97	r=0.135 p=0.425	*r=-0.327* *p=0.048*
Time Spent in Photopic Light Daytime (mins)	623.69	r=0.024 p=0.890	r=-0.035 p=0.839
Time Spent Outdoors Daytime (mins)	83.63	r=-0.171 p=0.311	r=0.199 p=0.238
Time Spent in Scotopic Light Night-time (mins)	468.43	r=-0.070 p=0.679	r=0.235 p=0.161
Time Spent in Mesopic Light Night-time (mins)	67.98	r=0.207 p=0.219	r=-0.312 p=0.060
Time Spent in Photopic Light Night-time (mins)	44.39	r=-0.101 p=0.551	r=-0.039 p=0.820
Night-time Light Exposure (lux)	0.44	r=-0.254 p=0.129	r=0.288 p=0.083

Weekend Evening Time Spent in Mesopic Light (mins)	46.38	r=0.100 p=0.555	*r=-0.384* *p=0.019*
Clouclip Light Exposure Parameter	**Average for all Participants**	**Correlation with SER Change**	**Correlation with AL Change**
Light Exposure (lux)	540.75	r=-0.072 p=0.743	r=0.160 p=0.466
Time Spent in Mesopic Light (mins)	13.59	*r=0.481* *p=0.020*	*r=-0.469* *p=0.024*
Time Spent in Photopic Light (mins)	496.20	r=-0.004 p=0.986	r=-0.096 p=0.663
Time Spent Outdoors (mins)	71.66	r=-0.153 p=0.487	r=0.196 p=0.371
Illumination During Near Work (lux)	139.73	r=-0.124 p=0.581	r=0.242 p=0.278
Sunlight Exposure Duration (mins)	72.41	r=-0.221 p=0.324	r=0.199 p=0.374
Sunlight Exposure Frequency per Day	11.05	r=-0.327 p=0.137	r=0.199 p=0.376
Weekday Afternoon Time Spent in Mesopic Light (mins)	2.49	r=0.421 p=0.051	*r=-0.450* *p=0.036*
Weekday Evening Time Spent in Mesopic Light (mins)	6.51	*r=0.454* *p=0.034*	r=-0.387 p=0.075

Weekend Evening Time Spent in Mesopic Light (mins)	11.59	*r=0.468* *p=0.028*	*r=-0.512* *p=0.015*

Table 7.4.5. The average daily light exposure parameters for all the participants combined and the Pearson's correlations between each light exposure parameter with change in SER and change in AL over the 12-month period. Light exposure was analysed in two ways; using the original cut-offs to define the category, and using the adjusted cut-offs determined by the validation study of the devices (Chapter 3), with the latter being presented in the table. There were no notable differences between the outputs using the original and new cut-offs hence the new classifications alone were used for all further analysis. The statistically significant durations of light exposures during specific time periods were included in the table also.

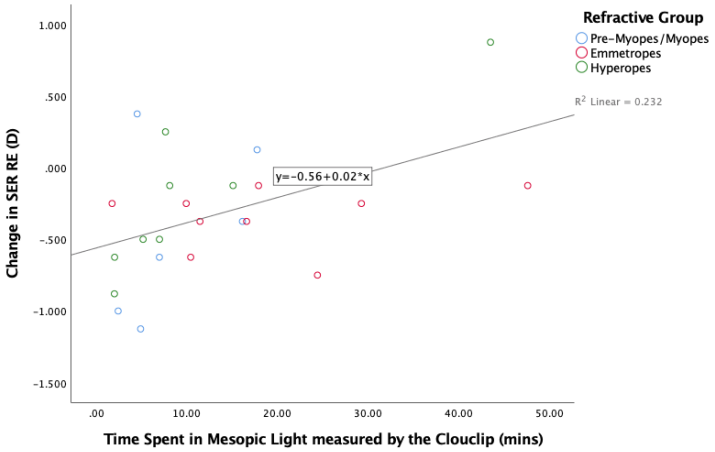


Figure 7.4.4. Scatterplot of time spent in mesopic light (measured by the Clouclip) against change in SER (D). Pearson's correlation shows a statistically significant positive correlation (r=0.481, p=0.020).

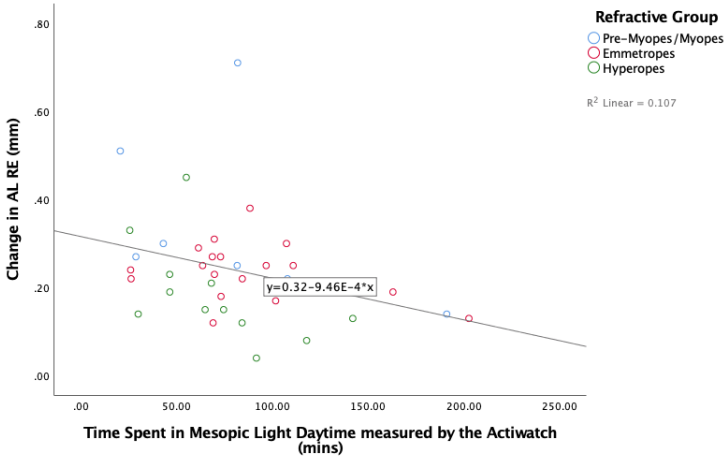


Figure 7.4.5. Scatterplot of time spent in mesopic light during the day (measured by the Actiwatch) against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.327, p=0.048).

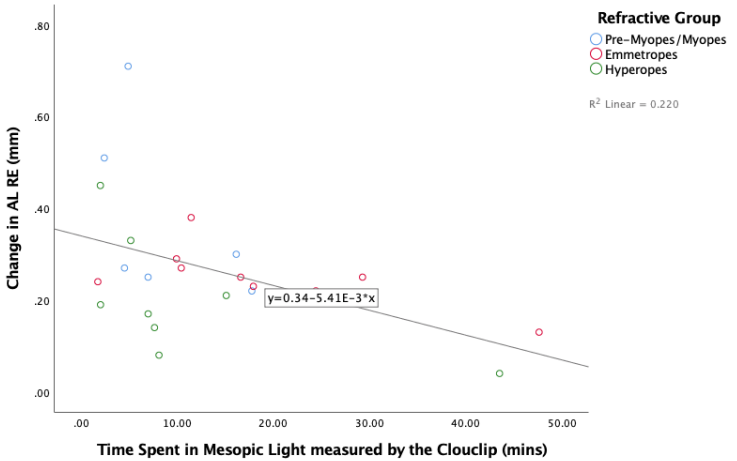


Figure 7.4.6. Scatterplot of time spent in mesopic light (measured by the Clouclip) against the change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.469, p=0.024).

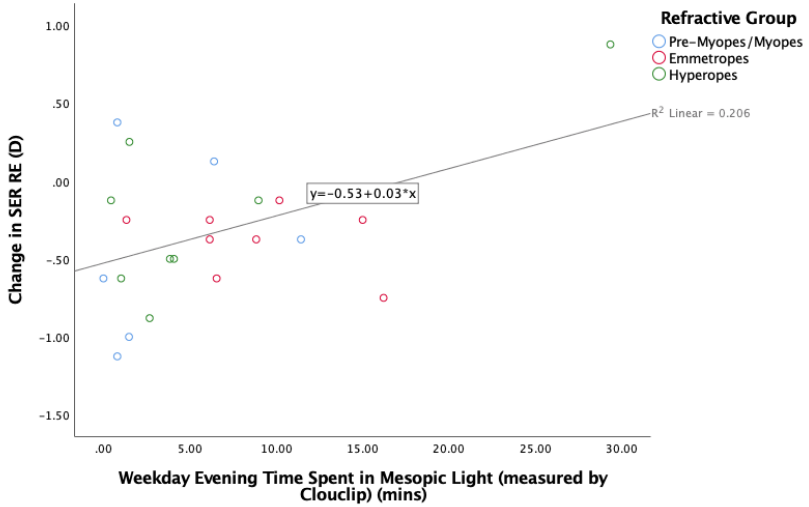


Figure 7.4.7. Scatterplot of time spent in mesopic light on weekday evenings (measured by the Clouclip) against change in SER (D). Pearson's correlation shows a statistically significant positive correlation (r=0.454, p=0.034).

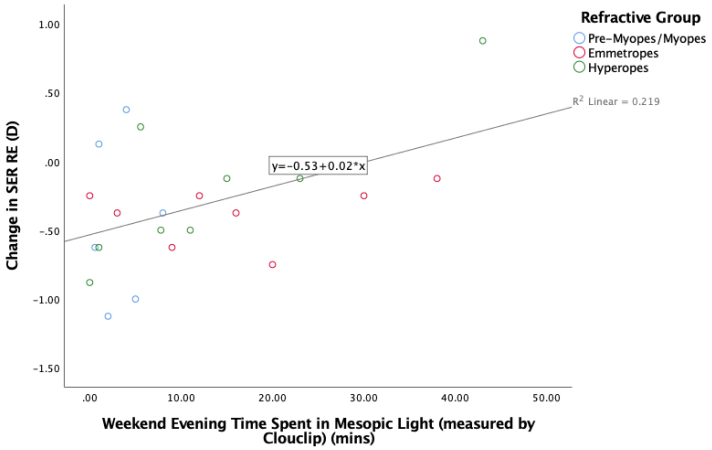


Figure 7.4.8. Scatterplot of time spent in mesopic light on weekend evenings (measured by the Clouclip) against change in SER (D). Pearson's correlation shows a statistically significant positive correlation (r=0.468, p=0.028).

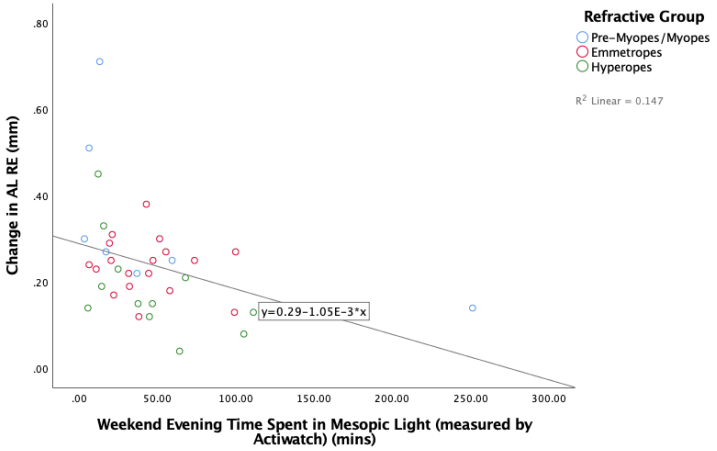


Figure 7.4.9. Scatterplot of time spent in mesopic light on weekend evenings (measured by the Actiwatch) against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.384, p=0.019).

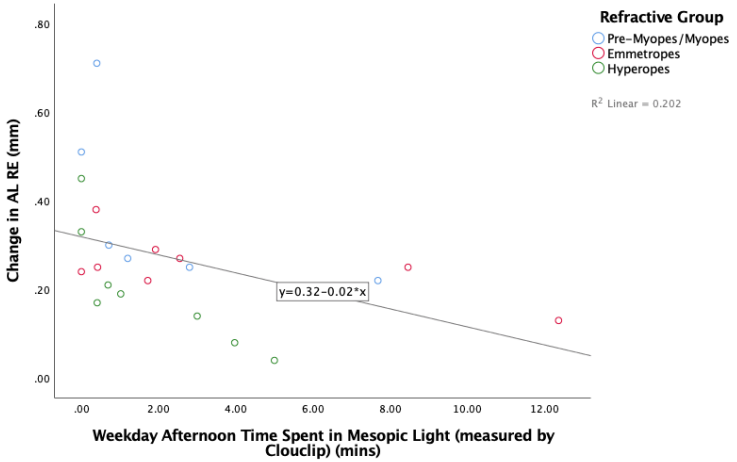


Figure 7.4.10. Scatterplot of time spent in mesopic light on weekday afternoons (measured by the Clouclip) against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.450, p=0.036).

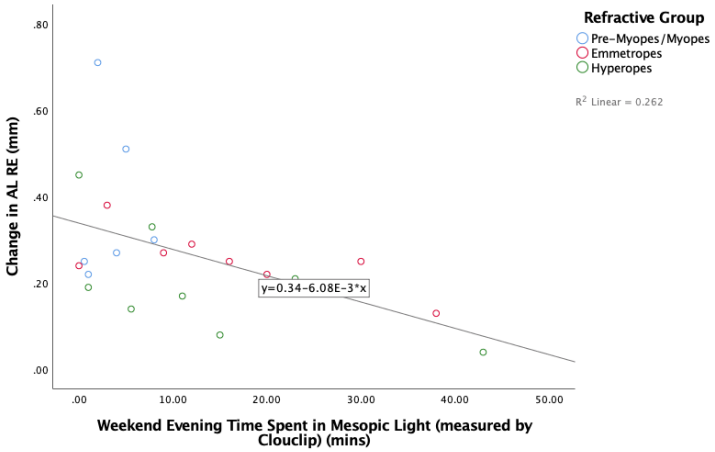


Figure 7.4.11. Scatterplot of time spent in mesopic light on weekend evenings (measured by the Clouclip) against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.512, p=0.015).

7.4.3. Physical Activity and Change in SER and AL (Actiwatch and PAQ-C)

The physical activity parameters and the duration of the physical activity levels during different periods of the day, and their respective correlations with SER and AL change are presented in Table 7.4.6.

Actiwatch Physical Activity Parameter	Average for all Participants	Correlation with SER Change	Correlation with AL Change
Physical Activity (cpm)	333.43	r=-0.160 p=0.345	r=-0.017 p=0.922
Time Spent Sedentary (mins)	335.90	r=0.313 p=0.060	r=-0.195 p=0.247
Time Spent on Light Activity (mins)	356.59	r=-0.203 p=0.229	r=0.078 p=0.647
Time Spent on Moderate Activity (mins)	91.77	r=-0.142 p=0.400	r=0.080 p=0.636
Time Spent on Vigorous Activity (mins)	74.93	r=-0.098 p=0.565	r=-0.006 p=0.973
PAQ-C Score	3.14	r=0.061 p=0.705	r=0.049 p=0.761
Weekend Morning Time Spent on Moderate Activity (mins)	24.54	r=-0.218 p=0.194	*r=0.338* *p=0.041*

Table 7.4.6. The average daily physical activity parameters for all participants and the Pearson's correlations between each physical activity parameter and the change in SER and change in AL over the 12-month period. The statistically significant durations of physical activity levels during different periods of the day were included in the table also.

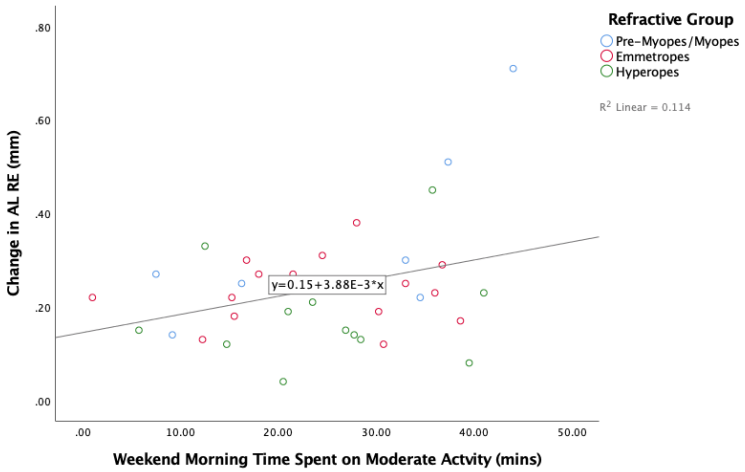


Figure 7.4.12. Scatterplot of time spent on moderate activity against change in AL (mm). Pearson's correlation shows a statistically significant positive correlation (r=0.338, p=0.041).

7.4.4. Sleep and Change in SER and AL (Actiwatch and PSQI)

The sleep parameters measured by the Actiwatch and PSQI, and their respective correlations with SER and AL change are presented in Table 7.4.7.

Actiwatch Sleep Parameter	Average for all Participants	Correlation with SER Change	Correlation with AL Change
Bedtime (hh:mm:ss)	21:12:07	r=0.019 p=0.911	r=-0.124 p=0.464
Get Up Time (hh:mm:ss)	07:15:51	r=0.062 p=0.717	r=-0.197 p=0.243
Time in Bed (hh:mm:ss)	10:03:43	r=0.038 p=0.823	r=-0.045 p=0.791
Hours of Sleep (hh:mm:ss)	8:41:12	r=-0.126 p=0.459	r=0.137 p=0.418
Sleep Onset (mins)	9.57	r=0.081 p=0.632	r=-0.135 p=0.426
Sleep Efficiency (%)	86.37	r=-0.261 p=0.119	r=0.296 p=0.075
Wake After Sleep Onset (WASO) (mins)	55.42	r=0.238 p=0.157	r=-0.316 p=0.057
Number of Awakenings	41.88	r=0.187 p=0.268	r=-0.155 p=0.361
PSQI Sleep Parameter	**Average for all Participants**	**Correlation with SER Change**	**Correlation with AL Change**
Bedtime (hh:mm)	20:03	r=-0.185 p=0.246	r=-0.062 p=0.698

Sleep Onset (mins)	20.66	r=0.215 p=0.177	r=-0.233 p=0.143
Get Up Time (hh:mm)	07:06	r=-0.077 p=0.631	r=0.027 p=0.868
Hours of Sleep (hours)	10.20	r=-0.148 p=0.356	r=0.117 p=0.465
PSQI Score	2.56	r=0.170 p=0.287	r=-0.103 p=0.523

Table 7.4.7. The average daily sleep parameters for all participants and the Pearson's correlations between each sleep parameter and the change in SER and change in AL over the 12-month period.

Sleep quality defined as good or poor by the score on PSQI was positively correlated with change in SER (r=0.229, p=0.149) and negatively correlated with change in AL (r=-0.156, p=0.331), but neither were statistically significant.

7.4.5. Near Activity and Change in SER and AL (Clouclip and Screen-Time Questionnaire)

The near activity parameters and the duration of the near activities during different periods of the day, and their respective correlations with SER and AL are presented in Table 7.4.8.

Clouclip Near Activity Parameter	Average for all Participants	Correlation with SER Change	Correlation with AL Change
Average Viewing Distance (cm)	94.19	r=-0.376 p=0.077	r=0.224 p=0.304
Time Spent on Very Close Viewing (mins)	161.75	r=0.388 p=0.067	r=-0.266 p=0.219
Time Spent on Near Viewing (mins)	69.61	r=-0.299 p=0.166	r=0.144 p=0.512
Time Spent on Intermediate Viewing (mins)	79.12	*r=-0.435* *p=0.038*	r=0.175 p=0.423
Time Spent on Distance Viewing (mins)	233.30	r=-0.327 p=0.128	r=0.181 p=0.409
Average Duration of Near Work (mins)	112.14	r=-0.203 p=0.366	r=0.155 p=0.492
Maximum Duration of Near Work (mins)	20.27	r=0.239 p=0.284	r=-0.163 p=0.469
Average Near Work Distance (cm)	30.09	r=-0.398 p=0.066	r=0.253 p=0.255
Weekday Evening Time Spent on Very Close Viewing (mins)	64.78	*r=0.522* *p=0.013*	*r=-0.489* *p=0.021*
Weekday Evening Time Spent on Intermediate Viewing (mins)	25.46	*r=-0.430* *p=0.046*	r=0.196 p=0.383

Weekend Morning Time Spent on Distance Viewing (mins)	55.48	*r=-0.555* *p=0.007*	r=0.382 p=0.080
Weekend Afternoon Time Spent on Near Viewing (mins)	17.18	*r=-0.436* *p=0.043*	r=0.350 p=0.110
Weekend Afternoon Time Spent on Intermediate Viewing (mins)	24.17	*r=-0.489* *p=0.021*	r=0.302 p=0.172
Weekend Evening Time Spent on Very Close Viewing (mins)	65.61	r=0.280 p=0.206	*r=-0.430* *p=0.046*
Weekend Evening Time Spent on Intermediate Viewing (mins)	21.16	*r=-0.435* *p=0.043*	r=0.161 p=0.475

Table 7.4.8. The average daily near activity parameters for all participants and the Pearson's correlations between each parameter and the change in SER and change in AL over the 12-month period. The statistically significant durations of near activities during different periods of the day were included in the table also.

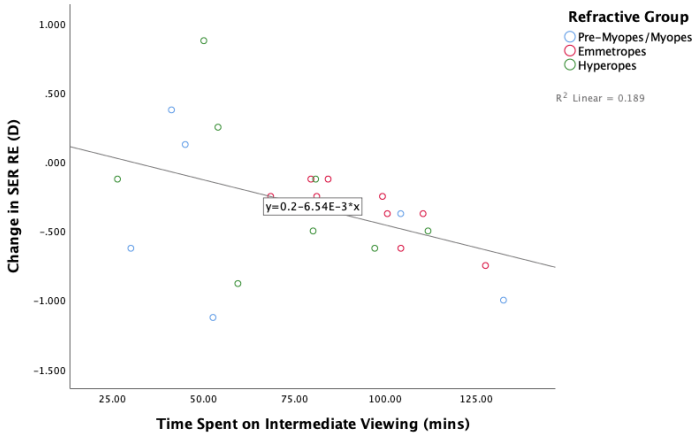


Figure 7.4.13. Scatterplot of time spent on intermediate viewing against change in SER (D). Pearson's correlation shows the statistically significant moderate negative correlation (r=-0.435, p=0.038).

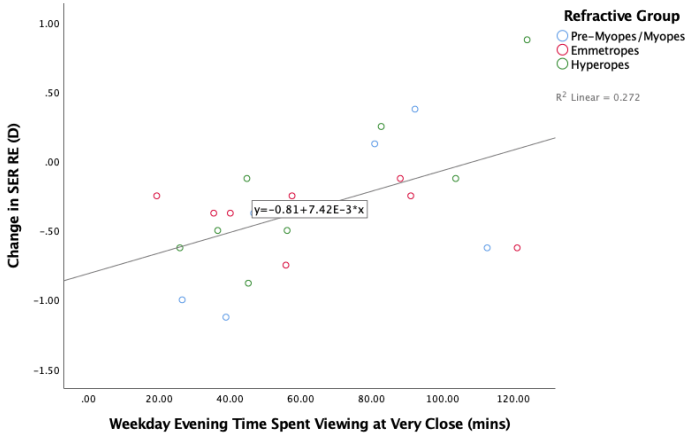


Figure 7.4.14. Scatterplot of time spent viewing at very close on weekday evenings against change in SER (D). Pearson's correlation shows a statistically significant positive correlation (r=0.522, p=0.013).

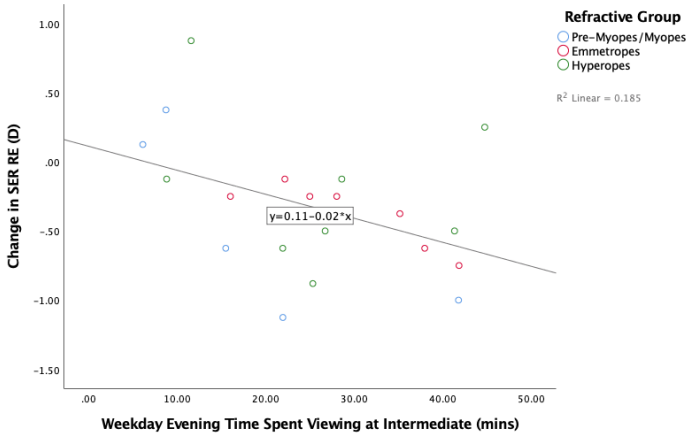


Figure 7.4.15. Scatterplot of time spent viewing at intermediate on weekday evenings against change in SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.430, p=0.046).

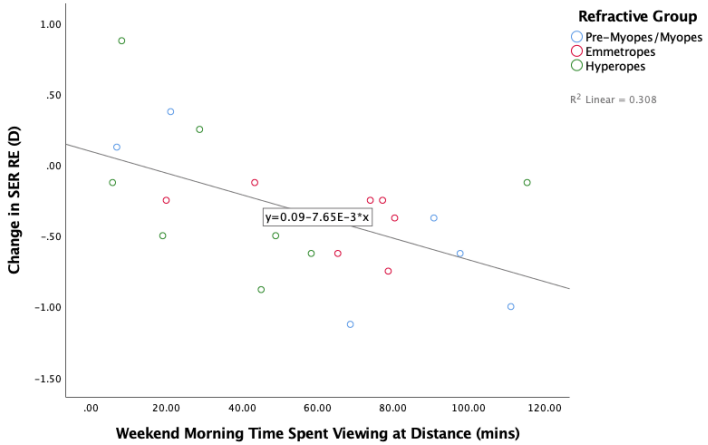


Figure 7.4.16. Scatterplot of time spent viewing at distance on weekend mornings against change in SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.555, p=0.007).

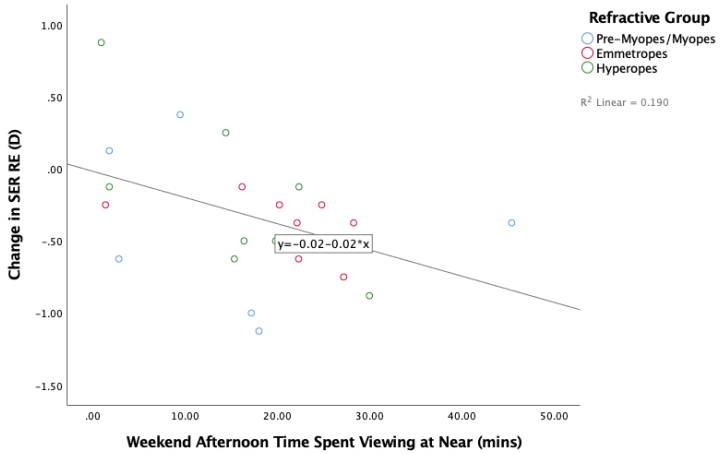


Figure 7.4.17. Scatterplot of time spent viewing at near on weekend afternoons against change in SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.436, p=0.043).

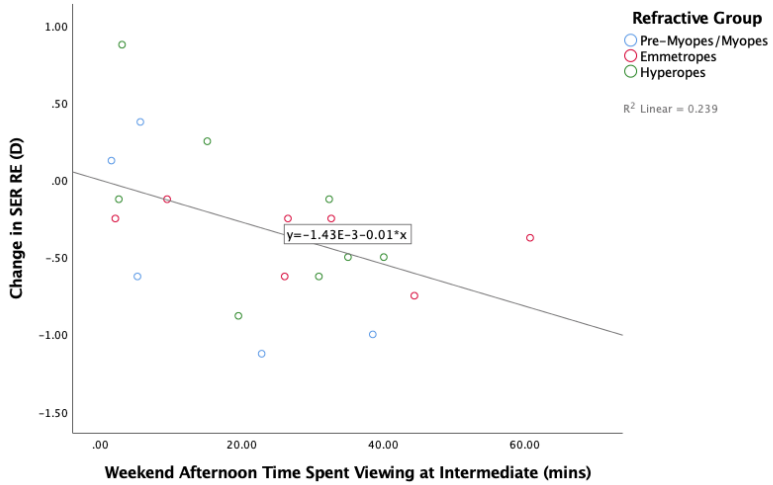


Figure 7.4.18. Scatterplot of time spent viewing at intermediate on weekend afternoons against change in SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.489, p=0.021).

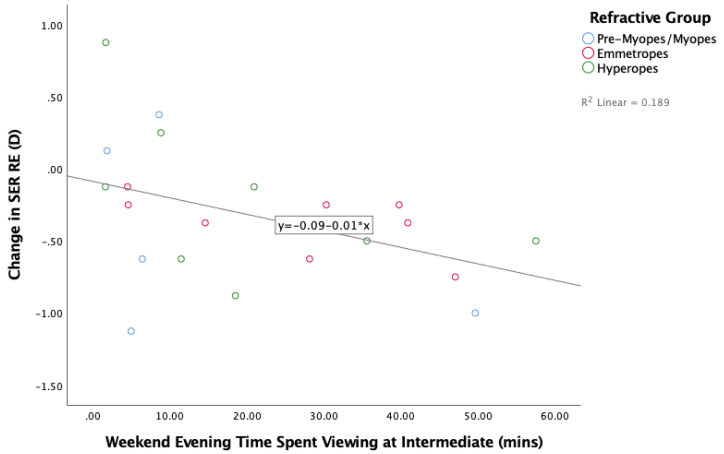


Figure 7.4.19. Scatterplot of time spent viewing at intermediate on weekend evenings against change in SER (D). Pearson's correlation shows a statistically significant negative correlation (r=-0.435, p=0.043).

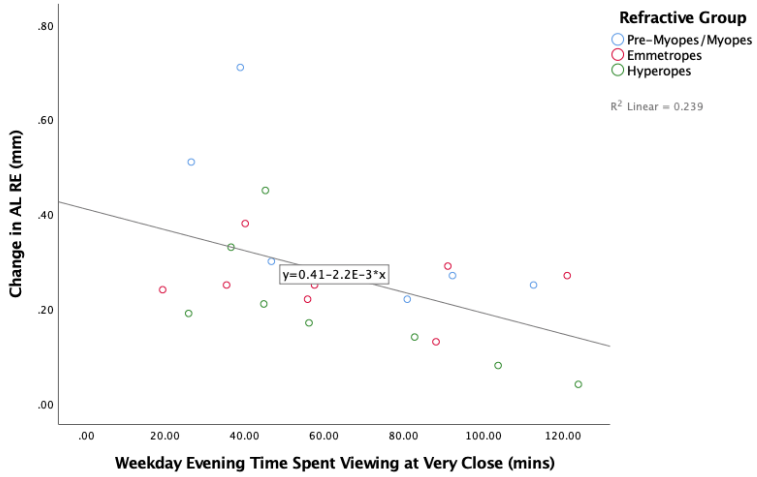


Figure 7.4.20. Scatterplot of time spent viewing at very close on weekday evenings against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.489, p=0.021).

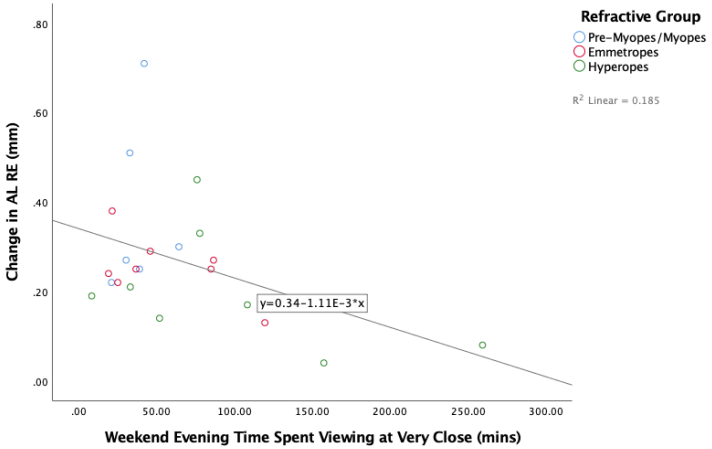


Figure 7.4.21. Scatterplot of time spent viewing at very close on weekend evenings against change in AL (mm). Pearson's correlation shows a statistically significant negative correlation (r=-0.430, p=0.046).

Parameter	Change in SER (D)	One-Way ANOVA	Change in AL (mm)	One-Way ANOVA
Time Spent on TV/Video Games	None=-0.47 <1 hour=-0.06 1-2 hours=-0.36 2+ hours=-0.46	p=0.101	None=0.25 <1 hour=0.23 1-2 hours=0.27 2+ hours=0.19	p=0.811
Time Spent on Phone/Tablet	None =-0.38 <1 hour=-0.24 1-2 hours =-0.31 2+ hours =0.50	p=0.160	None=0.24 <1 hour=0.22 1-2 hours=0.33 2+ hours=0.13	p=0.226
Time Spent on Computer/Laptop	None=-0.28 <1 hour=-0.13 1-2 hours n/a 2+ hours n/a	p=0.693	None=0.25 <1 hour=0.08 1-2 hours n/a 2+ hours n/a	p=0.185
Time Spent on Device before Sleep	None =-0.29 1-30 mins =-0.29 30 mins-1 hour n/a 1+ hours=0.50	p=0.120	None=0.25 1-30mins=0.22 30 mins-1 hour n/a 1+ hours=0.13	p=0.598

Table 7.4.9. Table showing the mean change in SER and AL for each duration of screen time. There were no statistically significant differences in SER or AL change for any of the screen time data using one-way ANOVAs. The durations with n/a had no participants spending that duration on screens.

7.4.6. Multiple Regression Analysis for Change in SER and AL

Hierarchical multiple regression analysis revealed no significant independent associations between any sleep, light exposure, or physical activity parameters and change in either SER or AL after controlling for age, gender, parental history of myopia, time of year of data collection or baseline SER. The named controlled variables explained 22% of the variance in change in SER but there were no significant independent associations from any of the parameters, F (5, 12) =0.68, p=0.645. The named controlled variables explained 35% of the variance in change in AL but there were no significant independent associations from any of the parameters, F (5, 12) =1.32, p=0.321.

7.4.7. Odds Ratios for Classification as Accelerated Eye Growth using 90th Centile Cut-Offs

Univariate logistic regression analyses were performed for all variables to define their odds ratios for classification as accelerated eye growth, and only those that were significant are presented in Table 7.4.10.

Parameter	Univariate Odds Ratios (95% confidence intervals) and p values
Age at Follow Up	*0.065 (0.006-0.686), p=0.023*
Average Daily Duration of Near Work at Baseline	*1.031 (1.001-1.062), p=0.042*
Parental Myopia (no [reference group], 1 myopic parent, 2 myopic parents, or at least 1 myopic parent)	*1 myopic parent: 6.29 (1.02-38.65), p=0.047* 2 myopic parents: 2.75 (0.16-46.79), p=0.484 At least 1 myopic parent: 5.50 (0.94-32.21), p=0.059
Average Daily Duration of Phone/Tablet Use at Baseline (not used [reference group], less than 1 hour, 1-2 hrs, 2-3 hrs, 3+hrs)	<1 hour: 1.60 (0.231-11.08), p=0.634 *1-2 hours: 20.00 (1.42-282.45), p=0.027* 2-3 hours: no participants 3+ hours: no participants
Average Daily Duration of TV/Video game Use at Baseline (less than 1 hour [reference group], 1-3 hrs, 3+hrs)	*1-3 hours: 7.50 (1.14-49.26), p=0.036* 3+ hours: no participants

Table 7.4.10. Results of the univariate analyses with the parameters that are significant underlined and in italics. None of the parameters remained significant on multivariate analysis.

7.5. Discussion

This is the first study to explore baseline quantitative measures of light exposure, physical activity, sleep, and near activity in young children (aged 7-9-years) in the UK and their relationship to refractive error progression and axial elongation over a 12-month period. The patterns of ocular growth and refractive change between the different refractive groups were also explored.

7.5.1. Change in SER and Ocular Biometry over 12-months

Over the 12-month period between visits, the mean SER became significantly less hyperopic, the axial length and anterior chamber depth became significantly longer, and the lens thickness reduced significantly for the whole cohort. On average, children who were pre-myopic/myopic at baseline showed clinically significantly greater myopic shift (-0.41 D) than emmetropes (-0.15 D), and hyperopes (-0.20 D). These findings are comparable to the 3-year follow up data from the original NICER 1.0 6-7-year-old cohort, where the median annual SER change for the cohort as a whole was -0.13 D, and mean SER change in the emerging myopes (risk of myopia onset before 10-years-old) was -0.41 D (McCullough *et al.*, 2020). In the present study there was a downward trend in mean axial elongation from pre-myopes/myopes (0.34 mm) to emmetropes (0.23 mm) to hyperopes (0.18 mm), but the difference was only statistically significant between pre-myopes/myopes and hyperopes. These results are comparable to Tideman *et al.* (2018) who reported axial increases of 0.34 mm, 0.19 mm, and 0.15 mm/year for myopes, emmetropes and hyperopes respectively, in a large cohort of European children.

Data from NICER 1.0 were used to define a criterion of >0.26 mm/year of axial elongation (90% centile) as accelerated eye growth for children aged between 6-7 to 9-10-years old. There were 12 participants in the present study who demonstrated accelerated eye growth and 30 participants with normal eye growth according to this criterion. Younger age at follow up was related to increased OR for classification as exhibiting accelerated eye growth on univariate regression analysis, OR 0.065 (95% CI 0.006-0.686), p=0.023. This translates that for every additional year younger the child is 15.4 times more likely to exhibit accelerated eye growth. This agrees with the finding that axial elongation is faster in younger children than older children (McCullough *et al.*, 2020).

The increase in ACD in the present study was significantly greater in the pre-myopes/myopes (0.08 mm) compared to the hyperopes (0.04 mm) and the difference between pre-myopes/myopes and emmetropes was approaching statistical significance (0.04 mm), p=0.051. The pre-myopes/myopes lens thickness decreased significantly more (-0.06 mm) than the hyperopes (-0.03 mm) in line with the findings of Mutti *et al.* (2012) who reported that the lens thins while the axial length increases to try and maintain emmetropia in young children.

7.5.2. Light Exposure and Change in SER and AL (start here)

The present study found that increased time spent in mesopic light in the daytime (dim light e.g., TV or side light only on and main room lights off) was related to less myopic shift and less axial elongation. These findings support those of Landis *et al*. (2018) where the authors report that non-myopes spent a greater amount of time in light levels between <1-1 lux compared with myopic children, however they defined this light condition as scotopic in their paper. The light levels in Landis *et al.*'s study attributed as 'scotopic' could have been anywhere between scotopic and mesopic light. Therefore, there is the potential that dim light has a role to play in the prevention of myopia. An interesting finding by Flanagan *et al.* (2020) was a unique significant contribution of time spent in mesopic light (measured by the Actiwatch) to morning serum melatonin levels; less time spent in mesopic light (defined as 0.01-<3 lux) was related to higher levels of morning serum melatonin, which in turn was associated with more myopic SER in a population of young UK adults (Flanagan *et al.*, 2020) indicating a possible link between dim light exposure and myopia. When broken down into different time periods the present study demonstrated that time spent in mesopic light (measured by Clouclip) by the participants in the present study on weekday and weekend evenings was associated with less myopic shift and time spent in mesopic light (measured by Actiwatch and Clouclip) on weekend evenings was associated with less axial elongation, as was time spent in mesopic light (measured by Clouclip) on weekday afternoons. These findings reinforce the role of dim light in the prevention of myopia and the likely mechanism for this is via regulation of the circadian rhythm (Flanagan *et al.*, 2020). Phillips, Backhouse and Collins (2012) reported that bright light in the middle of the day does not affect the circadian rhythms but, bright light at dawn and dusk are more disruptive. The findings from the present study reinforces the notion that dim light exposure (in this case in the evenings) is protective against myopic shift and axial elongation.

Time spent outdoors, and increased levels of light exposure did not appear related to myopia progression over a 12-month period in the present study. This could support the literature that increased light exposure and/or time spent outdoors are effective at delaying the onset of myopia but not slowing the progression of myopia (Xiong *et al.*, 2017).

More time spent in mesopic light at night was associated with less axial elongation (approaching statistical significance, p=0.060) indicating the protective effect of lower levels of illumination during sleep in agreement with the findings from the cross-sectional study (Chapter 5). Conversely, it could be that more time spent in mesopic light at night reduces the time spent in brighter light at night (indoor photopic), which is deemed to be more myopiagenic (Quinn *et al.*, 1999; Gooley *et al.*, 2011). Quinn *et al.* (1999) reported a dose dependant relationship between refraction and night-time light with those children sleeping with a room light on before the age of 2 years, having a higher prevalence of myopia and high myopia (>-5.00D) by adolescence than those under 2-years-old who slept with a night-light and higher again than those sleeping in darkness. The mechanism through which such early night-time light exposure may influence refractive outcome could be through the disruption of the circadian rhythm by decreasing melatonin (Gooley *et al.*, 2011; Chakraborty *et al.*, 2018; Leger *et al.*, 2019; Ostrin, 2019). Melatonin levels are known to rise in the evenings and to promote sleep onset and exposure to light at night suppresses melatonin, interfering with sleep timing and sleep quality (Gooley *et al.*, 2011; Bedrosian and Nelson, 2017). A study of young adults found significantly more myopic progression in those with ≤5.6 hours of darkness per day again supporting a role for the light-dark cycle on refractive development, but these findings were limited by questionnaire-based data (Loman *et al.*, 2002).

7.5.3. Sleep and Change in SER and AL

There were a number of associations between objectively measured sleep parameters and change in AL that were moderately correlated but did not reach statistical significance. Those with more axial elongation over the 12-month period tended to have higher sleep efficiency (total sleep time/total time in bed x100) and less wake after sleep onset (WASO). These findings are comparable to the associations between these two sleep parameters and baseline axial length in the cross-sectional study (Chapter 5). The findings lead us to reaffirming our discussion in Chapter 5, where the pre-myopes/myopes and those with faster axial elongation go to bed later, have a faster sleep onset and less wake during sleeping hours therefore having a higher sleep efficiency than the more hyperopic

individuals and those with slower axial elongation. Ostrin *et al.*, (2020) reported that these findings could be indicative of greater sleep debt and deprivation among those with faster sleep onset.

7.5.4. Near Activity and Change in SER and AL

Those individuals with more myopic shift of SER tended to spend increased time viewing at intermediate distances. Guo *et al.* (2017) reported greater axial elongation and increased incidence of myopia in those spending more time indoors studying. We need to be cautious when interpreting the results of increased incidence of myopia in Guo *et al.*'s study as they did not use cycloplegia to determine refractive error and therefore could be overestimating the presence of myopia, but the axial length measures are reliable without cycloplegia. When broken down into different time periods, increased time viewing at intermediate on weekday and weekend evenings was related with more myopic shift. Increased time spent viewing at near and intermediate on weekend afternoons were related with more myopic shift. These intermediate viewing distances by participants within our study would occur at 50-120 cm and would include time spent on computers/laptops/tablets. This finding would agree with Yi and Li (2011) where the authors reported that more myopia progression was found in those spending more time on computers. Phones are more likely to viewed closer than 50 cm, e.g., one such study reported viewing distances of 36.2 and 32.2 cm for text messages and internet use, respectively (Bababekova *et al.*, 2011). A systematic review found higher odds of myopia (OR's=1.14) with longer periods of time spent on near work, but there is no randomised control trial reducing near work as an intervention for myopia progression (Mak *et al.*, 2018). A previous study from Taiwan reported faster progression of myopia in 7-8-year-old "already myopes" with a shorter viewing distance (<30cm), and without a 10-min rest after 30 minutes of near work (Hsu *et al.*, 2017). Huang *et al.* (2019) reported that 9-11-year-olds in Taiwan with closer self-reported working distances had an increased risk of myopia progression over a 6-month period. In contrast to this, the present study found increased time spent viewing at very close on weekday evenings was related with less myopic shift and increased time spent viewing at very close on weekday and weekend evenings were associated with less axial elongation, because there were some hyperopes who spent a lot of time on this type of near activity.

Average duration of near work was related to a slightly increased risk for accelerated eye growth (OR 1.031, 95% CI 1.001-1.062 per minute increase in average duration of near

work, p=0.042). This translates to each additional 30 minutes of consistent near work increasing the risk for accelerated eye growth by 1.93 times. Ip *et al.* (2008) found that continuous reading >30 mins/day increased the odds of having myopia in a sample of 12-year-old Australian children, while Li *et al.* (2015) reported greater odds for myopia in 12-year-old Chinese children with >45 minutes of continuous reading/day. Those who spent longer periods on continuous reading also had more myopic progression per year (Jones-Jordan *et al.*, 2012; Öner *et al.*, 2016) in agreement with the findings from the present study.

The assumption that the increased accommodation associated with time spent on near work was controlling eye growth leading to myopia has been widespread. However, the evidence is inconsistent with muscarinic agents blocking the elongation of chick eyes by a non-accommodative mechanism, highlighting the potential for alternative sites of action (McBrien, Moghaddam and Reeder, 1993). Given the similarities between eye growth of humans and chicks it does seem likely that there is another mechanism by which increased near work increased the risk of myopia. Chakraborty *et al.* (2020) note that the link between near work and myopia development could be due to increased hyperopic defocus and a lack of outdoor light exposure or could be a combination of both risk factors as the typical pattern of retinal focus experienced in outdoor environments (less near focusing and less exposure to hyperopic blur), may also play a protective role over the progression of myopia. These findings indicate the need to vary children's visual activities to reduce the risk of myopia development and progression.

7.5.5. Screen Time and Change in SER and AL

The findings indicate an association between use of screens and risk of accelerated eye growth. Using a phone/tablet for 1-2 hours/day was associated with a significantly increased risk for accelerated eye growth (OR 20.0, 95% CI 1.42-282.45, p=0.027) compared to those spending no time on a phone/tablet each day. Additionally, watching TV/video games for 1-3 hours per day was associated with an increased risk for accelerated eye growth (OR 7.50, 95% CI 1.14-49.26, p=0.036) compared to those watching TV/video games for <1 hour per day.

More robust evaluation of screen time using objective measures in the future would help provide further refinement of advice for parents regarding children's eye health. This would also reduce the potential for both recall and social desirability bias which is

associated with the use of questionnaire data (Neumann, 2015). Some participants parents in the present study reported that their child spent no time using devices at all over the course of the week, which could be an example of social desirability bias in action.

7.5.6. Physical Activity Parameters and Change in SER and AL

Participants with less myopic shift over the 12-month period were found to spend more time sedentary, although the difference was not statistically significant, p=0.060. This finding regarding the progression of myopia over 12-months is contrary to the cross-sectional findings of NICER 1.0 and the Ireland Eye Study (IES), where increased time spent sedentary was associated with being myopic as a teenager (O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019). Increased time spent on moderate activity on weekend mornings was statistically significantly associated with increased axial elongation but not with change in SER whereas in Chapter 6, time spent on moderate and vigorous activity on weekend afternoons and evenings were significantly associated with classification as pre-myopic/myopic. In Chapter 6, it was previously hypothesised that higher levels of physical activity later in the day was potentially disrupting children's circadian rhythms (Yamanaka *et al.*, 2006; Rubio-Sastre *et al.*, 2014), which could be to be promoting myopia development; however, these longitudinal findings that higher levels of moderate activity on weekend mornings is promoting axial growth over a 12-month period suggest that the exact mechanism behind this is currently unclear.

7.5.7. Parental Myopia and Change in SER and AL

Kurtz *et al.* (2007) found that the rate of myopia progression over a 5-year period was associated with having more myopic parents. The present study found SER changes of -0.15, -0.41 and -0.13 D for children with no, one and two myopic parents, respectively. The axial elongation for these three groups were 0.22, 0.26 and 0.25 mm for no, one and two myopic parents, respectively, and having one myopic parent was associated with increased risk for accelerated 12-month eye growth (OR 6.29, 95% CI 1.02-38.65, p=0.047). This association between accelerated eye growth and parental myopia could be explained by both genetic and environmental factors, with myopic parents potentially providing their children a more myopiagenic environment in addition to the genetic risk their eye condition confers (Zhang, Qu and Zhou, 2015; Enthoven *et al.*, 2019). Having two myopic parents was associated with an increased risk of accelerated eye growth (OR

2.75, 95% CI 0.16-46.79, p=0.484), but the result was not statistically significant, and this could be due to the group with two myopic parents being limited to three children.

7.5.8. Strengths and Limitations

This study has many strengths including, the younger 6-9-year-old cohort enabling us to determine if differences in behaviours were evident prior to or just after the onset of myopia. Additionally, this study is the first of its kind in the UK and Ireland where objective measures of the potential risk factors for myopia were taken alongside a robust evaluation of refractive error via cycloplegic autorefraction over a 12-month period to examine the impact of these potential risk factors on axial elongation or myopic shift. Another benefit is use of the definition of accelerated eye growth, enabling exploration of differences in behaviours between those children whose eyes are growing faster than the expected normal physiological growth occurring in childhood.

The present study has several limitations. Firstly, the study is limited by the smaller sample that were available for follow-up data collection (n=42), this potentially reduced the statistical power to find relationships between the objectively measured parameters and change in refractive error and ocular growth. The loss of participants to follow-up enhanced the uneven number of participants in each baseline refractive group; 7 pre-myopes/myopes, 21 emmetropes and 14 hyperopes, which could make it difficult to help solidify trends in ocular growth with behavioural patterns. However, the numbers for each group were reflective of the proportion of refractive errors in the general population at this age. Additionally, the potential risk factors for myopia were only measured at baseline and in a single season and might not necessarily be reflective of the participants' patterns of behaviour over the whole 12-month period.

Future studies could examine the change in axial length over a 6-month period at two or more intervals in order to determine seasonal differences in axial growth. This could be done without the use of cycloplegia as Huang *et al.* (2012) determined that there was no statistically significant difference between measures of axial length made with and without cycloplegia. This would be useful to tease out how light exposure and time spent outdoors affects the progression of myopia as our study was limited by data collection year-round. This was due to limited resources for maintaining data collection at times of year where the day length was more consistent and could be a reason why no statistically

significant differences in myopic progression were found in those spending more time outdoors or in higher light intensities.

7.6. Conclusion

To conclude this study of objective environmental and behavioural risk factors along with change in SER and AL over a 12-month period further supports the theory that regulated circadian rhythms promote normal eye growth and are protective against myopia with evidence of time spent in mesopic light, particularly later in the day and during sleeping hours having a protective effect against myopic eye growth. Time spent on near and intermediate viewing at different time periods were significantly associated with more myopic shift, and longer durations of continuous near work increased the odds ratios for accelerated eye growth, highlighting the potential for increased near work influencing the progression of myopia. Increased time spent on phones/tablets and watching TV/video games also increased the risk of demonstrating accelerated eye growth also. Time spent outdoors and increased levels of light exposure did not appear related to myopia progression over a 12-month period in the present study, therefore supporting the literature that they are possibly not protective over myopic progression.

Chapter 8: Thesis Conclusions & Further Research

Chapter 8: Thesis Conclusions & Further Research

8.1. Summary of Main Findings

Chapter 3 studied the inter-device reliability of two wearable devices (Actiwatch 2 and Clouclip M2) and their validity for measuring illumination and near vision metrics. It was found that the Actiwatch 2 and Clouclip M2 demonstrated good or excellent inter-device reliability for measuring light exposure, physical activity and viewing distance. The Clouclip illumination measures taken in real-world settings more closely reflected 'true' illumination measured by a gold-standard calibrated photometer than those obtained with the Actiwatch 2, particularly at higher levels of illumination. The Clouclip more accurately classified illumination levels ≥2 lux than the Actiwatch 2, but the restricted operating range means it cannot discriminate between time spent in scotopic vs low mesopic light. Interestingly, photometry measurements of >1000 lux were obtained from indoor as well as outdoor locations. This should be considered when using the widely accepted >1000 lux (Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018) as a proxy for time spent outdoors.

Chapter 4 examined whether obtaining seven days' worth of data is a valid way of profiling a persons' lifestyle in relation to their physical activity, light exposure, sleep quality and near viewing behaviours using the Actiwatch 2, Clouclip and the screen time monitoring apps. The results have confirmed the hypothesis that measures taken over seven days provide average values which are in the main, not significantly different from those obtained over 14-days. The participants in this study were all adults, and most adults tend to have less regimented lifestyles than children. Therefore, the findings that 7-days of data collection is a reliable way to profile most of the parameters mentioned in this study, should also be applicable to young participants. This is supported by Trost *et al.'s* (2005) literature review in which they report that 4-5 days of data are sufficient for profiling physical activity, as children exhibited less day-to-day variability in daily habitual physical activity than adolescents and adults. The findings that seven days is an appropriate data collection period to evaluate an individuals' habitual light exposure patterns also agrees with Ulaganathan *et al.'s* (2017) research which found that a measurement duration of at least one week and a measurement frequency of two minutes or less provides the most reliable estimates of personal outdoor light exposure measures in both children and young adults. To conclude, seven days of data collection proves to be a reliable and more efficient way of examining an individual's habitual sleep, physical

activity, light exposure, viewing distance and screen time habits, with the limits of agreement (LOAs) for each parameter investigated in the present study falling within validated limits of repeatability or published LOAs for those metrics (Phillips Respironics, 2008; Clemes *et al.*, 2012; Shin, Swan and Chow, 2015).

Chapter 5 describes the first study to quantify light exposure, physical activity, sleep, and near activity in young children in the UK and to explore relationships between children's refractive error, axial length and these objectively measured risk factors. Average light exposure was statistically significantly higher in non-myopes than pre-myopes but only during winter months, indicating that the non-myopes managed to achieve higher levels of light exposure within the limited hours of daylight available in winter which previous studies have noted is the time which most myopic eye growth occurs (Fulk, Cyert and Parker, 2002; Gwiazda *et al.*, 2014; Ulaganathan *et al.*, 2019). A notable finding from the present study was that pre-myopic/myopic children spent significantly more time in photopic light at night-time during sleep compared to emmetropes and time spent in photopic light at night significantly increased the odds of classification as pre-myopic/myopic, meaning that for every additional hour in photopic light at night during sleep, the child is 1.3 times more likely to be pre-myopic/myopic than non-myopic. This finding agrees with those of Landis *et al*. (2018) who propose that scotopic light is deemed protective against the onset of myopia and Quinn *et al.* (1999) who reported a dose dependant relationship between refraction and night-time light before the age of two years, with those children sleeping with a room light on having a higher prevalence of myopia and high myopia (>-5.00D) than those with a night-light, and higher again than those sleeping in darkness. Pre-myopes within the present study were found to be experiencing an average of 27 times higher illumination (in lux) during sleep than emmetropes, and 13.5 times more than hyperopes. This exposure to light at night may alter the natural rhythm of melatonin synthesis and release (Gooley *et al.*, 2011) leading to a disrupted circadian rhythm which is potentially a mechanism for myopic development (Chakraborty *et al.*, 2018). In the present study, higher sleep efficiency (%) was statistically significantly related to more myopic spherical equivalent refraction (SER) and longer axial length (AL) and could be related to the later bedtime and shorter sleep duration measured in the pre-myopic/myopic participant group compared to the non-myopic participants. The Pittsburgh Sleep Quality Index (PSQI) scores also indicated a trend for poorer subjective sleep quality (parental-reported) in those with more myopic refractive error. This finding agrees with those of Ostrin *et al.* (2020) who reported that

myopes aged 10-15-years had a significantly faster sleep onset than non-myopes and the authors reported that shorter sleep onsets can be associated with greater sleep debt and sleep deprivation. Higher amounts of near viewing were found in those with less hyperopic SER and pre-myopes/myopes tended to have a shorter average viewing distance compared to the non-myopes and these findings may be indicative of near activity as a myopic risk factor or in contrast, may be task avoidance related to near work activities among those with hyperopia (French *et al.*, 2009). Interestingly, time spent on moderate physical activity in the present study was found to be associated with refractive error, with those more myopic/less hyperopic children spending slightly more time on moderate activity and those with higher levels of moderate activity were more likely to be classified as pre-myopic/myopic. This translates that every additional hour of moderate activity per day increased the likelihood of pre-myopia/myopia classification by 2.2 times. Interestingly, these findings could be socio-economic in nature as those children that are myopic by 12-13-years old in NI are more likely to be grammar-school educated (O'Donoghue *et al.*, 2015), and could therefore have more access to organised sporting activities, where there are often fees to pay.

Chapter 6 was designed to examine if any patterns of activity (light exposure, physical activity and near activity) throughout the course of the day, both weekday and weekend, were associated with refractive status or axial length. There were no statistically significant associations between the timing of light exposure parameters and either SER or AL. This agrees with the findings of Li *et al.* (2021) where no significant associations between the timing of light exposures and SER, AL or risk of myopia were found in children aged 9-years-old in Singapore. Within the present study, considering the cohort of 6-9-year-olds as a whole, they spent more time in darkness and dimmer light first thing in the morning and last thing in the evening and most time outdoors during midday which are conducive behaviours for a healthy circadian rhythm as described by Phillips, Backhouse and Collins (2012). Increased time spent on moderate and vigorous activity on weekend afternoons and evenings were statistically significantly associated with increased odds for classification as pre-myopic/myopic. However, Read *et al.* (2014) reported no significant differences between refractive groups (myopes and emmetropes) and time spent on moderate to vigorous physical activity or between time of day and refractive error interaction for activity. The potential reason for this difference between studies could be age of the cohorts, as our cohort were younger (6-9-years old) than Read *et al.'s* (10-15-years old) meaning our younger cohort were more likely to have higher

levels of physical activity in general (Jago *et al.*, 2017). Additionally, the difference could be due to the classifications of refractive grouping, as our pre-myopic/myopic group contained low hyperopes (<+0.75 DS) which Read *et al.* classified as emmetropes. The findings of the present study are also contrary to previous findings of increased sedentary time being linked to an increased prevalence of myopia (O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019). There is the potential that high levels of physical activity late in the day could impair the child's circadian rhythms and might not be as beneficial to ocular growth control as physical activity earlier in the day (Yamanaka *et al.*, 2006; Rubio-Sastre *et al.*, 2014), which could be to be promoting myopia development. However, the exact mechanism behind this is currently unclear. There is also the possibility that the participants in the present study have seen other eye care professionals and have been advised that they are at risk of future myopia based on their current refractive error, and parents might be getting them outdoors and active to avoid the onset or progression of myopia. On weekday mornings those with less hyperopic SER's were spending more time viewing at near. But those with more hyperopic SER's spent more time on very close viewing on weekend evenings. Multiple regression analysis for SER found that time spent viewing at near on weekday mornings was independently associated with more myopic refractive error after controlling for age, gender, ethnicity, and parental myopia. This means that on schooldays those less hyperopic individuals are more likely to be doing more viewing at near than their more hyperopic peers. This may be indicative of near activity as a myopic risk factor or in contrast, may be task avoidance of near work among those with hyperopia (French *et al.*, 2009).

Chapter 7 was designed to elicit which potentially modifiable risk factors were related to myopic shift and axial elongation in this young cohort over a 12-month period. Pre-myopes/myopes had more myopic shift (-0.41 D) than emmetropes (-0.15 D) and hyperopes (-0.20 D), and more axial elongation (0.34 mm) than emmetropes (0.23 mm) and hyperopes (0.18 mm), which was comparable to Tideman *et al.* (2018) and McCullough *et al.* (2020). Twelve participants were defined as having accelerated eye growth and 30 participants had normal eye growth. This was defined as axial elongation of greater than the 90th centile of growth (>0.26 mm/year) derived from analysis of data from the NICER 1.0 study[*] for children aged between 6-7 to 9-10-years old. Increased exposure to mesopic light throughout the day was related to smaller myopic shifts and

[*] derived from analysis of NICER 1.0 data

less axial elongation which support the findings of Landis *et al*. (2018) who report that non-myopes spent a greater amount of time in light levels between <1-1 lux compared with myopic children, however they defined this light condition as scotopic in their paper. The light levels in Landis *et al.*'s study attributed as 'scotopic' could have been anywhere between scotopic and mesopic light. Therefore, our findings of mesopic light having a protective effect over the progression of myopia support Landis *et al*.'s suggestion that dim light has a role to play in healthy refractive development. When light exposure patterns were considered in relation to the time of day they were experienced, mesopic light exposure on weekday and weekend evenings was statistically significantly positively correlated with less myopic shift and less axial elongation. Alternatively, pre-myopes/myopes whose axial elongation may be expected to be more rapid than those non-myopes (Mutti *et al.*, 2007), spent more time in brighter light later in the day, indicating that the time spent in brighter light later in the day is more likely to result in myopic shift and axial elongation, and the likely mechanism for this is via deregulation of the circadian rhythm (Flanagan *et al.*, 2020). Time spent in mesopic light at night during sleeping hours was associated with less axial elongation indicating the protective effect of minimal illumination during sleep. The mechanism through which this occurs could be through the brighter light at night disrupting the circadian rhythm by altering melatonin secretion patterns (Gooley *et al.*, 2011; Chakraborty *et al.*, 2018; Leger *et al.*, 2019; Ostrin, 2019). Melatonin levels are known to rise in the evenings to promote sleep onset and exposure to bright light at night strongly suppresses melatonin which therefore interferes with sleep timing and sleep quality (Gooley *et al.*, 2011; Bedrosian and Nelson, 2017). Higher sleep efficiency (total sleep time/total time in bed x100) and less wake after sleep onset (WASO) were moderately correlated with more axial elongation but did not reach statistical significance. These findings lead us to reaffirming our discussion in Chapter 5, where the pre-myopes/myopes tended to go to bed later, have a faster sleep onset and less wake during sleeping hours therefore having a higher sleep efficiency than the more hyperopic individuals, which Ostrin *et al.* (2020) reported could be associated with greater sleep debt and sleep deprivation.

Increased time spent viewing at intermediate distances in the evenings, is associated with larger myopic shifts over a 12-month period. Increased time spent viewing at near and intermediate on weekend afternoons were also significantly related to more myopic shifts. These intermediate viewing distances were between 50-120 cm and included time spent on computers/laptops/tablets, whereas phone use is likely to involve closer viewing

distances (Bababekova *et al.*, 2011). Yi and Li (2011) also reported that more myopia progression was found in those spending more time on computers. In the present study, spending more time on consistent near work significantly increased odds ratios (OR) for classification as having accelerated eye growth on univariate regression analysis (OR 1.031, 95% CI 1.001-1.062, p=0.042). This finding indicates that for every additional 30 minutes a child spends undertaking sustained near viewing per day, they are 1.93 times more likely to exhibit faster axial elongation. Ip *et al*. (2008) found that continuous reading over more than 30 minutes increased the odds of having myopia by 1.5 times in a sample of 12-year-old Australian children. In the present study, the screen time questionnaire results indicated a slight association between use of screens and potential risk of accelerated eye growth, however more robust evaluation of screen time using objective measures in the future would refine potential advice for parents regarding the influence of screen use on children's eye health. Objective measures through application of embedded screen time apps would also reduce the potential for both recall and social desirability bias by use of questionnaire data.

8.2. Strengths and Limitations

The strengths of these studies included the validation of the Clouclip and Actiwatch 2 for measuring light exposure for the first time and validating the time frame for data collection of environmental and behavioural risk factors. Chapter 5, 6, and 7 all included robust assessment of refractive error and ocular biometry measures alongside device measured environmental and behavioural risk factors for future myopia in a young UK cohort which is the first of its kind to the best of my knowledge. Additionally, to counteract limitations of light exposure and time outdoors data differences across seasons (because of the year-round data collection with differences in day length), the light exposure and time outdoor parameters were assessed for winter and summer separately. Interestingly, the differences between the light exposure experienced by the different refractive groups were only found in those children who had their objective measures of risk factors taken in winter and the trends found in winter were not apparent in summer. A basic screen time questionnaire was utilised to estimate average time spent on phone/tablets as well as time spent on computers/tablets, TV/video games and on any of the respective devices prior to sleep since very few children aged 6-9-years old owned their own phone or tablet. This was to prevent overestimation of the children's screen time by using data from a shared device. However, this type of questionnaire filled out

by the participants parents would be limited by both recall and social desirability bias (Neumann, 2015).

Chapter 5, 6, and 7 were limited by the few children who could be classified as 'already myopic' (<-0.50 D) in this young UK cohort, with most children in the pre-myopic/myopic group being pre-myopic at this age. The initial plan for the thesis was to collect the same cross-sectional data on 12-13-year-olds, to determine if there were differences in behavioural patterns between myopes and non-myopes at this age, however this age group proved to be non-compliant with the wearable devices. This was likely due to increased image awareness meaning they did not want to wear the spectacles with the Clouclip attached. The decision was made to cease data collection on this cohort after a short pilot study.

A potential reason for lack of statistically significant differences between light exposure/time spent outdoors in pre-myopes/myopes and non-myopes, as well as pre-myopes/myopes spending statistically significantly more time on higher levels of physical activity than non-myopes, could be attributed to increased optometrist and parental knowledge on the benefits of time outdoors/reduced time sedentary in myopia prevention. Professional advice provided to children at 'high risk' of future myopia could have influenced the behaviour of participants in the present study. There is also the potential that the previously measured risk factors for pre-myopes/myopes might not necessarily be reflective of the participants continual patterns of behaviour, as they were only measured once at baseline. These patterns may also change with season and time of year. The participants in the present study were also significantly affected by COVID-19 lockdowns, so what was recorded at baseline may not have reflected what happened during the 12-month follow-up period. Children over that period were subjected to more time indoors, no organised sports or activities, home-schooling via computers/laptops/tablets/phones and loss of regular sleep routines. There are published data suggesting that lockdown had increased incidence and progression of myopia among children aged 6-8-years old compared to previous years, indicating sensitivity of young children to environmental influences on myopic eye growth (Wang *et al.*, 2021).

8.3. Translational Application of the Thesis

By evaluating associations between environmental light exposure and behavioural profiles of children whose refractive status indicates a high risk for future myopia (pre-

myopes), the findings of the thesis highlight some potential modifiable risk factors for future myopia and accelerated eye growth in addition to increased time outdoors. Eye care professionals should be providing up to date advice to parents and their children who are already myopic or pre-myopic at 6-9-years. The key list of messages for parents arising from the outcomes of this thesis are:

- Promote less near work or a variety of visual activities to reduce constant periods of near work
- Reduced time spent on phones and tablets and watching TV/video games
- Promoting dimming of lighting in the evening and reduce physical activity levels in the evening before bed to encourage the production of melatonin and onset of sleepiness to increase sleep quality
- Promote earlier bedtimes and provide a fully dark environment for sleeping in.

8.4. Further Areas of Research

8.4.1. Screen Time Assessment

Using screen time monitoring apps to objectively measure screen time is likely to be a more robust method to capture screen use once children own their own personal device. Ofcom Communications Market Report (2021) found only 14% of children aged 5-7-years have their own smartphone and 57% have their own tablet, whereas 91% of children aged 12-15-years have their own smartphone and 59% have their own tablet. The present study found too few children with access to their own devices and instead were using a shared device for which the use of a screen time app could have resulted in overestimation of a child's screen time.

8.4.2. Seasonal Measures of Eye Growth

A number of studies have reported that myopia progresses faster in the winter and slower in the summer, a finding which can be attributed to increased time spent outdoors and/or more time in higher light intensities, but could also be a side effect of reduced near work and reduced educational pressures when children are on their summer holidays from school (Fulk, Cyert and Parker, 2002; Donovan *et al.*, 2012; Cui, Trier and Munk Ribel-Madsen, 2013; Gwiazda *et al.*, 2014). Northern Ireland has a large variation in daylight hours between winter and summer (winter daylight hours 7-8 hours, summer daylight hours, 16-17 hours) (https://www.timeanddate.com/worldclock/uk/belfast). The winter daylight hours coincide almost entirely with the school/workday hence the amount of light exposure and time spent outdoors (in lux >1000) is significantly more limited than

in summertime. Interestingly, the present study was only able to identify differences in the light exposure profiles experienced by children in different refractive groups when measures were taken in winter. The trend for non-myopic children to achieve greater exposure to more outdoor light than their myopic/pre-myopic peers were not replicated in summer. It may be that during the winter months when there is limited amount of time available for children to be exposed to higher intensities of light, the average daytime light exposure achieved by the pre-myopes/myopes is insufficient to reach a protective threshold and myopic eye growth is encouraged.

Future studies could examine the change in axial length over a 6-month period at two or more intervals in order to determine seasonal differences in axial growth. Axial length changes are easier to detect than refractive error especially over short time frames. This could be done without the use of cycloplegia as Huang *et al.* (2012) determined that there was no statistically significant difference between axial length measured with or without the use of cycloplegia, and this could to aid compliance and efficiency of data collection. These future studies would assess whether seasonal changes have an impact on the progression of myopia in children in the UK or Ireland.

8.4.3. Light Exposure Interventions

To date, there have been several clinical intervention studies in Asian countries, where light exposure or time spent outdoors has been increased in an intervention group and the control groups behaviours were not modified. A three-year randomized clinical trial in Guangzhou, China involved the scheduling of one 40-minute outdoor activity class at the end of every school day for 6-year-olds. They found a statistically significantly reduced 3-year cumulative incidence rate of myopia of 30.4% in the intervention group compared to 39.5% in the control group (He et al., 2015). In Taiwan, the intervention group participated in recess outside the classroom for the full 80 mins of recess per day for one year compared to the control group who remained inside for recess. At the end of the year, the new cases of myopia onset during the study period were significantly lower in the intervention group than in the control group (8.41% vs. 17.65%). The mean progression of myopia was also significantly lower in the intervention group than the control (-0.25D/year vs -0.38D/year) but there was no statistically significant difference in progression in the "already myopes" in the intervention and control groups. (Wu et al., 2013). Based on the evidence in this thesis regarding increased time spent in brighter light conditions during sleep for pre-myopes than non-myopes and time spent in dim (mesopic)

light in the evening hours prior to bedtime be associated with less myopic progression and axial elongation, future studies should consider an intervention to the evening/bedtime lighting conditions of young children to determine if bright light exposure before bed or during sleeping hours is related to increased incidence and progression of myopia in a randomized control trial.

8.4.4. Serum Melatonin Measures on a Younger Cohort

Kearney *et al.* (2017) identified significantly increased levels of circulating melatonin in myopic adults compared with non-myopes. Subsequently, Flanagan *et al.* (2020) reported that adult myopia is associated with significantly elevated levels of circulating melatonin in both morning and evening samples but that circadian phase, does not differ between myopes and emmetropes. Flanagan *et al.* (2020) also established that associations between melatonin and refractive error are detectable through non-invasive saliva sampling and circulating levels of melatonin are significantly different in adult myopes compared with their emmetropic peers. The authors note that future studies are required to ascertain the relevance of these findings of differences in salivary and circulating melatonin to the onset and development of myopia, particularly whether elevated melatonin levels are evident before and during myopia development. This may provide insight into the factors promoting childhood myopia.

Considering the evidence in this thesis regarding pre-myopes/myopes having increased light exposure during sleep, higher levels of physical activity in the evening, later bedtimes, higher sleep efficiency but poorer subjective sleep quality compared to non-myopes, there is evidence of a disrupted circadian rhythm even in this young cohort of primarily pre-myopic children. Therefore, by having an objective measurement of disrupted circadian rhythm via melatonin levels, future studies could determine if this is promoting the onset and development of childhood myopia. A similar study could be carried out on child participants as done by Flanagan *et al.* (2020) on adult participants to determine melatonin levels throughout the day alongside the same device measured environmental and behavioural risk factors listed above.

8.4.5. Objective Measures of Risk Factors on an Older Cohort

Initially, objective data collection was planned for 12-13-year-old children as well as 6–9-year-olds, to determine if there were differences in behavioural patterns between myopes and non-myopes at this age. However, in the initial pilot phase where 29

participants were recruited, only eight wore the devices reliably, and this age group were deemed non-compliant with the wearable devices. This was likely due to increased image awareness at this age. Future research on an older Caucasian cohort could provide useful information on which risk factors are linked to the progression of myopia as there will be significantly more manifest myopes in this age group compared to the 6-9-year-old cohort. Further consideration would need to be given on what appropriate wearable devices would aid compliance with measurement of visual behaviours.

Use of an older cohort would be helpful to more thoroughly assess the screen-time usage of children to check if screens are an independent risk factor for myopia or myopia progression. Additionally, examining the physical activity of an older cohort with the aid of wearable devices might tease out whether time spent on higher levels of physical activity, particularly later in the day constitutes a risk factor for myopia progression or if the finding was an anomaly due to high activity and lack of manifest myopia in younger children.

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Appendix

Image References

Figure 2.7.1. http://www.clouclip.com

Figure 2.7.2. https://www.newswise.com/articles/media-article/525641

Figure 2.7.3. https://www.actigraphcorp.com

Figure 2.7.4. http://www.actigraphy.com/solutions/actical

Figure 2.7.5. https://www.usa.philips.com/healthcare/product

Figure 2.7.6. https://www.verywellhealth.com/what-to-expect-in-a-sleep-study-3015121

Figure 5.3.1. https://bmedical.com.au/product/actiware-software/

Appendix A

Filter Committee Report Form

Project Information

Project Title: Assessment of the Reliability of Actiwatch2 and ClouClip Data on Physical Activity, Light Exposure, Sleep and Near Vision Tasks over a One or Two Week Period

Category: Cat A (No significant risk to researchers or participant)

Project Number: FCBMS-18-180-A

Chief Investigator: Saunders, Kathryn

Collaborators: Colleen Howell, Sara McCullough, Marie Murphy

Start / End Dates 01-12-2018 / 31-12-2018

Student Information

Students Names: Colleen Howell

RG3 Filter Committee Report

Dear Kathryn Saunders
Thank you for your project proposal application to the School of Biomedical Sciences Ethics Filter Committee (FCBMS) which has now been considered.
Your project, as proposed, may proceed.
Please find a signed RG3 form within your online project submission folder here https://biomed.science.ulster.ac.uk/portal/ethics/mysubmissions.
Sincerely
Chair of FCBMS

Comments: Thank-you for fully addressing the reviewers comments.

For the power calculations, investigators have stated that 11 participants should be sufficient to provide useful information for this study (as stated in the RG1a), please consider that you may need to recruit more than 11 participants to ensure that you have accounted for drop-out. If you do want to recruit more than 11 participants, please notify the ethics filter committee before beginning the study.

Peer review: Favourable peer review report(s) submitted

Appendix B1

Participant Information Sheet

Assessment of the Reliability of Actiwatch2 and ClouClip Data on Physical Activity, Light Exposure, Sleep and Near Vision Tasks over a One- or Two-Week Period

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for considering this invitation.

What is the purpose of the study?

The purpose of this study is to confirm/deny the hypothesis that measures of physical activity, light exposure, near vision tasks and sleep quality taken over one week provide average values (for weekdays and for weekends) which are not significantly different from those obtained over two weeks. This would help us understand whether taking just 7 days' worth of data is a valid way of profiling a person's lifestyle.

Why have I been chosen?

You have been chosen because you are an adult aged between 18-60 and you wear glasses full-time.

Do I have to take part?

It is up to you to decide whether you want to take part. If you decide to take part, you will be given this information sheet to keep. You will also be asked to sign a consent form. You can withdraw from the study at any time, and do not have to give a reason for withdrawing.

What will happen to me if I take part?

You will be fitted with a wristwatch called Actiwatch2 and a clip-on device called ClouClip that attaches to your glasses. You will be asked to wear both devices for 2 weeks, (the wristwatch even during sleeping hours). These devices will measure the amount of time you spend on physical activity, near tasks, and your sleep quality and how much light exposure you get. The wristwatch must be worn over sleeves/coats in order to measure the light exposure. We will also help you to download an app onto your phone/ tablet for free which will only monitor the time spent on the devices not what you use them for. On collection of the Actiwatch2 and ClouClip device we will download the data from the app or alternatively you can screenshot this information and email it to us. The free app that will be used for iPhones is 'Moment-Screen time tracker' for Android it is 'QualityTime-my digital diet' and for Windows it is 'Perfect screen time tracker'.

What are the possible disadvantages and risks of taking part?

There are no major risks associated with participation and all your details will be kept confidential. All the devices used are lightweight and non-invasive.

What are the potential benefits of taking part?

There are no direct benefits of this study, except that you might find out a bit more about the time you spend on near vision tasks, outdoors and exercising. But your assistance will aid in the development of further research studies.

What if new information becomes available?

If new information becomes available during the course of this study, you will be kept informed and any options or requests will be fully explained.

What happens when the study ends?

Once the study ends the researchers can contact you with the results from your two weeks of device wear. If you are interested, please provide your email address in the appropriate section in the consent form. Otherwise we do not need to contact you further in relation to this research study.

What if something goes wrong?

It is very unlikely that anything will go wrong, but Ulster University has procedures in place for reporting, investigating and handling adverse events. Any complaint should be made, in the first instance, to the Chief Investigator (Professor Kathryn Saunders) identified for this particular study. Complaints will be reported to the appropriate authority and treated seriously. The University is insured for its staff and students to carry out research involving people. Further details on the complaint's procedure can be found in the University's "Research Ethics and

Governance" webpage.

Will my taking part in the study be kept confidential?

To ensure that any personal data/information is kept confidential all data will be anonymised and participants will be identified using a numerical identifier. Your personal data will not be disclosed to anyone other than the chief investigator (Kathryn Saunders) and the additional investigators (Colleen Howell, Sara McCullough and Marie Murphy). Data will be held securely in a secure filing cabinet in a locked office and all electronic information will be stored on a password protected computer.

Who is organising and funding the research?

Ulster University Vision Science Research Group has organised this study. The Department for Economy student stipend has funded this study.

What will happen to the results of the research study?

The results of this study will be kept at Ulster University, Coleraine.

Who has reviewed the study?

This study has been reviewed by the Biomedical Sciences Research Ethics Filter Committee.

Who can I contact for further information?

If you would like further information about this study, please contact:

Miss Colleen Howell
T: 02870123718
E: howell-c1@ulster.ac.uk

Professor Kathryn Saunders
T: 02870124433
E: kj.saunders@ulster.ac.uk

Both based at:
Vision Science Research Group
School of Biomedical Sciences
University of Ulster
Cromore Road
Coleraine

Appendix B2

Consent Form

Title of Study: Assessment of the Reliability of Actiwatch2 and ClouClip Data on Physical Activity, Light Exposure, Sleep and Near Vision Tasks over a One- or Two-Week Period

Chief Investigator: Professor Kathryn Saunders

Additional Investigators: Miss Colleen Howell, Dr Sara McCullough, Professor Marie Murphy

Please confirm, by marking the boxes that you agree with the following statements:

1. I have been given and have read and understood the information sheet (version 2) for the above study and have asked and received answers to any questions raised. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason and without my rights being affected in any way. ☐

3. I understand that the researchers will hold all information and data collected during the study securely and in confidence and that all efforts will be made to ensure that I cannot be identified as a participant (except as might be required by law) and I give permission for the researchers to hold relevant personal data. ☐

4. I agree to take part in the above study ☐

5. I would like a copy of my results from the study. Please provide email address_____ ☐

6. I am happy to be contacted to participate in future studies related to this study by this research group ☐

Name of Participant and DOB	Signature	Date (dd/mm/yy)
Name of Person taking consent (if different from researcher)	Signature	Date (dd/mm/yy)
Name of Researcher	Signature	Date (dd/mm/yy)

Appendix C

To: Professor K Saunders

From: Elaine Bell, Research Governance, 26A20, JN

Date 18 May 2020 Ref:

Dear Professor Saunders

Research Ethics Committee application number: REC/18/0102

Project Title: The Northern Ireland Childhood Errors of Refraction (NICER) Study 2.0: Is modern life bad for children's eyes?

Amendment Number: 8

Following submission of Amendment Number 8 for ethical approval, the Research Ethics Committee is pleased to confirm that the amendment should proceed.

The period for which the committee's decision is valid remains unchanged from the original approval.

If you need any further information please do not hesitate to contact me.

Thanks and best wishes.

Elaine Bell
Research Governance Officer
Research Governance Section
Ext. 66518
e.bell2@ulster.ac.uk

Appendix D1

Will my child's taking part in this study be kept private?

We will take great care to ensure that any information we collect is stored safely under an ID number rather than names or any other details that will allow someone to work out who they are. Yes. All the information we collect about your child's eyes will be kept locked away or on a password-protected computer.

What will happen to the results of the research study?

At the end of the study we will tell other researchers and the public about what we have found. Your child's name won't appear in any of the reports describing the study or its findings.

The saliva samples will be analysed for melatonin. Samples will be kept for up to 15 years according to the Human Tissue Act and the permissions that you gave on the consent form. All samples will be disposed of by incineration.

What if new information becomes available?

If new information becomes available which could affect the study, we will let you know and appropriate action will be taken.

Who is organising and funding the research?

Ulster University is organising the study and the researchers have received funding from the Department for the Economy and the College of Optometrists.

Who has reviewed the study?

This research has been reviewed by Ulster University's Research Ethics Committee, to protect you and your child's safety, rights, wellbeing and dignity.

What do I do now?

Please fill in the consent form enclosed to say whether or not your child can take part, put it in the envelope provided and give it to your child to return to school as soon as possible.

If you would like further information please telephone 02870123078 and leave a message for the researchers of the NICER study or email

howell-c1@ulster.ac.uk

Thank you for taking the time to read this

Parent Information Sheet

Ulster University

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Is Modern Life Bad for Children's Eyes?

Dear Parent/Guardian:
Your child recently took part in our study of eyes and we are well on our way to finding out whether the number of children in Northern Ireland who are short-sighted has increased further since our original study in 2006. Thank you for you and your child's help.

We are also trying to find out what it is about modern lifestyles that is making more and more children become short-sighted, You helped us with this question when you filled in a questionnaire about how much time your child spends doing things like using a tablet or playing outside. Now we want to use modern 'wearable' technologies to look at your child's activities in more detail. We want to give your child and some of the other children in their class wearable devices to monitor their physical activity, sleep quality, the amount of time they spend outdoors and their visual behaviour. The amount of time they spend on tablets and or smartphones if they own their own will be monitored using apps during this week. These apps do not monitor the content viewed, merely timing and duration.

We would like your child to take part in this study which will help us find out in more detail how modern life is affecting children's eyes. This parent information sheet tells you about the study and what will happen if your child take part. If anything is not clear you can contact the researchers and ask questions .

What is the study about?

Short-sight (myopia) is becoming more common across the world and is starting in children at younger ages than ever before. We know that some children are short-sighted because their parents are also short-sighted and they have inherited similar eyesight.

But this can't be the only reason so many children are becoming short-sighted these days. There must be something about the way children are using their eyes or living their lives that is also affecting their eyesight.

Researchers from other countries tell us that modern children spend less time outdoors, more time studying and more time using smartphones and tablets. They think that this might be why more children are becoming short-sighted.

We don't know if this is true in Northern Ireland or how being outdoors or using digital devices is affecting children's eyes here.

We want to find out more by measuring how much time your child spends studying, playing outside and using smartphones and/or tablets and compare this to children who are short-sighted.

Why has my child been chosen?

Your child took part in our recent study and is not short-sighted. We need 50 6-7 year olds who are not short-sighted to take part.

What will happen to my child if they take part?

Your child, and some other children in your school, will be given a 'smart' watch, to wear on their wrist for one week. This must be worn all day and night, and only take it off for swimming or in the bath. It should be worn **over** sleeves and coats. This watch measures measures your childs physical activity, sleep quality and light exposure.

You and your child will be given instructions to download a free app on to their smartphone and/or tablet if they own one themselves. The app will measure how much they use their smartphone and/or tablet during the week. It will **not** monitor what they are viewing on the device.

To measure your child's visual behaviour during the week we will put a small clip-on device onto the 'leg' or side of their glasses (if worn). If your child doesn't wear glasses they will be given a blank pair of glasses with the device attached to wear for the week! The device records the viewing distance of what your child is looking at during the week. It does not record what your child is seeing. We will come to your child's school to give them the wearables and will return at the end of the 7 days to collect the devices. We will ask them to bring their smartphone or tablet to download the usage data or you can send it to us electronically.

We will also help your child complete detailed questionnaires on your levels of physical activity and sleep quality. On collection we will ask your child to provide one saliva sample (approx. 2mls) by drooling into a plastic tube. We will use this sample to find out how much melatonin is in their saliva. Melatonin is an important hormone that tells us about your child's sleep cycle to see if there are difference with short-sighted and non short-sighted children.

Does my child have to take part?

It is up to you and your child. You can change your mind at any time. You can chose not to and you do not have to tell us why and it wont affect your child's eye care in the future.

If you and your child want to be part of the study then fill in the 'parental consent form' enclosed and send it back to school with your child. Your child will also be asked to sign a form (assent form) to say they are happy to be a part of the study when we see them at school. Please keep this information sheet.

What are the possible disadvantages and risks of taking part?

We have not identified any risks to you or your child in taking part in this study.

What are the possible benefits of taking part?

You and your child's help with the study is valuable because it will help us understand how modern lifestyles and eye problems relate. It will help us develop strategies to try and reduce the number of children becoming short-sighted and at risk for eye disease in later life.

What happens when the research study stops?

The information we collect will be kept for at least 15 years after the study is finished. After that, the information will be safely deleted or destroyed.

What if something goes wrong?

Every effort will be made to ensure no-one is put at risk or harmed in any way. It is unlikely anything will go wrong as part of this study. However the university has measures in place for handing adverse events and complaints should they occur. The university is insured for research involving human participant and they know about this study and approved it. Further details can be found at: http://research.ulster.ac.uk/rg/0208ResearchVolunteerComplaintsProcedure.pdf

Appendix D2

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Is Modern Life Bad for Children's Eyes?

Hi our names are Colleen, Rebecca and Sarah.

You helped us with an Eye Study we did at your school. You looked at some letters and we measured your eyes and how well they can see.

We would like you to help us again.

You do not have to help us if you do not want to. You can say Yes or No.

If you help us we will give you a special 'smart' watch to wear for a week; at home and at school. The watch tells us how much you run around and sleep. We will also give you a clip to put on your glasses, if you wear glasses. If you don't wear glasses, we will give you a special pair of glasses with the clip on. The glasses tell us how hard your eyes are working.

If you have a smartphone or a tablet, we will help you put an 'app' on your phone or tablet that tells us how much you use your tablet or phone. We will also help you complete questionnaires on how much you run around and how well you sleep.

One week later you will return all devices and we will ask you to provide a morning saliva sample.

Thank you for reading this. You can ask us to tell you more, if you are not sure about helping us. Please let your Mum, Dad or person who looks after you know if you want to help us with the study.

Thank you,

Colleen, Rebecca and Sarah

Appendix D3

Parent Consent Form

Title of Study:

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Is Modern Life Bad for Children's Eyes?

Chief Investigator: Professor Kathryn Saunders

Additional Investigators: Dr Sara McCullough, Dr Karen Breslin, Prof Marie Murphy, Mr Patrick Richardson, Dr Julie Sittlington

PhD researchers: Rebecca Leighton, Colleen Howell, Sarah Flanagan

Please confirm, by marking the boxes provided, that you agree with the following statements:

1. I have been given and have read and understood the information sheet (V2) for the above study and have been given the opportunity to ask questions. ☐

2. I understand that my child's participation is voluntary, and he/she has been informed that they are free to withdraw at any time without giving a reason and without their rights being affected in any way. ☐

3. I understand that the researchers will hold all information and data collected during the study securely and in confidence and that every effort will be made to ensure that my child cannot be identified as a participant (except as might be required by law) and I give permission for the researchers to hold relevant personal data. ☐

4. I consent for my child to provide a morning saliva sample to be stored and used for the analysis in the current study and confirm that I have been given details of how it will be stored, used and the method of disposal. ☐

5. I agree to take part in the above study and consent to the data collected being used for the purpose of this research study as outlined in the information sheet. ☐

6. I agree to receive follow-up advice about my child's vision or eye health which may arise as part of their participation in the study. ☐

7. I am happy to be contacted again by the researchers about follow-up studies. ☐

Childs Name (please print) Childs D.O.B (dd/mm/yy)

Name of Parent/Guardian (please print) Guardian's Signature

Date (dd/mm/yy)

Name of Researcher Signature Date (dd/mm/yy)

Parent/ Guardian Email address _____

Appendix D4

Optometry Clinic
Cromore Road
Coleraine
BT52 1SA
Tel: 028 7012 3047

Child Assent Form

The Northern Ireland Childhood Errors of Refraction (NICER) Study:

Is Modern Life Bad for Children's Eyes?

What will happen to me in this study?

This is a study about how you use your eyes and how active you are. We will measure how much time you spend exercising, sleeping and using a smartphone or tablet. We will use a special clip on a pair of glasses, a smart watch and apps on your phone and tablet to do this. One-week later we will ask you to provide one morning time saliva sample.

Can anything bad happen to me?

No, this is a safe study.

Can anything good happen to me?

You might find out a little bit more about the amount of time you spend on near vision tasks, outdoors and exercising!

Do I have other choices?

You can choose not to be in this study.

Who can I talk to about this study?

You can ask questions at any time. You can ask your parents to talk to us or you can ask us any questions you may have on the day.

What if I do not want to do this?

You don't have to be in this study. No one will be angry at you if you don't want to take part, you just have to tell us. And remember, you can say 'yes' now and change your mind later. It's up to you.

Do you understand this study and are you willing to participate?

Yes ☐ **No** ☐

Childs Name (please print) | Childs D.O.B (dd/mm/yy) | Childs Class

Name of Researcher | Signature | Date (dd/mm/yy)

Appendix E

Physical Activity Questionnaire for Children

Participant ID_____

We are trying to find out about your level of physical activity in the last 7 days (last week). This includes sports or dance that make you sweat or make your legs feel tired, or games that make you breath hard, like tag, skipping, running, climbing and others.

Remember:
There are no right or wrong answers- this is not a test. Please answer all the questions as honestly and accurately as you can-this is very important.

1. **Physical Activity in your spare time. Have you done any of the following activities in the past 7 days (last week)? If yes, how many times? (Mark like this X in one per row.)**

Activity	No	1-2	3-4	5-6	7 times or more
Skipping					
Rowing/Canoeing					
Tag					
Walking for exercise					
Bicycling					
Jogging/Running					
Aerobics					
Swimming					
Dance					
Gaelic Football					
Handball					
Hurling/ Camogie					
Soccer/Football					
Rugby					
Hockey					
Martial Arts					

Basketball					
Ice Skating					
Skiing					
Gymnastics					
Boxing					
Golf					
Horse riding					
Cricket					
Tennis					
Athletics					
Other…(please note below)					

2) In the last 7 days, during your physical education (PE) classes, how often were you very active? (playing hard, running, jumping, throwing) (Check one only)

☐ I don't do PE
☐ Hardly ever
☐ Sometimes
☐ Quite often
☐ Always

3) In the last 7 days, what did you do most of the time at break time? (Check one only)

☐ Sat down (talking, reading, doing schoolwork
☐ Stood around or walked around
☐ Ran or played a little bit
☐ Ran around and played quite a lot
☐ Ran and played hard most of the time

4) In the last 7 days, what did you normally do at lunchtime (besides eating lunch)? (Check one only)

- [ ] Sat down (talking, reading, doing schoolwork
- [ ] Stood around or walked around
- [ ] Ran or played a little bit
- [ ] Ran around and played quite a lot
- [ ] Ran and played hard most of the time

5) In the last 7 days how many days <u>right after school</u>, did you do sports, dance or play games in which you were very active? (Check one only)

- [ ] None
- [ ] 1 time last week
- [ ] 2/3 times last week
- [ ] 4 times last week
- [ ] 5 times last week

6) In the last 7 days, on how many <u>evenings</u> did you do sports, dance or play games in which you were very active? (Check one only)

- [ ] None
- [ ] 1 time last week
- [ ] 2/3 times last week
- [ ] 4/5 times last week
- [ ] 6/7 times last week

7) On <u>the last weekend</u> how many times did you do sports, dance or play games in which you were very active? (Check one only)

- [ ] None
- [ ] 1 time
- [ ] 2/3 times
- [ ] 4/5 times
- [ ] 6 or more times

8) Which one of the following describes you best for the last 7 days? Read all 5 statements before circling which one answer describes you.

A. All or most of my free time was spent doing things that involve little physical effort
B. I sometimes (1-2 times last week) did physical things in my free time
C. I often (3-4 times last week) did physical things in my free time
D. I quite often (5-6 times last week) did physical things in my free time
E. I very often (7 or more times last week) did physical things in my free time

9) Mark how often you did physical activity like playing sports, games, doing dance or any other physical activity for each day last week.

Day	None	Little Bit	Medium	Often	Very Often
Monday					
Tuesday					
Wednesday					
Thursday					
Friday					
Saturday					
Sunday					

10) Where you sick last week or did anything prevent you from doing your normal physical activities? (Check one)

☐ Yes

☐ No

If Yes, what prevented you?

_____

ID #:

Appendix F

THE PITTSBURGH SLEEP QUALITY INDEX (PSQI) Questionnaire

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

During the past month,

1. When have you usually gone to bed? _____

2. How long (in minutes) has it taken you to fall asleep each night? _____

3. When have you usually gotten up in the morning? _____

4. How many hours of actual sleep do you get at night? (This may be different than the number of hours you spend in bed) _____

5. During the past month, how often have you had trouble sleeping because you...	**Not during the past month (0)**	**Less than once a week (1**	**Once or twice a week (2)**	**Three or more times a week (3)**
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe, including how often you have had trouble sleeping because of this reason(s):				

6. During the past month, how often have you taken medicine (prescribed or “over the counter”) to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
	Very good (0)	Fairly good (1)	Fairly Bad (2)	Very Bad (3)
9. During the past month, how would you rate your sleep quality overall?				

Name:
ID:

Appendix G

Screen Time Diary

Please fill out this diary on your how much time you used screens during the week. Get your mum, dad or other grown-up to help you if you need to!

Tick/mark the appropriate box for each question and bring it with you to school on the final day of data collection. Try to be as honest and accurate as you can but there are no right or wrong answers!

How much time did you spend watching TV/ playing video games (PlayStation, Xbox etc.) during this week?

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Not at all								
Less than 1 hour								
1-2 hours								
2-3 hours								
3+ hours								

How much time did you spend using a phone/ tablet during this week?

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8

Not at all								
Less than 1 hour								
1-2 hours								
2-3 hours								
3+ hours								

How much time did you spend using a computer/laptop during this week?

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**
Not at all								
Less than 1 hour								
1-2 hours								
2-3 hours								
3+ hours								

How much time did you spend using any of the devices above in bed before going to sleep?

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**

Not at all							
1-30mins							
30 mins - 1 hour							
1-2 hours							
2+ hours							

For Parents:

Please fill out this short questionnaire about your own eye history. It should take no longer than 2 minutes to complete.

Do you or your child's other parent wear glasses or contact lenses?

Mother: Yes ☐ ☐ No Not Know ☐

Father: Yes ☐ ☐ No Not Known ☐

Have you or your child's other parent ever had laser eye surgery?

Mother: Yes ☐ ☐ No Not Know ☐

☐ ☐ ☐

Father: Yes No Not Known

If either parent wear glasses or contact lenses (or if they used to but have had laser eye surgery to correct this), are the glasses or contact lenses for myopia (short-sight)?

Short-sight means you have more difficulty seeing things further away without glasses e.g. TV, cinema, driving.

Mother: Yes ☐ ☐ No Not Know ☐

Father: Yes ☐ ☐ No Not ☐ Known

What is your glasses prescription to the best of your knowledge?

If you have a copy of your latest prescription from the Optician please write it down exactly as was given

{e.g. Right Eye: +3.00/-0.75x180. Left Eye: -1.25/-2.50x90}

Mother: Right Eye ☐

Left Eye ☐

Father: **Right Eye**

Left Eye

Appendix H

Ulster University

Ulster University
Shore Road
Newtownabbey
County Antrim
BT37 0QB
Northern Ireland
T: +44 (0)28 9036 6552/6518/6629
ulster.ac.uk

Our Ref: NC:GOV

31 October 2019

Professor K Saunders
Room G151
School of Biomedical Sciences
Ulster University
Coleraine Campus

Dear Professor Saunders

Research Ethics Committee Application Number: REC/19/0078

Study Title: The Northern Ireland Childhood Errors of Refraction (NICER) Study 2.0: Progression of Eye Growth and Associated Risk Factors-6-7-year-old cohort follow-up

Thank you for your recent response to matters raised by the committee. This has been considered and the decision of the committee is that the research should proceed.

Please also note the additional documentation relating to research governance and indemnity matters, including the requirements placed upon you as Chief Investigator.

The committee's decision is valid for a period of three years from today's date (this means that the study should be completed by that date). If you require this period to be extended, please contact the Research Governance section.

1. **Please complete and return the Chief Investigator Statement of Compliance prior to commencing the study and keep a copy for your file.**

2. **Please retain all other documents.**

Further details of the University's policy along with guidance notes, procedures, terms of reference and forms are available on the Ulster University Portal.

If you need any further information or clarification of any points, please do not hesitate to contact me.

Yours sincerely

Nick Curry
Head of Research Governance
028 9036 6629
n.curry@ulster.ac.uk

Appendix I1

Will my child's taking part in this study be kept private?

Yes. All the information we collect about your child's eyes will be kept locked away or on a password-protected computer. We will take great care to ensure that any information we collect is stored safely under an ID number rather than names or any other details that will allow someone to work out who they are.

What will happen to the results of the research study?

At the end of the study we will tell other researchers and the public about what we have found. Your child's name won't appear in any of the reports describing the study or its findings.

What if new information becomes available?

If new information becomes available which could affect the study, we will let you know and appropriate action will be taken.

Who is organising and funding the research?

Ulster University is organising the study and the researchers have received funding from the Department for the Economy (DfE).

Who has reviewed the study?

This research has been reviewed by Ulster University's Research Ethics Committee, to protect you and your child's safety, rights, wellbeing and dignity.

What do I do now?

Please fill in the consent form enclosed to say whether or not your child can take part, put it in the envelope provided and give it to your child to return to school as soon as possible.

If you would like further information please telephone 02870123078 and leave a message for the researchers of the NICER study or email

howell-c1@ulster.ac.uk

Thank you for taking the time to read this Parent Information Sheet

QR code will be created and attached here!!

Ulster University

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Eye Growth and Modern Lifestyles

Dear Parent/Guardian:

In P3 your child took part in Part 1 and 2 of our eye study. We measured their eyes and vision and how much time they spent outdoors, sleeping, exercising, using screens and how far away their eyes were focused from them.

If you scan the QR code on this leaflet with your phone this will link you to our website where we have some feedback on the results to date.

Now we would like their help again to see how much their eyes and vision have changed over the past 9-15 months. We want to see if the eye size and vision is affected by the amount of time they spent outdoors, sleeping, exercising, using screens and how far away their eyes were focused from them. This study will help us to understand how modern children's lifestyles impact on eye growth.

We are writing to all the parents/guardians of the P3 children who participated in Part 1 and 2 of our eye study to participate in this stage of our study now that they are a bit older.

This information leaflet tells you about the study and what will happen if your child takes part. If anything is not clear you can contact the researchers and ask questions.

Why has my child been chosen?

Your child has been invaluable in helping us with Part 1 and 2 of our study so far when they were P3. You child, alongside 100 other P3 children, took part in both parts and we would love for them all to help us again!

What is the study about?

We want to find out:

1). How much your child's eyes have grown and how their refractive error (how long or short sighted they are) has changed since we first tested them 9-15 months ago.

2). How things like time spent outdoors, sleeping, exercising, using screens and reading distance affect any changes in eye growth and refractive error.

Does my child have to take part?

It is up to you and your child to decide whether they take part or not. You or your child can change your mind in the future and withdraw from the study. You don't have to tell us why and it won't affect your child's eye care in the future. **Please let us know if you and your child would/would not like to take part in the study by completing the enclosed 'Parental consent form' and send it back to school with your child.** Your child will also be asked to sign an 'informed assent' form to say they would like to take part when we see them at school. Please keep this information sheet.

What will happen to my child if they take part?

Your child (and their relevant classmates) will have their eyes tested at school by an Optometrist, the test should take about 1 hour. We will measure how well your child sees (without/with glasses if they wear them). They will have eye drops instilled to aid accuracy of the results and after 30 minutes, we will ask them to look into a piece of equipment so we can measure the size and shape of their eyes and how long- or short-sighted they are. Nothing touches their eyes and these measurements are taken very quickly whilst they look at a small target, usually a light. After the eye test we will check the results carefully. If we find your child needs glasses or needs to update his/her glasses we will write to you advising that your child should visit your local Optometrist to have a full eye test.

What are the possible disadvantages and risks of taking part?

Taking part in this study involves your child having eye drops which make their vision a little blurry for a couple of hours and enlarge their pupils for up to 24 hours afterwards. We used these drops on your child the last time we saw them and there were no problems. Other studies have reported that the drops can cause a reaction (facial flush and feeling hot and light-headed) but this is very rare (less than 1 in 10,000 people). These reactions go away naturally the same day without treatment. We will closely monitor all children taking part in this study for any reactions. You will also receive an information leaflet on these eye drops on the day of your child's eye test.

What are the possible benefits of taking part?

You and your child's help with the study is invaluable because it will help us better understand the eye care needs of children in Northern Ireland. This will help us develop strategies to try and reduce the number of children becoming short-sighted and at risk for eye disease in later life.

What happens when the research study stops?

The information we collect will be kept for at least fifteen years after the study is concluded. After that, the information we have on computer and on paper will be safely deleted or destroyed.

What if something goes wrong?

Every effort will be made to ensure that no one taking part in this study is put at risk or harmed in any way. It is unlikely that anything will go wrong as a result of taking part in this study. However, the University has measures in place for reporting, investigating, recording and handling adverse effects and complaints from study volunteers should they occur. The University is insured for its staff and students to carry out research involving human participants. The University knows about this research study and has approved it. Further details on the complaints procedure can be found in the University 's 'Research Ethics and Governance ' webpage, internet address:

http://research.ulster.ac.uk/rg/0208ResearchVolunteerComplaintsProcedure.pdf

Any complaints are made, in the first instance, to the Chief Investigator (Professor Kathryn Saunders) identified for this particular study. Any complaint you make will be treated seriously and reported to the appropriate authority.

Appendix I2

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Eye Growth and Modern Lifestyles

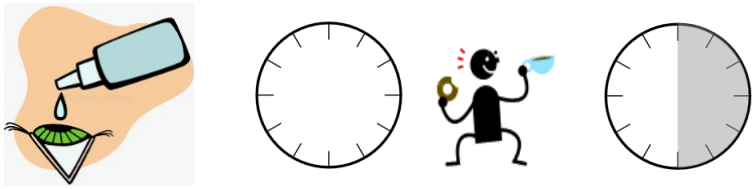
Hi our names are <names of researchers>.

<INSERT HEAD SHOT OF RESEARCHERS>

You helped us with an Eye Study we did at your school last year. We measured your eyes and how well they see and also checked how much time your spent exercising, sleeping, being outdoors and reading. We would like you to help us again. You do not have to help us. You can say Yes or No.

We will be doing the same tests we did when we first saw you so that we can find out how much your eyes have changed as you have gotten older. First we will measure how well you can see on the letter chart.

Then we will put in the eyedrops which may sting a little, but this does not last long as you might remember. You will then get a 30 minute break!



When your break is finished, you will look into two machines that measure the shape and size of your eye (we do not need to touch your eyes).

Thank you for reading this. You can ask us to tell you more if you are not sure about helping us. Please let your mum, dad or person who looks after you know if you want to help us. They need to fill in a 'consent form' and you need to bring it back into school to let us know you want to take part in the Eye Study.

Thank you,

<Name of researchers>

Appendix I3

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Eye Growth and Modern Lifestyles

Chief Investigator: Professor Kathryn Saunders
Additional Investigators: Dr Sara McCullough, Dr Karen Breslin, Prof Marie Murphy, Ms Colleen Howell, Ms Rebecca Leighton, Ms Sarah Flanagan, Mr Patrick Richardson, Dr Julie Sittlington

Parent/ Guardian Consent Form: ***Please confirm, by marking the boxes provided, that you agree with the following statements:***

1. I have been given and have read and understood the information sheet for the above study and have been given the opportunity to ask questions. ☐
2. I understand that my child's participation is voluntary, and he/she has been informed that they are free to withdraw at any time without giving a reason and without their rights being affected in any way. ☐
3. I understand that the researchers will hold all information and data collected during the study securely and in confidence and that all efforts will be made to ensure that my child cannot be identified as a participant (except as might be required by law) and I give permission for the researchers to hold relevant personal data. ☐
4. I agree to take part in the above study and consent to the data collected being used for the purpose of this research study as outlined in the information sheet. ☐
5. I agree to receive follow-up advice about my child's vision or eye health which may arise as part of their participation in the study. ☐
6. I am happy to be contacted again by the researchers about follow-up studies. ☐

Are you willing for your child to participate in this study? YES / NO

Name of Child (please print).	**Child's Date of birth**	**Class/Teacher**
Name of Parent/ Guardian (please print)	**Signature**	**Date (dd/mm/yy)**
Name of Researcher (please print).	**Signature**	**Date(dd/mm/yy)**

Parent/ Guardian's Email Address: _____

Parent/ Guardian's Phone Number: _____

Appendix I4

Optometry Clinic
Cromore Road
Coleraine
BT52 1SA
Tel: 028 7012 3047

The Northern Ireland Childhood Errors of Refraction (NICER) Study: Eye Growth and Modern Lifestyles

Child Assent Form

What will happen to me in this study?
This is a study about children's eyes. We will test your eyes to see how well you can see and whether you need to wear glasses. You will have had these tests done before by us in school when you were in P3.

Can anything bad happen to me?
We will need to put some drops into your eyes to make sure our results are more accurate. These drops sting for a few seconds; most children do not find them too uncomfortable. They are used during children's eye tests very often and you have already had them in your eyes at least once!

Can anything good happen to me?
If we find that you are not seeing as clearly as you should be, we will advise your parent/guardian to take you to your Optometrist to have a full eye test.

Do I have other choices?
You can choose not to be in this study.

Who can I talk to about this study?
You can ask questions at any time. You can ask your parents to talk to us or you can ask us any questions you may have on the day of your eye test.

What if I do not want to do this?
You don't have to be in this study. No one will be angry at you if you don't want to take part; you just have to tell us. And, remember, you can say 'yes' now and change your mind later. It's up to you.

Do you understand this study and are you willing to participate?

Yes ☐ **No** ☐

Name of Child (write in capitals)	Signature of Child	Date
Name of Researcher	Signature of Researcher	Date

Appendix J1

Actiwatch Parameter	Average for all Participants	Correlation with SER	Correlation with AL	New Actiwatch Light Exposure Parameter	Average for all Participants	Correlation with SER	Correlation with AL
Original Time Spent in Mesopic Light Daytime (mins)	198.23	r=0.016 p=0.875	r=-0.016 p=0.875	New Time Spent in Mesopic Light Daytime (mins)	94.48	r=0.070 p=0.489	r=-0.079 p=0.437
Original Time Spent in Photopic Light Daytime (mins)	547.37	r=-0.022 p=0.829	r=0.033 p=0.748	New Time Spent in Photopic Light Daytime (mins)	637.62	r=-0.054 p=0.591	r=0.047 p=0.644
Original Time Spent Outdoors Daytime (mins)	38.40	r=0.023 p=0.824	r=0.065 p=0.521	New Time Spent Outdoors Daytime (mins)	51.89	r=0.024 p=0.812	r=0.075 p=0.455
Original Time Spent in Mesopic Light	78.18	r=0.116 p=0.252	r=-0.117 p=0.246	New Time Spent in Mesopic Light	56.54	r=-0.082 p=0.415	r=-0.144 p=0.154

Night-time (mins)				Night-time (mins)			
Original Time Spent in Photopic Light Night-time (mins)	20.64	r=-0.101 p=0.316	r=0.010 p=0.923	New Time Spent in Photopic Light Night-time (mins)	41.19	r=-0.028 p=0.780	r=0.004 p=0.968
Clouclip Parameter	**Average for all Participants**	**Correlation with SER**	**Correlation with AL**	**New Clouclip Light Exposure Parameter**	**Average for all Participants**	**Correlation with SER**	**Correlation with AL**
Original Time Spent in Mesopic Light (mins)	59.43	r=-0.120 p=0.369	r=0.066 p=0.625	**New Time Spent in Mesopic Light (mins)**	20.19	r=-0.147 p=0.271	r=0.135 p=0.312
Original Time Spent in Photopic Light (mins)	517.23	r=-0.067 p=0.619	r=-0.012 p=0.931	**New Time Spent in Photopic Light (mins)**	512.74	r=-0.077 p=0.566	r=-0.007 p=0.959

Original Time Spent Outdoors (mins)	43.49	r=0.190 p=0.153	r=-0.033 p=0.806	**New Time Spent Outdoors (mins)**	47.97	r=0.198 p=0.135	r=-0.040 p=0.766

Appendix J1. Light exposure was analysed in two ways; using the original cut-offs to define the category, and using the adjusted cut-offs determined by the validation study of the devices (Chapter 3). The results of both Pearson's correlations between each light exposure parameter with SER and AL are presented above from the data in Chapter 5.

Appendix J2

Actiwatch Light Exposure Parameter	Pre-Myopes/Myopes Mean and (SD)	Non-Myopes Mean and (SD)	Independent t-test (Pre-Myopes/Myopes vs Non-Myopes	Emmetropes Mean and (SD)	Hyperopes Mean and (SD)	One-Way ANOVA	Between Groups (P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes)
Original Time Spent in Mesopic Light Daytime (mins)	204.21 (98.99)	196.73 (82.84)	p=0.729	197.68 (74.45)	195.05 (97.26)	p=0.934	
New Time Spent in Mesopic Light Daytime (mins)	92.77 (49.79)	94.91 (45.16)	p=0.853	93.89 (43.17)	96.72 (49.21)	p=0.950	
Original Time Spent in Photopic Light Daytime (mins)	557.05 (83.47)	544.95 (76.64)	p=0.565	542.63 (76.12)	549.03 (78.74)	p=0.804	

New Time Spent in Photopic Light Daytime (mins)	652.37 (100.57)	633.94 (66.44)	p=0.444	634.83 (67.02)	632.36 (66.57)	p=0.609	
Original Time Spent Outdoors Daytime (mins)	44.49 (61.36)	36.88 (49.49)	p=0.559	32.22 (46.37)	45.08 (54.42)	p=0.481	
New Time Spent Outdoors Daytime (mins)	60.62 (73.52)	49.71 (61.83)	p=0.499	43.81 (58.23)	60.09 (67.49)	p=0.441	
Original Time Spent in Mesopic Light Night-time (mins)	67.53 (76.55)	80.84 (122.94)	p=0.646	80.21 (110.43)	81.94 (144.45)	p=0.898	
New Time Spent in Mesopic Light	44.21 (46.16)	59.63 (83.83)	p=0.431	65.70 (90.44)	48.94 (70.97)	p=0.480	

Night-time (mins)							
Original Time Spent in Photopic Light Night-time (mins)	67.36 (142.67)	8.96 (24.43)	p=0.084	5.90 (15.72)	14.36 (34.58)	*p=0.003*	*p=0.002 P/M vs E* *p=0.020 P/M vs H* p=0.849 E vs H
New Time Spent in Photopic Light Night-time (mins)	90.68 (161.82)	28.82 (71.85)	p=0.110	20.25 (37.28)	43.90 (108.23)	*p=0.024*	*p=0.018 P/M vs E* p=0.220 P/M vs H p=0.542 E vs H
Clouclip Light Exposure Parameter	**Mean and (SD) Pre-Myopes/Myopes**	**Mean and (SD) Non-Myopes**	**P-value results of independent t-test between pre-myopes/myopes and non-myopes**	**Mean and (SD) Emmetropes**	**Mean and (SD) Hyperopes**	**P-value from one way ANOVA P/M=Pre-myopes/Myopes E=Emmetropes H=Hyperopes**	

Original Time Spent in Mesopic Light (mins)	51.70 (41.16)	61.45 (40.38)	p=0.461	68.67 (41.91)	43.12 (30.40)	p=0.116	
New Time Spent in Mesopic Light (mins)	16.33 (13.29)	21.20 (14.06)	p=0.285	24.04 (14.00)	13.98 (11.80)	*p=0.046*	No significant difference between groups
Original Time Spent in Photopic Light (mins)	497.69 (84.97)	522.32 (85.89)	p=0.379	541.22 (83.53)	474.34 (74.72)	*p=0.036*	p=0.265 P/M vs E p=0.758 P/M vs H *p=0.041 E vs H*
New Time Spent in Photopic Light (mins)	492.71 (85.20)	517.97 (86.16)	p=0.369	537.66 (83.30)	467.98 (74.57)	*p=0.028*	p=0.242 P/M vs E p=0.732 P/M vs H *p=0.032 E vs H*
Original Time Spent Outdoors (mins)	59.10 (58.24)	39.42 (38.27)	p=0.286	30.38 (26.78)	62.36 (52.78)	*p=0.026*	No significant difference between groups

New Time Spent Outdoors (mins)	64.09 (61.07)	43.77 (41.05)	p=0.175	33.94 (29.17)	68.72 (55.75)	*p=0.025*	p=0.112 P/M vs E p=0.962 P/M vs H *p=0.048 E vs H*

Appendix J2. The average time spent in both the original and adjusted light exposures for the Actiwatch and Clouclip for each of the refractive categories and the results of independent t-tests and one-way ANOVAs between these categories from Chapter 5 data.

Appendix K

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Reliability and Validity of the Actiwatch and Clouclip for Measuring Illumination in Real-World Conditions

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Purpose

To compare real-world measures of illumination obtained with an Actiwatch 2 and a Clouclip M2 with 'gold standard' photometry measures and evaluate the ability of the Actiwatch 2 to correctly identify photometer-defined conditions: scotopic (≤0.01 lux), mesopic (0.02-3 lux), indoor photopic (>3-1000 lux) and outdoor photopic (>1000 lux) and the Clouclip to correctly identify photometer-defined conditions within its operating range (>1 lux). Additionally, the inter-device reliability of the Clouclip for illumination and viewing distance measures was investigated.

Methods

A Hagner-S2 photometer was used as reference for illumination readings taken with Actiwatch 2 and Clouclip M2 devices across a range of real-world light conditions. To investigate inter-device reliability of the Clouclip, five Clouclips were simultaneously exposed to varied light conditions and object distances.

Results

Strong correlations were found between illumination measured with the photometer and both the Actiwatch 2 (ρ=0.99, $p<0.0001$) and Clouclip (ρ=0.991, $p<0.0001$). However, both devices underestimated illumination when compared to the photometer; the disparity increased with increasing illumination and was greater for the Actiwatch 2 than Clouclip measures. The Actiwatch 2 successfully categorised illumination level (scotopic, mesopic, indoor and outdoor photopic) in 71.2% of cases. The Clouclip successfully categorised illumination levels as scotopic/mesopic (≤3 lux), indoor and outdoor photopic in 100% of cases. The mean differences and limits of agreement (LOA) across the illuminations measured were 430.92 ± 1828.74 and 79.35 ± 407.33 lux, between the

photometer and Actiwatch 2 and photometer and Clouclip, respectively. The Intra-class Correlation Coefficients (ICCs) for illumination and viewing distance measured with the Clouclips were 0.853 and 0.958 respectively.

Conclusion

These data illustrate that different Clouclip devices produce comparable measures of viewing distance and illumination in a real-world setting. Both Actiwatch 2 and Clouclip devices underestimate illumination in the field when compared to gold standard photometer measures. The disparity increases at higher levels of illumination and the discrepancy was greater for Actiwatch 2 measures. For researchers interested in categorising light exposure, the Clouclip more accurately classifies illumination levels above 2 lux than the Actiwatch 2 but cannot discriminate between scotopic and low mesopic light.

Key Points

- Illumination measures taken in real-world settings by Clouclip more closely reflect 'true' illumination measured by photometer than those obtained with the Actiwatch 2, particularly at higher levels of illumination.
- Clouclip more accurately classifies illumination levels ≥2 lux than the Actiwatch 2, but the restricted operating range means it cannot discriminate between time spent in scotopic vs low mesopic light.
- Photometry measurements of >1000 lux were obtained from indoor as well as outdoor locations. This should be considered when using illumination measures as a proxy for time spent outdoors.

Introduction

Wearable devices which monitor aspects of daily living such as light exposure(Read, Collins and Vincent, 2014; Ostrin, Sajjadi and Benoit, 2018), sleep(Rosenberger *et al.*, 2016), physical activity(Read, Collins and Vincent, 2014; Rosenberger *et al.*, 2016) and near work behaviours(Wen *et al.*, 2016; Bhandari, Lan and Ostrin, 2019; Cao *et al.*, 2020) are increasingly being used by researchers to provide objective data pertinent to systemic(Humphreys, McLeod and Ruseski, 2014) and ocular health issues(Sherwin, Hewitt, *et al.*, 2012; French, Ashby, *et al.*, 2013; Read, Collins and Vincent, 2015; Cao *et al.*, 2020; Ostrin *et al.*, 2020) including obesity, diabetes, hypertension, mental well-being, and the development of myopia (short-sightedness).

Research from around the world has identified that based on current trends, half the world's population will be myopic by 2050,(Holden *et al.*, 2016) and that modern lifestyles could be contributing to the rise in myopia worldwide.(Morgan *et al.*, 2018) Ulster University's Northern Ireland Childhood Errors of Refraction (NICER) study has demonstrated that the prevalence of myopia amongst white UK teenagers has more than doubled in the last 50 years and is appearing in children at a younger age than in previous decades.(McCullough, O'Donoghue and Saunders, 2016) An earlier onset of myopia results in an increased risk of progression to high myopia, inflating the risk of secondary sight threatening ocular pathologies.(Flitcroft, 2012) The prevalence of myopia is increasing at a rate that cannot solely be attributed to genetic pressures and is therefore a cause for global concern.(P. C. Wu *et al.*, 2016; Morgan *et al.*, 2018) Researchers are seeking a better understanding of the environmental and lifestyle factors that may contribute to the earlier incidence of myopia in order that strategies for delaying myopia onset may be applied. The potentially modifiable risk factors for childhood myopia include; spending less time spent outdoors,(Sherwin, Reacher, *et al.*, 2012; French, Ashby, *et al.*, 2013; Read, Collins and Vincent, 2014) increased educational pressure,(Saw *et al.*, 2007; Guggenheim and Williams, 2015; Mountjoy *et al.*, 2018) spending more time on near activities,(Saw, Chua, *et al.*, 2002; Saw *et al.*, 2007; Ip, Saw, *et al.*, 2008) leading less active lifestyles,(Deere *et al.*, 2009; O'Donoghue *et al.*, 2015; Harrington, Stack and O'Dwyer, 2019) having poor sleep quality,(Gong *et al.*, 2014; Ayaki *et al.*, 2016; Jee, Morgan and Kim, 2016; Kearney *et al.*, 2017; Xu *et al.*, 2017) and increased time spent using hand-held electronic devices.(Harrington, Stack and O'Dwyer, 2019; Liu *et al.*, 2019)

Wearable devices can provide objective measures of multiple risk factors and remove the limitation of recall-bias from self-/parental-reports of childhood behaviours collected through questionnaire or diaries.(Alvarez and Wildsoet, 2013; Ostrin, 2017; Ostrin, Sajjadi and Benoit, 2018) Wearable devices are generally lightweight, easy to wear and allow for data collection in the free-living setting.(Verkicharla *et al.*, 2017; Smith *et al.*, 2018) These features make wearable devices an attractive method with which to collect myopia-related risk factor data. Furthermore, self-reported measures of time spent outdoors are not able to record the intensity of the light to which the individual is exposed and previous research has determined that time spent outdoors is often misreported and poorly correlated to objective sensor-derived data.(Alvarez and Wildsoet, 2013; Ostrin,

Sajjadi and Benoit, 2018) To date, it is not clear which elements of the outdoor experience are beneficial in relation to reducing the risk for myopia, but further information on children's light exposure in terms of timing of exposure to different levels of illumination and the duration and frequency of these exposures is needed. Therefore, it is important to determine which devices are valid and reliable for estimating the intensity of light as well as the amount of time spent outdoors. Time spent in illumination levels >1000 lux is often used as a proxy for time spent outdoors.(Read, Collins and Vincent, 2014; Ostrin, 2017; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020)

The devices employed to objectively measure illumination in the present study were the Respironics Actiwatch 2 (Philips, NV, USA), the Clouclip Model M2 (HangZhou Glasson Technology Co) and the Hagner Universal Photometer S2 (B Hagner AB, Solna, Sweden). The Actiwatch 2 is a wristworn device which records physical activity and illumination. The Clouclip is a spectacle-mounted device which records near viewing distance and eye-level illumination.

The inter-device reliability of the Actiwatch 2 for illumination and activity measures has been reported as excellent; with intraclass correlation coefficients of 0.99 and 0.98 for light and activity, respectively.(Read, Collins and Vincent, 2014) The Actiwatch brand refers to a family of wearable devices including; the Actiwatch 2, Actiwatch-L, Actiwatch Spectrum and Actiwatch 64, and this family of devices have previously been validated against both 'gold standard' polysomnography and room respiration calorimetry (measures total energy expenditure) and found to be a reliable method for measuring sleep(Hyde *et al.*, 2007; Weiss *et al.*, 2010) and physical activity, respectively.(Puyau *et al.*, 2002, 2004; Ekblom *et al.*, 2016; Neil-Sztramko *et al.*, 2017) Actiwatch 2 measures of illumination have also been compared with a 'gold standard' photometer in both laboratory and outdoor lighting conditions by Joyce *et al*.(Joyce *et al.*, 2019) The authors found that the Actiwatch 2 underestimated the 'true' level of illuminance in comparison to the photometer. However, the linear relationship illustrated between the two devices suggests that it may be possible to apply a conversion factor in order to estimate 'true' illumination.(Joyce *et al.*, 2019) The Actiwatch-L has also been compared to eye-level illumination from a Daysimeter. Comparison between these devices demonstrated that their measures were correlated under 5000 lux, but that at higher illuminations the Actiwatch-L underestimated the light exposure by more than 100 lux. In contrast, at night in lower illuminations the Actiwatch-L was found to overestimate the illumination

compared to the Daysimeter.(2011) Two other studies compared the Actiwatch Spectrum measures to calibrated photometer measures, with one study also comparing readings between the Actiwatch Spectrum and Daysimeter. Both studies found the Actiwatch Spectrum to consistently overestimate illumination in comparison to the calibrated photometers,(Figueiro *et al.*, 2013; Markvart, Hansen and Christoffersen, 2015) and the Daysimeter devices.(Figueiro *et al.*, 2013) There are currently no data examining how well the Actiwatch 2 is able to categorise illumination into scotopic, mesopic, and photopic (indoor/outdoor) levels.

Previous published abstracts[4,5] and a recently published paper[36] have shown that the Clouclip is highly accurate for measurements of illumination and viewing distance in a laboratory setting, and that the Clouclip could accurately distinguish between indoor (<1000 lux) and outdoor (>1000 lux) environments.(Bhandari, Lan and Ostrin, 2019; Bhandari and Ostrin, 2020) As the Clouclip is relatively new there are currently no studies where the inter-device reliability of the Clouclip is investigated; hence the consistency of measures taken by different Clouclip units is unknown. Recently, Bhandari and Ostrin(2020) reported that the Clouclip slightly underestimated 'true' illumination in comparison to a photometer in a range of real-world conditions in Houston, Texas (29°N, 95°W). They also report that the Clouclip could accurately distinguish between indoor (<1000 lux) and outdoor (>1000 lux) environments.(Bhandari, Lan and Ostrin, 2019; Bhandari and Ostrin, 2020) It is not yet clear how well the device discriminates between indoor photopic and mesopic levels of illumination.

Landis *et al.*(Landis *et al.*, 2018) reported significant differences in the light exposure profiles experienced by myopic and non-myopic children in Australia and hypothesise that these differences suggest that both scotopic and outdoor photopic light have a potential role in the prevention of myopia development. However, at present we have limited information on how accurately either the Clouclip M2 or the Actiwatch 2 classify illumination into different categories.

The present study aims to:

- Assess the inter-device reliability of the Clouclip M2 for illumination and viewing distance measures.
- Assess the ability of the Actiwatch 2 and Clouclip M2 to measure and accurately categorise illumination using 'gold standard' photometry as the reference.

Methods

Devices Employed

The devices employed to objectively measure illumination in the present study were the Respironics Actiwatch 2 (Philips, NV, USA), the Clouclip Model M2 (HangZhou Glasson Technology Co) and the Hagner Universal Photometer S2 (B Hagner AB, Solna, Sweden).

The Actiwatch 2 is a lightweight and waterproof wrist-worn 'actigraphy' device measuring 43 x 23 x10 mm. The Actiwatch 2 contains a silicone photodiode light sensor to measure visible light illuminance with a range of 0.01-100,000 lux and a solid-state piezoelectric accelerometer to measure physical activity ranging from 0.35-7.5 Hertz (recorded as activity counts per minute [cpm]).(Read, Collins and Vincent, 2014) The Actiwatch 2 has an adjustable epoch from 15, 30, or 60 seconds. The device is connected to a computer containing the Actiware software using a docking station for charging and data retrieval. The data are uploaded onto the Actiware software and from here can be exported as a CSV file and converted to an Excel (Microsoft, www.microsoft.com) spreadsheet for further analysis.

The Clouclips were provided by Aeir Eye Hospital Group, China. The Clouclip M2 is a 45.3 x 13.4 x 8.0 mm device, designed for attachment to the right temple of a spectacle frame using a rubber sleeve. The devices have a built-in infrared distance sensor to determine near viewing distance (ranging from 5-120 cm), a light intensity sensor to record eye-level ambient illumination (ranging from 1-65536 lux) and a three-axis accelerometer (X, Y, Z axis) to determine when it is being worn. The Clouclip records near viewing distance every 5 seconds and illumination every 2 minutes. The device is Bluetooth capable and has a magnetic USB charger for syncing the device to an app and uploading the data to the cloud, from here raw data can be downloaded as an Excel spreadsheet using login credentials.(Wen *et al.*, 2016; Bhandari and Ostrin, 2020)

The Hagner Universal Photometer S2 is a combined luminance and illuminance (illumination) meter which is designed for measurements in the field and laboratory. The light sensitive components of the photometer are two silicon diodes, filtered to give a spectral response close to that of the human eye. Illumination is measured directly with an external cell connected to the instrument by a cable approximately 3 metres long. The external cell is cosine corrected and therefore reads the level of incident light correctly,

independent of the direction of the light source. The reading is obtained from the deflection of the external meter. Illumination can be measured in the range 0.1-100,000 lux.(B Hagner AB, 1968) The Hagner S2 photometer used to determine the 'true' level of illumination was calibrated prior to data collection by the manufacturers B Hagner AB (16th October 2019). All measurements for the present study were taken between May and June 2020 in Northern Ireland (UK, 55° North).

1.1.1.1 Clouclip Inter-Device Reliability

Five Clouclip M2 devices (HangZhou Glasson Technology Co.) were used to evaluate the inter-device reliability of illumination (lux) and viewing distance (cm) measures. The number of Clouclips under evaluation was restricted to five in order that the spectacle frames on which they were mounted, could be fixed to a moveable surface in such a way that the devices would receive uniform illumination (see Figure 1). The moveable surface was sized to ensure it could be transported efficiently through a variety of spaces over a 60-minute period of data collection whilst maintaining the horizontal orientation of each Clouclips' light sensor. Light levels were not manipulated; they represented the normal variation experienced in a range of real-world settings both indoors and outside (spanning the illumination categories under investigation; scotopic through to outdoor photopic).

Clouclips are activated through a mobile phone app and it was not possible to simultaneously start recording on all the devices. In order to ensure that the time of data logging of the Clouclips matched one another, each unit was activated consecutively and then all devices were left in darkness before illumination was introduced, and the test protocol commenced. The point at which the devices detected the onset of illumination was used to synchronise data after download. To evaluate the reliability of viewing distance measures the board was held at a range of distances from a solid, flat surface (e.g., a wall or door). The actual distances from the solid surface to the Clouclips were not independently recorded. Data were uploaded from each device to a cloud location using the Clouclip app. A synchronised 60-minute sample of both the illumination and viewing distance data was extracted from each device and the inter-device intraclass correlation coefficients for both illumination (lux) and viewing distance (cm) were calculated.

Figure 1. Schematic drawing of the Clouclips mounted on spectacle frames attached to a solid, portable board for inter-device reliability measures. Diagram not to scale.

1.1.1.2 Validity of Actiwatch 2 and Clouclip Measures and Categorisation of Illumination: Comparison with Hagner-S2 Universal Photometer

In order to evaluate how well the two wearable devices classified ambient illumination into previously published categories (Table 1), a free-standing anatomically accurate adult-sized skeleton (height: 176cm [comparable to UK average male height of 175.3cm(Moody, 2012)]) was employed to 'wear' the devices. A skeleton was chosen in order to maintain consistent, device-appropriate positioning of each devices' light sensors throughout data collection. To enable measures of illumination to be taken by the photometer at the same plane as each wearable device's light sensor, the two devices could not be compared to the photometer at the same time and were not worn concurrently. The skeleton was stationed in a range of locations spanning all four light exposure categories (Table 1) over a period of 100 minutes per device, including locations with illumination close to the boundaries of each category. The locations included indoor and outdoor locations in a family home (e.g., cupboard without windows, living room, kitchen by window, outdoors in shade, outdoors in bright light) providing a range of illuminations from near darkness indoors to outdoor sunshine (nine conditions in total), and included locations with illumination close to the boundaries of each light exposure category.

LIGHT EXPOSURE CATEGORIES	LUX VALUE	REFERENCES
SCOTOPIC LIGHT	≤0.01 lux	SolarLight(2014)
MESOPIC LIGHT	0.02-3 lux	Rosenfield and Logan(2009)
INDOOR PHOTOPIC LIGHT	>3-1000 lux	Bhandari and Ostrin(2020)
OUTDOOR PHOTOPIC LIGHT	>1000 lux	Ulaganathan *et al.*(2019)

Table 5. Categories used to classify light exposure

Clouclip vs. Photometer: The photometer's light sensor was held at eye level, to match the position of the Clouclip mounted on a pair of spectacles worn by the skeleton (Figure 2), and readings taken for periods of 12 minutes (an expansion of Bhandari and Ostrin's

four minute measuring period (2020)) in each condition. The Clouclip has a fixed illumination collection epoch of two minutes and the photometer readings were taken every 15 seconds. Coinciding time points from the Clouclip raw data sheets were matched with the photometer's readings (averaged across two minutes) to reflect the two-minute measurement epoch of the Clouclip. As noted by Bhandari and Ostrin,(2020) the skeleton's head needed to be 'wobbled' from side to side between illumination measurements in order to prevent the Clouclip from going into sleep mode (if no motion detected for 40 seconds).

Actiwatch 2 vs Photometer: The protocol described above was repeated with the skeleton wearing an Actiwatch 2. The photometer's light sensor was held at wrist level, to match the position of the Actiwatch 2 (Figure 2), and readings taken for periods of 12 minutes in each condition. The Actiwatch 2 illumination epoch was set to 15 seconds throughout and recordings were taken from the photometer every 15 seconds. Data were extracted from the Actiwatch 2 raw data sheets and matched with measures taken by the photometer at corresponding time points.

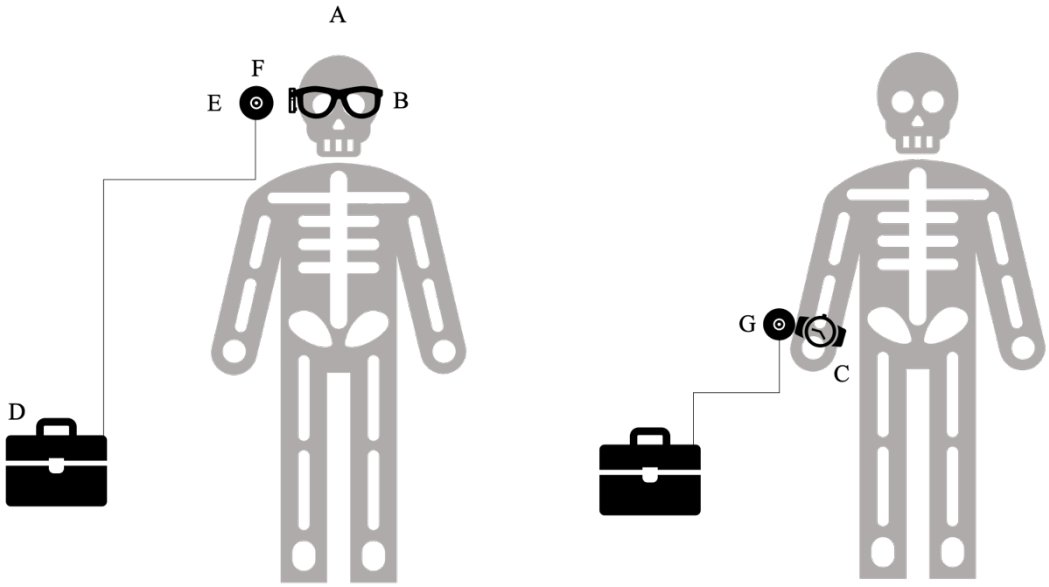

Figure 2. The skeleton (A) setup with the spectacle mounted Clouclip (B) and Actiwatch 2 (C). The photometer (D) was setup with the light sensor (E) held at eye-level (F) and wrist-level (G) to allow comparison of outputs with the Clouclip and the Actiwatch 2, respectively. Diagram not to scale.

Statistical Analysis

1.1.1.3 Clouclip Inter-Device Reliability

1.1.1.4 SPSS Version 25 was used for all statistical analyses. Reliability analysis using two-way mixed, average measures, absolute agreement models were used to calculate the inter-device intraclass correlations for the Clouclip metrics under test (illumination and viewing distance). This enabled comparison of the 60-minute sample of illumination (every 2 minutes) and viewing distance (every 5 seconds) for all five Clouclips under investigation.

1.1.1.5 Validity of Actiwatch 2 and Clouclip Measures and Categorisation of Illumination: Comparison with Hagner-S2 Universal Photometer

Scatterplots were constructed to illustrate the relationship between measures made with the Actiwatch 2 and the photometer, and the Clouclip and the photometer across a range of illuminations. Illumination data from the photometer, Actiwatch 2 and Clouclip were tested for normality using the Shapiro-Wilk test and were found to follow a non-normal distribution (all $p<0.001$) therefore, Spearman's Rank Order Correlations were used. Illumination category 'cut-offs' were included in a graphical representation to illustrate the capability of the Actiwatch 2 to successfully categorise ambient light levels into each of the four categories described in Table 1(Rosenfield and Logan, 2009; SolarLight, 2014; Ulaganathan *et al.*, 2019; Bhandari and Ostrin, 2020); scotopic (≤0.01 lux), mesopic (0.02-3 lux), indoor photopic (>3-1000 lux) and outdoor photopic (>1000 lux) light. As the Clouclip cannot measure illumination below 1 lux, environmental illuminations of ≤1 lux are recorded as 1 lux on the output Excel file. Therefore, Clouclip is unable to differentiate between scotopic and low mesopic illumination. Hence for the purpose of this study, the scotopic and mesopic categories were combined and the ability of the Clouclip to successfully categorise ambient light levels within its operating range was evaluated in terms of the following categories, scotopic/mesopic (≤3 lux), indoor photopic (>3-1000 lux) and outdoor photopic (>1000 lux) light and was also presented in graphical and numerical format. The agreement between measures recorded by the wearable devices and the photometer were compared using Bland and Altman analyses.(Bland and Altman, 1986) The mean difference in illumination measures and 95% limits of agreement (LOAs) were plotted for each wearable device against the

photometer and regression analyses were used to check for proportional bias. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the area under curve (AUC), sensitivity and specificity of the photometer, Actiwatch 2 and Clouclip in identifying a measurement taken indoors and outdoors using the traditional cut-off >1000 lux.

Results

1.1.1.6 Clouclip Inter-Device Reliability

The inter-device intraclass correlation coefficients (ICCs) for the Clouclip devices under test are shown in Table 2 below. The ICCs indicate good and excellent inter-device reliability for illumination and viewing distance measures, respectively.

CLOUCLIP PARAMETER	INTER-DEVICE INTRACLASS CORRELATION COEFFICIENTS (ICC)
ILLUMINATION (LUX)	0.853
VIEWING DISTANCE (CM)	0.958

Table 6. Inter-device intraclass correlation coefficients for the Clouclip parameters

1.1.1.7 Validity of Actiwatch 2 and Clouclip Measures and Categorisation of Illumination: Comparison with Hagner-S2 Universal Photometer

The natural light measured (by the photometer) ranged between 0-3700 lux and 0-6850 lux when comparing the photometer and Clouclip and photometer and Actiwatch 2, respectively. Strong correlations were found between 'true' photometer-measured illumination and both the Actiwatch 2 (ρ=0.99, $p<0.0001$) and the Clouclip (ρ=0.991, $p<0.0001$) measures (Figure 3). Both devices underestimated the illumination levels in comparison to the photometer when exposed to high levels of outdoor light (>2500 lux). However, the Actiwatch 2 consistently underestimated the illumination in all lighting conditions to a greater degree than the Clouclip (Figure 3). The disparity between both wearable devices' recordings and the photometer output increased with increasing illumination. Table 3 presents how successfully the Actiwatch 2 and Clouclip devices categorised illumination levels, using the photometer reading as the reference value.

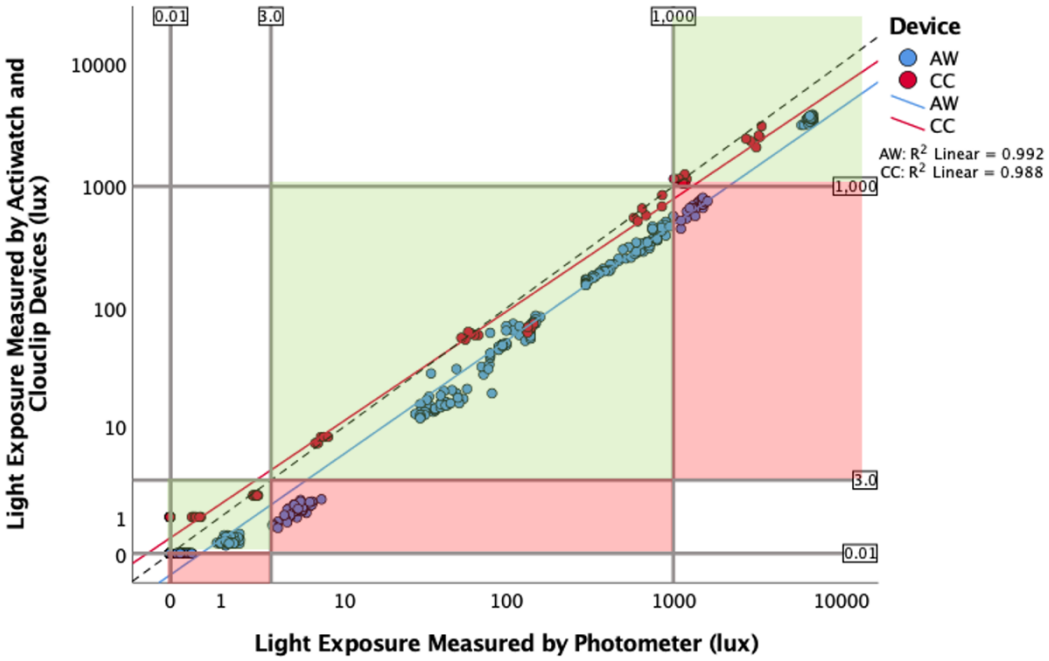

Figure 3. Illumination measures taken with the photometer vs Clouclip (CC) and the photometer vs Actiwatch 2 (AW) plotted on a logarithmic scale. The measures taken by the Clouclip every 2 minutes and the photometer measures averaged over the corresponding 2 minutes are represented by a single data point (red). The measures taken by the Actiwatch 2 and photometer every 15 seconds are also represented by a single data point (blue). The black dashed line represents the line of unity (1:1). The solid red and blue lines indicate the correlation between the photometer and Clouclip measures and the photometer and Actiwatch 2 measures, respectively. Data points falling in the shaded green areas represent the measurements made by the wearable devices provided a classification of light level which agreed with the photometer, while the shaded red areas represent incorrect classification by the wearable devices. The Actiwatch 2 and photometer are unable to differentiate between illumination levels lower than 0.01 and 0.1 lux, respectively. Lower illuminations are recorded as 0.01 lux and 0 lux, respectively. The Clouclip is unable to differentiate between illumination levels less than or equal to 1 lux. Lower illuminations are recorded by the Clouclip as 1 lux.

LIGHT EXPOSURE MEASUREMENT BY PHOTOMETER	CATEGORY	ACTIWATCH 2 CATEGORISATION
≤ 0.01 LUX	Scotopic	100% (44/44)
0.02-3 LUX	Mesopic	50% (44/88)
>3-1000 LUX	Indoor Photopic	77.3% (150/194)
> 1000 LUX	Outdoor Photopic	62.9% (44/70)
OVERALL	All categories	71.2% (282/396)

LIGHT EXPOSURE MEASUREMENT BY PHOTOMETER	CATEGORY	CLOUCLIP CATEGORISATION
≤3 LUX	Scotopic/Mesopic	100% (18/18)
>3-1000 LUX	Indoor Photopic	100% (24/24)
> 1000 LUX	Outdoor Photopic	100% (12/12)
OVERALL	All categories	100% (54/54)

Table 7. The agreement between the photometer and both wearable devices when categorising illumination levels with the number of measures in each condition noted. The scotopic and mesopic categories are combined for the Clouclip due to the device's floor effect preventing it from distinguishing between scotopic and low mesopic illuminations.

As seen in Figure 3, while the Clouclip outputs are more closely aligned with the photometer's categorisation, neither the Actiwatch 2 nor the Clouclip correctly categorised all the illumination levels to which they were exposed. Adjusted cut-off criteria for scotopic, mesopic, indoor and outdoor photopic categories calculated from application of the linear fit equations from Figure 3 are presented in Table 4 for both devices.

LIGHT EXPOSURE CATEGORIES (LUX)	**EMPIRICALLY DERIVED ACTIWATCH 2 CRITERIA (LUX)**
SCOTOPIC ≤ 0.01	≤0.01
MESOPIC 0.02-3	0.02-0.78
INDOOR PHOTOPIC 3-1000	>0.78-533.15
OUTDOOR PHOTOPIC >1000	>533.15
LIGHT EXPOSURE CATEGORIES (LUX)	**EMPIRICALLY DERIVED CLOUCLIP CRITERIA (LUX)**
SCOTOPIC/MESOPIC ≤3	≤3
INDOOR PHOTOPIC 3-1000	>3-850
OUTDOOR PHOTOPIC >1000	>850

Table 4. The adjusted criteria for Actiwatch 2 and Clouclip devices to better align classification with that defined by the photometer. These criteria were derived from the application of linear fit equations from Figure 3. A combined 'scotopic/mesopic' category for measures ≤3 lux has been applied to the Clouclip because the operating range of the device does not allow for measurements ≤1 lux to be differentiated.

Figures 4 and 5 illustrate the Bland and Altman analyses evaluating the agreement between measures of illumination taken with the photometer and the two wearable devices. The mean differences between the Actiwatch 2 and photometer, and Clouclip and photometer are 430.92 and 79.35 lux, respectively. The limits of agreement (LOAs) between measures made with the Actiwatch 2 compared with the photometer (±1828.74 lux) are wider than those derived by the Clouclip comparison with the photometer (± 407.33 lux). Regression analyses demonstrated significant proportional bias for both the Actiwatch 2 compared to the photometer ($r=0.998$, $p<0.001$) and the Clouclip compared to the photometer ($r=0.778$, $p<0.001$).

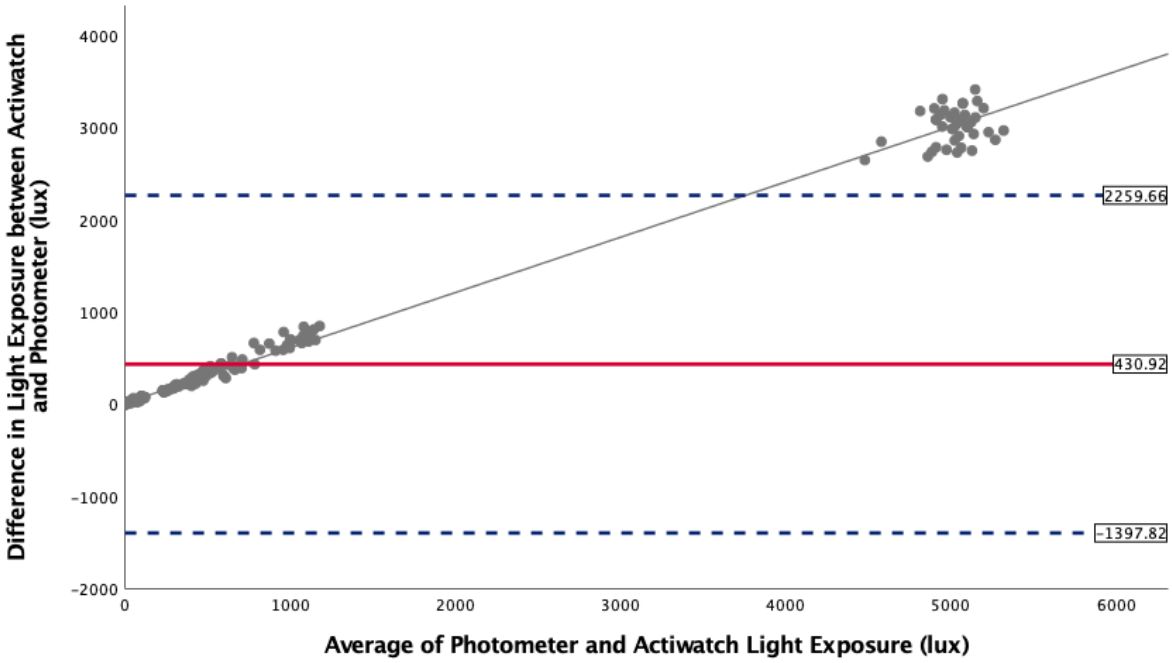

Figure 4. Bland and Altman plot for illumination measures recorded with the photometer and Actiwatch 2. The red line represents the mean difference between illumination measures. The dashed blue lines represent the upper and lower limits of agreement and the grey line illustrates the proportional bias (r=0.998, p<0.001).

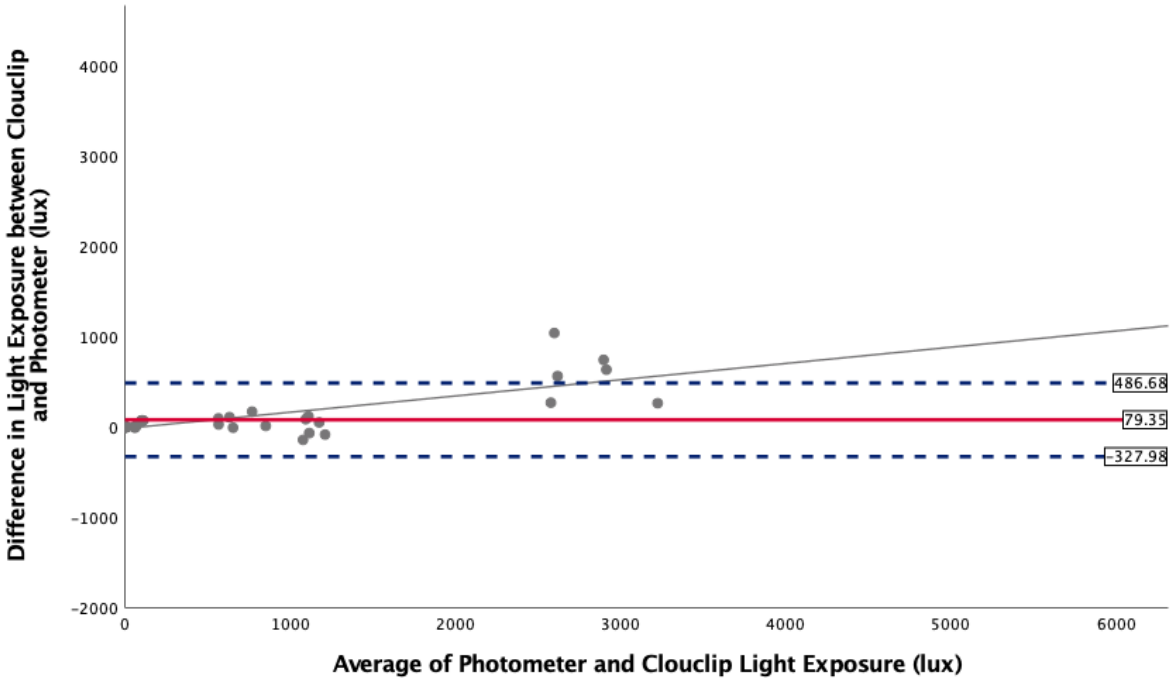

Figure 5. Bland and Altman plot for illumination measures recorded with the photometer and Clouclip. The red line represents the mean difference between illumination measures. The dashed blue lines represent the upper and lower limits of agreement and the grey line illustrates the proportional bias (r=0.778, p<0.001).

During testing it was noted that light levels of >1000 lux were occasionally recorded in indoor environments such as when the skeleton was situated adjacent to a window/door. ROC curve analysis was carried out to determine the sensitivity (i.e., a measurement of >1000 lux results in correct identification of an outdoor position) and specificity (i.e., a measurement of ≤1000 lux results in correct identification of an indoor position) of each device, for determining between an indoor and outdoor setting using the traditional cut-off of >1000 lux. The results are presented in Table 5.

DEVICE USED	AREA UNDER CURVE (AUC)	SENSITIVITY (%)	SPECIFICITY (%
PHOTOMETER	1.00	90.5	100
ACTIWATCH 2	1.00	99.7	100
CLOUCLIP	1.00	91.7	100

Table 5. The results of ROC curve analysis reporting the sensitivity and specificity of using >1000 lux to identify whether the measurement was taken outdoors or indoors for each of the devices.

Discussion

This is the first study that has examined the Clouclip's inter-device reliability for both near viewing distance and illumination measures. Moreover, this is the first to investigate the ability of the Actiwatch 2 and the Clouclip to identify different illumination categories (scotopic, mesopic, indoor photopic and outdoor photopic) used by researchers to explore and compare children's activity and light exposure profiles.

The present real-world data clarifies the strengths and limitations of using the Clouclip to study illumination measures in Northern Ireland (UK, 55° North), demonstrating for the first time good and excellent inter-device reliability with intraclass correlation coefficients of 0.853 and 0.958 for illumination and near viewing distance measures, respectively.(Koo and Li, 2016) Bhandari and Ostrin[36] report that the Clouclip slightly underestimated 'true' illumination in comparison to a photometer. Our findings support those of Bhandari and Ostrin, illustrating that the Clouclip underestimates 'true' lux values in higher levels of illumination, but to a lesser degree than the Actiwatch 2 outputs.

Underestimation of the 'true' illumination value results in the Actiwatch 2's relatively poor ability to successfully identify environmental light as scotopic, mesopic, indoor

photopic or outdoor photopic. Misclassification was most prevalent in dimmer illumination; low levels of mesopic light were classified by the Actiwatch 2 as scotopic, indoor photopic light as mesopic, and outdoor photopic light as indoor photopic (Figure 3). Given that outdoor photopic light is generally in the range 1000 to 10000 lux,(ATP Instrumentation, 1989) but can be as high as 100,000 lux on a very bright summer day,(Ostrin, 2017) the opportunities for misclassification of outdoor light (between 1000-2500 lux) by the Actiwatch 2 are likely to be limited to measures made at dusk or dawn, particularly in the winter months. The empirically calculated criteria presented in Table 4 can be applied to both Actiwatch 2 and Clouclip outputs to allow categorisation that aligns more closely with photometer measures. Joyce *et al.* also recommended the use of a conversion factor when using the Actiwatch 2 to accurately quantify ambient illumination.(Joyce *et al.*, 2019)

In findings similar to the present study, Joyce *et al.* (2019) found that the Actiwatch 2 underestimated the true illumination in comparison with a calibrated photometer, but that the relationship between the illumination outputs by the Actiwatch 2 and photometer was strongly linear.(Joyce *et al.*, 2019) Jardim *et al.* (2011) also report that both eye-level (Daysimeter) and wrist-level (Actiwatch-L) illumination measures were correlated with each other at <5000 lux but above that, the Actiwatch-L underestimated the illumination. The average difference across the entire day between the eye-level and wrist-level illumination was 130 lux, with a range of differences of 5-1000 lux.(2011) In contrast to two previous studies which found the Actiwatch Spectrum to consistently overestimate illumination in comparison to calibrated photometers,(Figueiro *et al.*, 2013; Markvart, Hansen and Christoffersen, 2015) our data demonstrate consistent underestimation of the 'true' illumination value by the Actiwatch 2. The Actiwatch-L and Actiwatch 2 both have a silicon photodiode light sensor while the Actiwatch Spectrum has colour sensitive photodiodes which could explain the variation in under- and overestimation of illumination when compared to photometer measures.

The present study demonstrates that the Clouclip measures of illumination are more comparable to the 'true' illumination measured by a calibrated photometer than those achieved with the Actiwatch 2. The relationship between the Clouclip and photometer measures found in the present study (ρ=0.991) are similar to those reported by Bhandari and Ostrin(2020) who also report a strong relationship between measures made by the Clouclip and photometer (r= 0.96). In higher levels of illumination (>2500 lux), the

Clouclip underestimates the 'true' lux value in comparison with the photometer, but this is unlikely to result in misclassification of the outdoor photopic light category. The Clouclip is unable to distinguish between scotopic and mesopic light ≤1 lux, and therefore is not a useful tool to explore exposure to extremely low light levels as it cannot discern between scotopic and low mesopic illumination. However, when used to distinguish between mesopic and indoor photopic, and indoor and outdoor photopic light levels, the Clouclip performed more successfully than the Actiwatch 2 (Table 3). Classification by the Clouclip remained accurate even when illumination levels measured by the photometer were close to the category borders. Bhandari and Ostrin(2020) report that the Clouclip could reliably detect outdoor illumination (defined as >1000 lux) in a more southerly location than (Houston, Texas 29° North) than the present study.

Several studies have used the Actiwatch 2 to quantify differences between myopes and non-myopes in terms of time spent in different lighting conditions.(Read, Collins and Vincent, 2014, 2015; Landis *et al.*, 2018) However, the criteria used to delineate one type of illumination from another has been inconsistent, making comparison between data sets challenging. Landis *et al.* report that non-myopes spent a greater amount of time in scotopic light conditions compared with myopic children. [48] When combined with the rather extended definition of scotopic used by Landis et al (<1-1 lux) compared to more commonly accepted values (≤0.01 lux)(SolarLight, 2014) as used in the present study and the underestimation of illumination by the Actiwatch 2 reported here, the light levels in Landis *et al.*'s study attributed as 'scotopic' could have been anywhere between scotopic and low mesopic. While the non-myopic children spent more time in these lower lighting levels than their myopic peers it is not clear whether the illumination was truly rod activating as the authors suggest. It has also been reported using Actiwatch 2 data that non-myopes spend more time in outdoor photopic (>1000 lux) light levels than myopes.(Read, Collins and Vincent, 2014, 2015; Landis *et al.*, 2018) The results of the present study suggest that the amount of time exposed to light of >1000 lux is likely to have been underestimated using a cut-off of >1000 lux measured by these wristworn devices, although the effect will be consistent across refractive groups. For researchers wishing to evaluate time spent in different light levels including the very dimmest illumination, the broader measurement range of the Actiwatch 2 makes it a more useful tool than the Clouclip, but researchers should be

aware of, and calibrate for, the underestimation of true illumination using empirically derived cut-offs.

The Bland and Altman analysis comparing illumination measures between the Actiwatch 2 and photometer (Figure 4), and the Clouclip and photometer (Figure 5), indicate the superior ability of the Clouclip to determine 'true' illumination compared to the Actiwatch 2, as illustrated by the smaller mean difference and narrower LOAs for the Clouclip (79.35 ± 407.33 lux) compared to the Actiwatch 2 (430.92 ± 1828.74 lux). However, there is significant proportional bias for both devices, illustrating that as the illumination increases the measures recorded by the wearable devices deviate more from the 'true' value.

A notable finding of the present study was that readings >1000 lux were recorded by the photometer in indoor domestic locations, when the sensor was near a window/door with bright sunlight streaming in. Illumination readings of >1000 lux are commonly used by researchers to denote time spent outdoors.(Read, Collins and Vincent, 2014; Ostrin, 2017; Landis *et al.*, 2018; Ulaganathan *et al.*, 2019) The present field study determined that even when using a calibrated photometer to measure illumination, a value of >1000 lux does not always indicate an outdoor location. Using this cut-off to indicate an outdoor location as measured by the calibrated photometer has a sensitivity (i.e., a measurement of >1000 lux results in correct identification of an outdoor position) of 90.5% and specificity (i.e., a measurement of ≤1000 lux results in correct identification of an indoor position) of 100% (Table 5). The Clouclip suffers from a similar limitation, but because the Actiwatch 2 consistently under-estimates 'true' lux, the >1000 lux values recorded with the Actiwatch 2 will reflect outdoor location more consistently than when recorded by the other devices used in the present study, with a sensitivity of 99.7% and specificity of 100%. Time spent outdoors not only confers higher light levels, but also more varied spectral content as well as differences in dioptric demand and spatial content experienced by the eye. Given that there is still debate about the mechanisms by which time spent outdoors protects against myopia,(Flitcroft, 2012; Ngo *et al.*, 2013) this distinction may be important. If researchers want to accurately discriminate between time spent indoors and outdoors, activity may need to be certified by video or GPS data when using the Clouclip. The use of activity diaries can also support objectively gathered data in profiling time spent outdoors.

The results of the present study highlight some benefits and limitations of the Actiwatch 2 and Clouclip devices for measuring illumination. Both devices are wearable and therefore ideal for field-use. The Actiwatch 2 can record illumination across a wider range of light levels and is therefore useful when investigating time spent in conditions ranging from near-dark scotopic illumination through to bright outdoor photopic light levels. However, the Actiwatch 2 underestimates light levels to a greater extent than the Clouclip and more often misclassifies illumination than the Clouclip, if the traditional criteria for categorisation are applied. The empirically derived cut-offs for illumination described in Table 4 are likely to be more appropriate for determining time spent in different types of illumination if researchers are using a categorical approach to analyse environmental light exposure. The Clouclip outputs more closely resemble 'true' illumination as measured by the photometer, and the spectacle mounted device accurately classifies light exposures >1 lux. However, the Clouclip's utility is limited by a short battery life, a restricted recording epoch and an inability to determine between scotopic and low mesopic light levels as illumination ≤1 lux is recorded as 1 lux in the output Excel. Additionally, the restricted two-minute recording epoch could result in under- or over-estimation of time spent in different categories of illumination if the wearer is moving rapidly between different environments. This may be particularly relevant when conducting research aimed at understanding light exposure profiles of children; the Clouclip will not capture dynamic changes in environment as readily as the Actiwatch 2, which has the option of shorter recording epochs (15, 30 or 60s).

The present study was intentionally carried out in the field rather than a laboratory setting to gain insight into the real-world utility of the devices. However, the non-laboratory setting resulted in reliance on the natural light conditions encountered and it was not possible to control the specific lux range to which the devices were exposed. The outdoor illumination values are reflective of the real-world light levels experienced in the present study's location (Northern Ireland, UK 55° North). Interpretation of the results is restricted to evaluation of the devices' performance in these naturally occurring light conditions. It should also be recognised that the devices were not compared with the photometer under identical conditions due to practical constraints, including the need to continually 'wobble' the skeleton's head to prevent the Clouclip entering 'sleep mode'. The Clouclip wasn't exposed to the same high illuminations that were available when undertaking testing with the Actiwatch 2, and therefore the two devices' outputs could not be directly compared to each other.

Conclusion

The present data illustrate that different Clouclip devices produce comparable measures of viewing distance and illumination in a real-world setting. Both Actiwatch 2 and Clouclip devices underestimate illumination in the field when compared to 'gold standard' photometer measures. This disparity increases at higher levels of illumination and is greater for the Actiwatch 2 measures. For researchers interested in categorising light exposure into different classifications from mesopic through to outdoor photopic levels, the Clouclip is a more useful tool, but when scotopic and low mesopic differentiation is required, the Actiwatch 2's broader measurement range is required. Empirically calculated criteria for defining scotopic, mesopic, indoor and outdoor photopic illuminations are presented for the Actiwatch 2 devices and empirically calculated criteria for defining scotopic/mesopic, indoor and outdoor photopic illuminations are presented for the Clouclip devices. These could be applied by researchers to improve the accuracy of categorisation, or researchers may consider undertaking such calibration activity for the devices used in their own research. Finally, caution should be applied when using a cut-off of >1000 lux as a proxy for outdoor settings.

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