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# RISK FACTORS OF MYOPIA DEVELOPMENT AMONG HONG KONG PRIMARY SCHOOL STUDENTS

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# Risk Factors of Myopia Development among Hong Kong Primary School Students

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A thesis submitted in partial fulfillment of the requirements

for the

degree of Master of Philosophy

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# **CERTIFICATE OF ORIGINALITY**

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LIANG Yuanyuan

### Abstract

**Purpose:** Myopia is a common cause of visual impairment, reaching "epidemic" proportions, especially in several East Asian countries. Most myopia emerge during childhood, particularly during the school years. Although some genes suspected to be involved in myopia development have been documented, currently most attention is paid to environmental factors, such as increasing educational pressures combined with reduced outdoor time. The main purposes of this thesis were: (1) to determine myopia proportion and compare risk factors of myopia among Hong Kong Chinese primary school children under two different educational systems; and (2) to determine myopia proportion after "study at home" during COVID-19.

**Methods:** *Study (1):* Vision screenings were conducted in one governmentfunded primary school and one international school in September and October, 2018, respectively. Measurements were performed on children aged 8 to 10 years old. Non-cycloplegic refraction and axial length were measured by an open-field autorefractometer (Shin-Nippon, NVision K5001, Japan) and an IOL Master (Carl Zeiss Meditec AG, Germany), respectively. A validated questionnaire focusing on demographic information, non-screen time (e.g., reading and writing on paper materials), screen time (i.e. smartphones and tablets usage), time spent on outdoor activities, and other myopia risk factors was completed by parents of participants. *Study (2):* The same vision screening as described in study 1 was conducted in the same local school after school closure in June 2020. The same ophthalmic instruments and school settings were adopted. We compared the vision screening and questionnaire results with those collected in 2018.

**Results:** *Study (1):* The proportions of myopia (SER  $\leq$  -1.00 D) and refractive astigmatism (Cyl  $\geq$  1.00 DC) were significantly higher in the local school than those in the international school. There were differences between two schools in demographic information such as the parental myopia history and their educational level received. Children in different schools were exposed to different risk factors of myopia. *Study (2):* the myopia proportion (SER  $\leq$  -1.00 D) in the same school had nearly doubled after the school lockdown. The surge in myopia proportion was accompanied by an increased axial length. Compared with the 2018 survey, the time spent on handheld digital devices (i.e. smartphone and tablet) increased while time spent on non-screen activities decreased (i.e. reading, writing, etc). The proportions of inappropriate visual habits were also increased in the 2020 survey.

**Conclusion:** The myopia proportion differed between the two school models in Hong Kong and students under different educational systems were exposed to different myopia risk factors. In addition, the proportion of myopia was doubled accompanied with increased axial length in the same school after home confinement.

|||

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# Abbreviations

- ALSPAC: Avon Longitudinal Study of Parents and Children
- ACES: Anyang Childhood Eye Study
- AL: Axial Length
- BMPS: Beijing Myopia Progression Study
- BCES: Beijing Children Eye Study
- CLEERE: The Collaborative Longitudinal Evaluation of Ethnicity and

**Refractive Error** 

- COMET: The American Study of the Correction of Myopia Evaluation Trial
- CREAM: the Consortium for Refractive Error And Myopia
- D: Dioptre
- EOM: Early Onset Myopia
- GWAS: Genome-Wide Association Studies
- HOA: Higher Order Aberration
- IMI: International Myopia Institute
- ICC: Intraclass Correlation Coefficient
- LOM: Late Onset Myopia
- NICER: Northern Ireland Childhood Errors of Refraction
- NITM: Near-work Induced Transient Myopia
- OLSM: Orinda Longitudinal Study of Myopia
- OR: Odds Ratio

- PAL: Progressive Addition Lens
- PISA: Programme for International Student Assessment
- RR: Risk Ratio
- **RCT: Random Clinical Trial**
- **RESC: Refractive Error Study in Children**
- ROAM: Role of Outdoor Activity in Myopia
- SER: Spherical Equivalent Refraction
- SCORM: Singapore Cohort Study of the Risk Factors for Myopia
- STARS: STrabismus, Amblyopia and Refractive error in Singaporean
- SPSS: Statistical Package for Social Science
- SMS: Sydney Myopia Study
- SAVES: The Sydney Adolescent Vascular and Eye Study

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## **Chapter 1: Introduction**

This literature review focused on three parts: (i) myopia and its impact on public health, (ii) emmetropization and myopia development, and (iii) risk factors associated with myopia and potential mechanism for myopia development.

#### 1.1 Myopia and Its Impact

#### 1.1.1 Definition of Myopia

Myopia is a kind of refractive error (Holden et al., 2016) due either to the ocular refractive power (i.e., cornea and lens) being too strong or the axial length being too long, consequently the retinal image is focused in front of the retina when eye is in relaxed state. The definition of myopia in terms of magnitude varies slightly between studies, but it has been defined in a White Paper recently as SER of  $\leq$  -0.50 D when the accommodation is relaxed (Flitcroft et al., 2019). The major cause of myopia among children is the excessive axial length (Morgan et al., 2012).

#### 1.1.2 Classification of Myopia

There are different classifications of myopia. Myopia has been classified as either physiologic or pathologic depending on whether there is any degenerative ocular complications (Curtin, 1985). According to the age of myopia onset, it can also be classified as congenital (onset at birth), early onset (myopia develops between 5 to 15 years old) or late onset (myopia develops 16 years or older) myopia (Grosvenor, 1987). Early onset myopia is also known as school myopia (Saw et al., 1996) since myopia begins to show and progresses during this period (Lam et al., 1991; Lin et al., 2004). Late-onset adult myopes can be further classified as either progressing or stable based on their myopia progression (Kinge et al., 2000). According to the main structural components associated with myopia, myopia can be classified into axial myopia, which is due to excessive eyeball elongation, and refractive myopia, which is due to strong refractive power in cornea and/or lens (Rosenfield et al., 1998). Nonetheless, the classification according to the degree of refraction is the most commonly used. The latest IMI review paper suggests myopia to be categorized as: low myopia (-6.00 D <SER $\leq$  -0.50 D), high myopia (SER  $\leq$  -6.00 D), and premyopia (-0.50 D <SER≤ +0.75 D) (Flitcroft et al., 2019). Children's baseline refractive error, together with age and other risk factors, are used to predict the future myopia development. The concept of premyopia calls for the attention to prevent myopia at early age.

#### 1.1.3 Interpretation of non-cycloplegic refraction

Lack of cycloplegia not only leads to the over estimation of the prevalence of myopia due to the strong accommodative amplitude among children, but also makes it difficult to compare cycloplegic with non-cycloplegic refractions (Zhao et al., 2004). It has been shown that differences between cycloplegic and noncycloplegic refractions were much greater for hyperopes and emmetropes than for myopes (Fotedar et al., 2007; Zhao et al., 2004). For example, in You's study investigating Chinese children (range: 7-18 years), the difference between precylcoplegic and post-cylcoplegic values was  $0.57 \pm 0.63$  D for the eyes with a refractive error ranging from hyperopia to myopia (SER  $\leq -0.50$  D), and it was  $0.29 \pm 0.40$  D in the eyes with myopia (SER  $\leq -0.50$  D) (You et al., 2012). Thus, a valid conclusion cannot be reached with non-cycloplegic refraction, especially when the primary outcome measure is myopia prevalence.

#### 1.1.4 Myopia Prevalence and Progression

Myopia is regarded as a worldwide public health issue (Pararajasegaram, 1999). Based on the data from 145 studies and 2.1 million participants, a recent metaanalysis study predicted that half of the world population will become myopic by 2050, and more alarmingly, the percentage of high myopia (defined as SER  $\leq$  -5.00 D in this study) will increase to 10% (Holden et al., 2016). However, it should be cautious that this prediction model did not consider the potential influence of myopia control on the future myopia prevalence, and the model also did not consider the potential influence of some studies with noncycloplegic refractions (see above). Table 1.1 summarizes the prevalence of myopia among schoolchildren in Hong Kong and other parts of the world from 2002. Random sampling methods were used in these cross-sectional studies. In addition, some longitudinal cohort studies were also included in Table 1.1. Despite the differences in methodology including the use of cycloplegic and myopia definition, it is observed that myopia prevalence varies by geographical location. In East and Southeast Asia, myopia has become an epidemic (Morgan et al., 2012). It has been reported that myopia begins to develop and progress when children start schooling (Lin et al., 2004; Fan et al., 2004). By the time they graduate from high school (around 18 years old), the myopia prevalence reaches 80%-90% (Jung et al., 2012; Sun et al., 2012., Wu et al., 2015). Furthermore, myopia has become more prevalent across Western and Northern Europe (Williams et al., 2015).

The myopia progression was the average change in spherical-equivalent refraction (SER) divided by the time of follow-up in years. The average progression is -0.63 D per year in Hong Kong myopic children (5 to 16 years) (Fan et al., 2004) and -0.70 D per year in Singapore myopic children (7 to 9 years) (Saw et al., 2005). In the Northern Ireland Childhood Errors of Refraction (NICER) study, the annual myopia progressions were -0.23 D and -0.10 D for European Caucasian children aged 6–7 years and 12–13 years, respectively (McCullough et al., 2016). In the Sydney Myopia Study (SMS), the annual shifts in myopia were -0.41 D and -0.31 D among children aged 6 years and 12 years, respectively (French et al., 2013). Younger children aged 6-9 years tended to progress faster than older children (Wolffsohn et al., 2019). Although myopia

progression varies between different ethnicities, delaying the onset of myopia is likely to slow the myopia progression and onset of high myopia (Chua et al., 2016; Hu et al., 2020).

Study	Location	Ethnicity	Age (Years)	Sample size	Cycloplegia	Муоріа	Myopia prevalence
						definition	
Yam et al., 2020	Hong Kong	Chinese	6-8	4257	Yes	SER ≤ -0.50 D	25.0%
He et al., 2019	Shanghai	Chinese	6-9	6295	Yes	SER ≤ -0.50 D	7.7%-8.9%
You et al., 2012	Beijing	Chinese	7-18	15066	No	SER ≤ -0.50 D	64.9%
Fan et al., 2004	Hong Kong	Chinese	6-15	7560	Yes	SER ≤ -0.50 D	36.7%
Lin et al., 2004	Taiwan	Chinese	7, 12, 15	920-937	Yes	SER ≤ -0.25 D	21%, 61%, 81%
He et al., 2004	Guangzhou	Chinese	5-15	4347	Yes	SER ≤ -0.50 D	35.1%
Saw et al., 2002	Singapore	Chinese	7-9	1453	Yes	SER ≤ -0.50 D	29.0%, 34.7%, 53.1%
McCullough et al., 2016	Northern Ireland	Caucasian	6–7, 12–13	212	Yes	SER ≤ -0.50 D	1.9%; 14.6%
Saxena et al., 2015	North India	NA	5-15	9884	Yes	SER ≤ -0.50 D	13.1%
Guggenheim et al., 2012	Southwest	Caucasian	7, 10, 11, 12,	4837-7747	No	SER ≤ -1.00 D	2.5%, 7.6%, 10.8%, 14.6%,
	England		15				21.6%
Rose et al., 2008	Sydney	Caucasian	6, 12	2511	Yes	SER ≤ -0.50 D	0.7%, 5.1%
Kleinstein et al., 2003	USA	40.5% Caucasian	6-14	2583	Yes	SER ≤ -0.75 D	10.1%

Table 1.1. Prevalence of myopia among schoolchildren in Hong Kong and other parts of the world since 2002.

#### 1.1.5 Adverse Effects of Myopia

The development of myopia has been strongly associated with structural changes of the eye, in particular eyeball elongation (Curtin et al., 1971, Flitcroft et al., 2019). With the increasing rate of early onset myopia accompanied with fast progression, high myopia is more likely to emerge in children, leading to a series of sight-threatening complications such as myopic macular degeneration (Ohno-Matsui et al., 2015), retinal detachment (Lam et al., 2005), and glaucoma (Shen et al., 2016). It has become a significant public health concern both for global economy (Zheng et al., 2013) and for individual visual consequences due to these ocular pathologies (Morgan et al., 2012).

#### 1.1.6 Myopia Control Methods

Currently there are many methods aimed to slow myopia progression and axial elongation. A meta-analysis study comparing different interventions for myopia (the last clinical registration was in August 2014) reported that pharmacological treatment is more effective than optical methods using contact lenses or spectacles (Huang et al., 2016). Pharmacological methods such as atropine (Yam et al., 2020), optical methods such as orthokeratology (Cho et al., 2017), MiSight (Chamberlain et al., 2019), Stellest<sup>™</sup> lens using highly aspherical lenslet target (Bao et al., 2021), and Defocus Incorporated Multiple Segments (DIMS) spectacle lenses (Lam et al., 2020) show effective treatment effects on myopia control. On the other hand, a recent RCT compared treatment effects

between 0.01% atropine combined with orthokeratology (AOK) versus orthokeratology (OK) alone. The one-year result showed an additive effect with mean axial elongation in the AOK group shorter than that in the OK group (0.07 mm/year vs. 0.16 mm/year) (Tan et al., 2020).

#### 1.2 Eye Growth

#### 1.2.1 Emmetropization

Emmetropization is a process in which infantile refractive errors disappear (i.e., achieving emmetropia) naturally over time observed in animal studies. Evidence shows that emmetropization is a visually guided process in both human (Flitcroft, 2014) and animals (Troilo et al., 2019). Emmetropia is the refractive state of the eye where the image of a distant object is sharply focused on the retina without an accommodative effort, any disruption to this process may lead to refractive errors (Brown et al., 1999).

Infants were typically born with hyperopia (+1.00 D to +2.50 D) (Flitcroft, 2014). The hyperopia decreases rapidly toward emmetropia during the first year and by 6 years of age, emmetropia or low hyperopia (approximately 1.00 D or less) is the predominant refractive status (Flitcroft, 2014). However, population-based studies at eight sites in the Refractive Error Study in Children (RESC) showed that mild hyperopia (+0.50 D <SER≤ +2.00 D) was the most prevalent

category in all ages (5 to 15 years old) (Morgan et al., 2010). It indicated that mild hyperopia was predominant, if refractive status drops below this level, emmetropia during childhood carries the risk of subsequent progression to myopia (Morgan et al., 2010). Optical changes in corneal curvature (Inagaki, 1986), axial length (Fledelius et al., 1996) and lens power also occurred during this period (Mutti et al., 2005). The process of emmetropization may continue after 6 years but becomes much slower (Flitcroft, 2014). Even in regions known to have high myopia prevalence such as Mainland China, Hong Kong, Japan and Singapore, the emmetropization process appears to be largely completed by this age (e.g., the prevalence of myopia was less than 5% when children were 6 years or younger) (Fan et al., 2004; He et al., 2009., Matsumura et al., 2009; Tan et al., 2000).

#### 1.2.2 Abnormal Refractive Development

#### 1.2.2.1 Form Deprivation

Animal studies improve our understanding of the mechanism underlying refractive error development. The induction of form deprivation myopia is due to the deprivation of a sharp retinal image. Imposing form deprivation by eyelid suture or translucent occluders in tree shrews (Norton, 1990), marmosets (Troilo et al., 1993), chickens (Wallman et al., 1978), fishes (Shen et al., 2005), and monkeys (Smith III et al., 2000; Wiesel et al., 1977) induced excessive ocular elongation and significant myopic shift in an open-loop condition without

a well- defined endpoint (Morgan et al., 2013).

Similarly, visual experience is important for normal eye growth in humans. Deprived of form vision in early childhood such as ptosis (Gusek-Schneider et al., 2001), congenital cataract (von Noorden et al., 1987), corneal opacity (Gee et al., 1988), and vitreous haemorrhage (Mohney, 2002) all lead to excessive eye growth when compared to children with normal vision.

#### 1.2.2.2 Lens Induced Defocus

In animal models, it is well established that eyes can compensate for the imposed optical defocus, within a certain range, in monkeys (Huang et al., 1995), chickens (Irving et al., 1992), marmosets (Benavente-Perez et al., 2012), fishes (Shen et al., 2007), and guinea pigs (Lu et al., 2009). Positive (converging) lens can impose myopic defocus in front of retina, this leads to a thickened choroid and reduced ocular growth rate to push the retina forwards to the focal plane. Whereas negative (diverging) lens can impose hyperopic defocus behind the retina, inducing a thinned choroid and axial elongation (Wallman et al., 2004). Once the animal eyes reach the new refractive endpoint, they stop elongating.

Studies showed that humans have similar bi-directional ocular responses to imposed defocus. Young emmetropic adults can respond to short-term (1 hour)

optically imposed defocus: in addition to the change in axial length, the change of choroidal thickness was also found by using instrument of high resolution (Read et al., 2010). Imposing myopic defocus (+3.00 D) caused the axial length to shorten by -13  $\mu$ m and the choroid to thicken by + 12  $\mu$ m; whereas hyperopic defocus (-3.00 D) caused the eye to lengthen (+8  $\mu$ m) and the choroid to thin (-3  $\mu$ m). An even longer exposure to defocus (12 hours, +1.5 D/-2 D) also led to similar axial elongation and choroidal thickness changes (Chakraborty et al., 2012, 2013).

In daily life, eyes are exposed to the combination of myopic and hyperopic defocus from time to time, and animal studies have demonstrated that these optical signals were integrated over time in a non-linear fashion (Wallman et al., 2004). In essence, not only do eyes respond more strongly to myopic than hyperopic defocus (Tse et al., 2007; Winawer et al., 2002; Zhu et al., 2003), presenting brief episodes of myopic defocus or clear vision can attenuate the influence of continuous hyperopic defocus (Delshad et al., 2020; Kee et al., 2007; Smith et al., 2002). Evidence from epidemiological studies also showed that continuous reading without a break may increase the risk of developing myopia (Ip et al., 2008; Li et al., 2015).

#### 1.2.3 Local Control Mechanism

The original study by Schaeffel showed that chicks' eyes treated with negative

lens grew longer and accommodated more compared with those treated with positive lens (Schaeffel et al., 1988). However, the findings from animal studies do not support the pre-requisite for accommodation in eye growth regulation, i.e., eyes can still compensate for imposed defocus in the absence of accommodation (i.e. Edinger-Westphal nucleus lesion (Schaeffel et al., 1990), lesion of ciliary nerve (Wildsoet, 2003), or pharmacological blockage of accommodation (Schwahn et al., 1994), although under these conditions the compensatory response was less accurate. Indeed, a brain-mediated mechanism appears to have additional effect on the accuracy of emmetropization process (Wildsoet, 2003).

Furthermore, localized visual deprivation or defocus resulted in vitreous chamber elongation that was confined to the affected areas only (Smith III et al., 2010; Wallman et al., 1987). Additionally, a series of studies found that the fovea or central retinal region is not essential for controlling refractive development (Smith III et al., 2005; Smith III et al., 2007; Smith III et al., 2009; Stone et al., 2006). Instead, peripheral retinal region can direct the axial elongation even when there were conflicting visual signals between the fovea and peripheral retina (Huang et al., 2009; Smith III et al., 2009; Huang et al., 2011; Smith III et al., 2020). Based on the finding from animal work that peripheral hyperopia can promote the development of central axial myopia, some myopia control methods such as orthokeratology (Kang et al., 2011) and

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multifocal lenses (Chamberlain et al., 2019; Lam et al., 2020) apply this principle to impose myopic defocus in the peripheral retina.

#### 1.3 Aetiology of Myopia

#### 1.3.1 Genetics

Parental myopia and ethnicity are considered as important factors for myopia development (Rudnicka et al., 2016; Wojciechowski, 2011). Myopia is prevalent among children with East Asian ethnicity (Ip et al., 2008; Rose et al., 2008; Twelker et al., 2009). Studies found that children with myopic parents have increased risk of myopia compared to those without myopic parents (French et al., 2013., Jones et al., 2007; Liang et al., 2004; Saw et al., 2002; Wu et al., 1999). Furthermore, the number of myopic parents appears to show a "dose response" effect (Kurtz et al., 2007). A meta-analysis included 16 studies (6 prospective cohort studies, 8 cross-sectional studies, and 2 case-control studies) showed that children with two myopic parent (Zhang et al., 2015).

Zadnik and coworkers proposed that parental myopia predisposed children to myopia development when they examined the role of genetic factor in the myopia development of non-myopic Caucasian children (6-14 years old) (Zadnik et al., 1994). Longitudinal studies in Hong Kong Chinese children (5-16 years old) (Lam et al., 2008) and Generation R Study in Rotterdam among children aged 6-9 years old (Tideman et al., 2019) showed that the number of myopic parents had influence on the growth rate of children's eye, rather than children's axial length, before the onset of myopia.

Twin eye study provided further evidence of the impact of parental myopia. Monozygotic twins demonstrated a greater similarity in refractive errors and ocular parameters to each other compared to dizygotic twins. It was estimated that the contribution of heritability (i.e. the contribution of genetic differences to the variability of a trait in the population) was between 50% to 93% for myopia, and 40% to 94% for axial length (Chen et al., 2016). Furthermore, Twins UK study showed that 77% of the variation can be explained by heritability, compared with only 2% explained by shared environmental effects on refractive errors (Lopes et al., 2009). Of note, twin study may underestimate the environmental influence because its assumption was based on the same environmental exposure. If genetic similarity is the key, it would predict a correlation of 0.125 in cousins by assuming one grandparent was myopic, but in the one study that focused on for axial length, the correlation was about 0.7 (Chen et al., 2007). This suggests that heredity is not the only major determinant. The heritability results of recent genome-wide association studies (GWAS) could explain about 8% of the phenotypic variance in adults and 2% in children (Enthoven et al., 2019; Tedja et al., 2018). These results suggest

that the impact of parental myopia is mediated by genetics, but it is plausible that the myopic parents impose myopiagenic patterns of behaviour (Ghorbani mojarrad et al., 2018).

Transgenerational epigenetic inheritance theory, proposed by Lamarck, agreed that genetic factors can be influenced by environmental factors (Kubota et al., 2012). Animal study found that chicks with high susceptibility to form deprivation myopia developed twice as much myopia as those from the low-susceptibility group after the same period of experimental manipulation (Chen et al., 2011). DNA methylation is now thought to be one of the mechanisms underlying myopia development. The Consortium for Refractive Error And Myopia (CREAM) study found 3 genome-wide loci interacted significantly with education in Asian populations (Fan et al., 2016). These results suggest that the methylation of DNA is probably involved in the development of myopia, it can serve as a marker for the development of myopia, but not be the determining factor. A recent study found the relative high myopia prevalence in college students with two farmer parents was similar to the myopic college students with two non-farmer parents (Li et al., 2017). These findings further suggest that environmental factors play a larger role and may have equal impact on both groups of students irrespective of their parental occupation (Li et al., 2017).

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The above studies show the influence of genetic factor on myopia development. "Genetics loads the gun but the environment pulls the trigger (Ramos & Olden, 2008)", since genetics is hard to modify, the increasing prevalence of myopia within a generation has brought specific attention to the role of environmental factors in the development of myopia.

#### 1.3.2 Environmental Factors

The acceleration of urbanization has increasing influence on the prevalence of myopia. Different generations of genetically related people show dissimilar myopia prevalence among Hong Kong people, with the impact of parental myopia decreasing from the 1<sup>st</sup> generation to 3<sup>rd</sup> generation (Wu & Edwards, et al., 1999). These factors have been widely studied in the epidemiological studies.

#### 1.3.2.1 Education

Education level is regarded as a risk factor for myopia development. There was nearly no myopia in Eskimos before the introduction of education (Young et al., 1969) compared with the higher prevalence of myopia in young and educated Eskimos (Morgan et al., 1973). Those who received higher education were found to have more myopia (Al-Bdour et al., 2001; Cohn, 1886; Jonas et al., 2016; Mirshahi et al., 2014; Saw et al., 2001; Wong et al., 2002). For examples, the age-standardized myopia prevalence was 25.4%, 29.1%, and 36.6%,

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respectively, for those who completed primary, secondary, and higher education in Europe (Williams et al., 2015). In Hong Kong, the prevalence of parental myopia ranged from 58.3% (primary school or lower education) to 86.0% (master degree or higher) (Yam et al., 2020).

Although such association was consistently observed in several studies, it is not clear whether education per se causes myopia, or myopic children tend to perform more near work and thus attain higher education. Applying the theory of Mendelian randomization which can reduce bias from confounding and reverse causation, one study revealed that the number of years in education causes the rising prevalence of myopia – with every additional year in education leads to -0.27 D more myopia in European Caucasians (Mountjoy et al., 2018).

#### 1.3.2.2 Near Work

The association between near work and myopia was first suggested by Kepler (Mark, 1971). According to Kepler, "those who do much close work in their youth become myopic." Earlier studies provided supporting evidence for this association. For examples, those who spent more time on reading the scientific literature were found to have faster myopia progression in Norwegian engineering students (Kinge et al., 2000). More involvement in near viewing and reading tasks after three years promoted myopia development in emmetropic children than those working as skilled laborers (48.8% versus

18.9%) (Hepsen et al., 2001).

Cohort study is one of the reliable methods to investigate the effects of suspected risk factors. The association between near work and myopia was studied in several cohort studies. In Singapore, the number of books read per week was used to quantify the workload of near work in the Singapore Cohort Study of the Risk Factors for Myopia (SCORM). Among children aged 7 to 9 years, those who read more than two books per week was associated with higher myopia (SER  $\leq$  -3.00 D) (Saw et al., 2002). However, the three-year longitudinal data in this study failed to find an association between reading time and incident myopia (Saw et al., 2006). They found that children with higher IQ scores had higher risks of incident myopia. The interaction between reading and IQ scores indicated that children who read more than two books per week were more likely to have higher IQ scores compared with those who read fewer books. Thus, the influence of near work on myopia development still exists (Saw et al., 2006). Another cohort study called STrabismus, Amblyopia and Refractive error in Singaporean (STARS) also investigated risk factors of myopia in Chinese preschool children aged 6 to 72 months old, parental myopia and height were associated with myopia rather than near work activities, which reflects the determining role of genetic factors during early childhood of children (Low et al., 2010).

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In Australia, Sydney Myopia Study (SMS) aimed to investigate the etiology of myopia and other eye conditions in year 1 (mean age: 6.7 years) and year 7 (mean age: 12.7 years) school children (Ojaimi et al., 2005). The results showed that time spent on near-work activities, including homework, reading, handheld computer use, and drawing was not related to myopia (Rose et al., 2008). Instead, near work parameters such as close reading distance and continuous reading time were associated with myopia (Ip et al., 2008). However, the longitudinal study The Sydney Adolescent Vascular and Eye Study (SAVES) found that more near work time were associated with incident myopia in the younger cohort while such association was not found in the older cohort (French et al., 2013).

In U.S., The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) is a multicenter, observational cohort study evaluating development of ocular components and risk factors for juvenile-onset myopia in children of different ethnicities (White, Asian, Hispanic, African-American and Native American). Diopter hour was used to quantify the time and accommodation required during each near work activity. The diopter hour (Dh) was defined as: Dh=3×(hours spent studying or hours spent reading for pleasure) + 2×(hours spent playing video games or working on the computer at home) + 1×(hours spent watching television) (Zadnik et al., 1994). The odds ratio of myopia was 1.02 for every "dioptre-hour" of near work spent per week,

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after controlling for parental myopia and educational achievement scores (Mutti et al., 2002). Comparing the near work time between future myopes and emmetropes before myopia onset, the longitudinal study showed that near work time was not the cause for myopia onset (Jones-Jordan et al., 2011), neither was it the cause of myopia progression (Jones-Jordan et al., 2012). However, near work activities (reading/writing, computer use and other forms of near work) was associated with myopia stabilization by age 15 in Correction of Myopia Evaluation Trial (COMET), which aimed to investigate the effect of using progressive addition lenses for myopia control among myopic children aged 6 to 14 years (Scheiman et al., 2014).

In China, a cohort study in which the methodology was very similar to SMS was conducted in Henan, called Anyang Childhood Eye Study (ACES). No association were found between time spent in near work and myopia among grade 7 students (Li et al., 2015). In contrast, the Beijing Myopia Progression Study (BMPS), a 3-year cohort study, aimed to investigate the relationship between near-work induced transient myopia (NITM) and permanent myopia among primary and secondary school students. They showed that children with a greater load of near work at baseline exhibited more myopic change and were also more likely to develop myopia (Lin et al., 2016). The Beijing Children Eye Study (BCES) found that more time spent on studying indoors was associated with axial elongation in a 4-year longitudinal study among primary school

students (Guo et al., 2017). In Taiwan, a 4-year longitudinal study showed that children in cram school who were involved in homework, assignments and examinations more than 2 hours every day was associated with incident myopia (Ku et al., 2019).

In other parts of the world, there were also cohort studies exploring the role of near work in myopia such as Avon Longitudinal Study of Parents and Children (ALSPAC) study (Williams et al., 2008), Generation R Study in Rotterdam (Tideman et al., 2019), and North India Myopia Study (NIM Study) (Saxena et al., 2017). These studies consistently found that the increasing near work activity increased the risk of becoming myopia.

Near work habits related to myopia have also been investigated. Donders was the first to focus on the near work hygiene such as reading or writing distance, room lighting, and the height of table and desk (Donders et al., 1864). A threeyear longitudinal study in Finland found that myopia progression was associated with a shorter reading distance, but it was only among girls (Parssinen et al., 1993). SMS study found that children who had closer reading distance (< 30 cm) or continuous reading habit (> 30 minutes) had a higher risk of having myopia after adjusted for age, sex and ethnicity (Ip et al., 2008). A one-year cohort study in Shanghai found that myopia progression was related to a shorter near work distance and continuous reading or writing for more than
40 minutes, and incident myopia was related to a shorter near work distance (You et al., 2016). In the Anyang Childhood Eye Study, head tilt when reading and writing was also associated with the presence of myopia, apart from continuous reading, after adjusted for age, sex, number of myopic parents and height (Li et al., 2015). In addition, lying down to read increased the likelihood of having myopia as well (Zhou et al., 2014). This abnormal posture may cause unequal amount of hyperopic defocus in the peripheral retina, which may be associated with myopia development (Charman, 2011; Logan et al., 2021).

# Mechanisms for The Link Between Near Work and Myopia

# **Mechanical Factor**

Mechanical factor has been proposed to explain how near work leads to myopia. The inward force, generated by ciliary muscle's contraction, creates tension on the choroid and adjacent sclera, causing axial elongation (Drexler et al., 1998). Further studies found that a significant axial elongation was associated with a brief period of accommodation, and the magnitude of change in axial length increased with a larger accommodative stimulus (Mallen et al., 2006; Read et al., 2010). In addition, the transient effect of the forces created by extraocular muscles on the eyeball has also been investigated. In the infero-nasal gaze direction, which occurs frequently in near work activities, the increases in axial length were greater in moderate myopes (-3.00 D to -6.00 D) than low myopes and emmetropes (Ghosh et al., 2012). Further study showed that ciliary muscle contractions during accommodation combined with extraocular muscle tension in downward gaze have additive effects on the magnitude of axial elongation (Ghosh et al., 2014).

## Optical Factor: Accommodative Lag

Accommodative lag is the dioptric difference between accommodative response and the accommodative demand. During near work, the eyes converge and accommodate to maintain a clear image on the retina. It is suggested that accommodative lag may provide visual error signals to induce myopia progression which is similar to that of the hyperopic defocus that induces compensatory axial elongation in animals (Gwiazda et al., 2003). Many studies compared the accuracy of the accommodative system during near work between myopes and emmetropes. Collectively, myopes had more accommodative lag than emmetropes (Goss, 1991; Gwiazda et al., 1993; Harb et al., 2006). Furthermore, a larger accommodative lag was found in progressive myopes than stable myopes (Abbott et al., 1998). However, longitudinal studies found that accommodative lag is not the cause for myopia onset (Mutti et al., 2006) or progression (Huang et al., 2016; Lan et al., 2008). Clinical trials of bifocals and progressive addition lens (PALs) which impose myopic defocus to reduce accommodation lag during near work did not achieve clinically significant effects on controlling myopia progression when compared with single vision glasses, i.e., axial elongation slowed by only 0.06 mm/year

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for bifocals and 0.04 mm/year for PALs in comparison to single vision spectacle lenses (Huang et al., 2016). In addition, no difference was found in myopia progression between children with greater accommodative lag and those with less than the mean amount of near accommodative lag after one year (Lan et al., 2008).

Near work induced transient myopia (NITM) is another optical factor related to accommodation. NITM is a transient myopic shift after sustained near work due to accommodative hysteresis (Ciuffreda & Ordonez, 1998). Normally the change is small and an average magnitude of 0.40 D difference was found between the pre- and post-task distance refraction among myopes (Ciuffreda et al., 2002; Ciuffreda & Wallis, 1998; Rosenfield et al., 1994). Because this magnitude was within the depth of defocus, it was thought that individuals might have clear images without obvious symptoms. However, studies reported that some individuals complained about blur distance vision after sustained near work (Ciuffreda & Ordonez, 1998). A link between NITM and permanent myopia was proposed. Later studies found that both early-onset and late-onset myopes were more susceptible to NITM than emmetropes and hyperopes, and myopes demonstrated a prolonged decay time before their refractions returned to the pre-task level (Ciuffreda & Ordonez, 1998; Vasudevan et al., 2009). For example, after a 10-minute near work activity which was performed at 20 cm (5 D accommodative demand), there was approximately 0.35 D myopic shift in both myopic groups, compared with 0.10 D myopic shift in emmetropes but nearly no myopic shift in hyperopes. About the decay time, myopes showed a significantly longer decay time than the other two groups, with LOM showed a longer decay time than EOM (62s versus 35s) (Ciuffreda & Ordonez, 1998). In addition, progressive myopes showed a larger magnitude of NITM and a longer decay time than stable myopes (Vasudevan et al., 2009; Vera-Díaz et al., 2002). Further research found no association between parental myopia and children's NITM characters, which suggests that NITM is an environmentally based myopigenic factor (Lin et al., 2013).

# **Optical Factor: Aberrations**

Higher order aberration (HOA) has been suggested as the potential cause for myopia development (Collins et al., 1995). HOA is defined as the residual aberrations after optimal corrections of defocus and astigmatism by spherocylindrical lens (Liang et al., 1997). Cross sectional studies found differences in wavefront aberrations between myopes and emmetropes (Cheng et al., 2004; He et al., 2002). Longitudinal studies further provided the negative association between HOA and axial elongation (Hiraoka et al., 2017; Lau et al., 2018; Lau et al., 2020; Philip et al., 2014).

Since the cornea is the most powerful refractive component of the eye, subtle change in cornea may have large influence on the ocular aberration, leading to a poor image quality (Buehren et al., 2003). There are studies investigating the change in aberration before and after near work activity (i.e. reading) because downward gaze may induce torsion on the cornea. For example, there was a "wave-like" change in the superior cornea caused by upper eyelid after reading. Significant changes in the against-the-rule astigmatism, spherical aberration and coma were also found after a period of near work, which may change the image quality or provide visual signals for myopia development (Buehren et al., 2003; Buehren et al., 2005).

### 1.3.2.3 Screen Time

With the rapid advancement of technology, electronic devices are popular and widely used among even the younger generation. Considering different characteristics between electronic devices and paper work with respect to brightness, contrast sensitivity and resolution, it is necessary to examine the impact of screen time on myopia development.

Before the massive use of smartphone and tablet, the association between TV/computers with myopia had been studied but the results were inconclusive. In SMS study which focused on student aged 12 years old, the average time spent per week on computer and console game were 6.4 hours and 3.7 hours, respectively. There were very weak correlations between SER and screen time (all  $r \le 0.1$ ), and between axial length and screen time (all  $r \le 0.1$ ). Computer use and console games play were not associated with refractive errors after adjusted for age, sex, ethnicity and school type (Ip et al., 2008). Computer use time was not significantly associated with SER, AL or myopia in the SCORM study (Chua et al., 2015). However, a cross sectional study of children aged 5 to 15 years old suggested that watching television for > 14 h per week (OR=5.4) and playing computer, video and mobile games for  $\geq$  1 h per week (OR=4.5) increased the risk of developing myopia after adjusted for age, sex, parental myopia, school type, socioeconomics and outdoor time (Saxena et al., 2015). In China, the odds of increased computer usage with myopia (OR=1.17) were also found among students aged 5 to 16 years old after adjusting for parental myopia, sex, age, height, time outdoors and time on reading (Qian et al., 2016).

The small screens and short working distance associated with tablet and smartphone usage have again raised public concern about the screen time as a risk factor for myopia development in children. A recent study assessed the association between different types of electronic devices with refraction among schoolchildren aged 6–14 years old. The results showed that more myopic SER and longer AL were both associated with more time spent on using smart phones and computers, but not with time spent on using tablets and watching television (Liu et al., 2019). A study objectively measured smartphone data usage as a surrogate for time spent on using smartphone, they found that data usage was independently associated with myopia (OR=1.08) (McCrann et al.,

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2020). Note, however, that data usage does not equal to the time spent on smart phones.

A meta-analysis involving 15 studies (nine cross-sectional and six cohort studies) conducted between 2002 to 2019 among children aged 3 to 19 years old found that screen time was not associated with prevalent or incident myopia (Lanca et al., 2019). The screen time here refers to computer use and playing video games. One possible reason for the lack of association was that only results of five studies which reported OR were analyzed, and results can be biased by the validity of the pooled estimates. Another possible reason was that it was hard to differentiate the independent influence of screen time. Since myopia typically emerges and progresses when children start schooling (Fan et al., 2004; Lin et al., 2004), intensive schooling may have a larger contribution to the increased myopia prevalence than the screen time. Therefore, it is better to investigate the influence of screen time on myopia development during a period without many confounders.

A large birth cohort study in Rotterdam (the Generation R study) found that computer use at age 3 years was associated with myopia at school ages (OR=1.005 when myopia at 6 years old and OR=1.009 when myopia at 9 years old) (Enthoven et al., 2020). A six-year longitudinal study in China suggested that the postnatal first year might be the sensitive period in early life for the association between screen exposure and preschool myopia. Their findings showed that even for children without myopic parents, initially exposed to electronic devices during the first year showed a higher risk of preschool myopia (Yang et al., 2020).

Although the exact contribution of screen time to the refractive development in children needs to be confirmed, the American Academy of Pediatrics recommends restricting screen time to 1 hour per day for children 2-5 years of age, and they have similar limits for children aged 6 years older. However, they lacked specific time limits for 6-year-old age group (Chassiakos et al., 2016).

#### 1.3.2.4 Outdoor Time

The association between outdoor time and myopia has been reported since 1993. Early studies emphasize the role of sports on the myopia development. For examples, the study in Finland first found that more time spent outdoors can slow the rate of myopic progression as well as the degree of myopia among primary school children (Parssinen et al., 1993). In CLEERE study, a total sport/outdoor time greater than 14 h/wk significantly reduced the risk of a child becoming myopic, regardless of the state of parental myopia (Jones et al., 2007). In Sydney Myopia Study, higher levels of time spent outdoors, rather than sport per se, was associated with more myopic refraction (Rose et al., 2008). A study comparing myopia prevalence in age-matched Chinese children in Sydney and Singapore further support the role of outdoor time in the myopia development. The myopia prevalence is almost 10 times higher in Singapore than in Sydney (29.1% vs. 3.3%, SER  $\leq$  -0.50 D) together with less outdoor time in Singapore (13.75 h/wk in Sydney vs. 3.05 h/wk in Singapore), considering no significant difference in the proportion of parental myopia (Rose et al., 2008). This finding revealed the important impact of outdoor time because the potential effects of genetic variances from ethnicity and parental myopia had been controlled in the study. The Avon Longitudinal Study of Parents and Children (ALSPAC) also stressed the importance of time spent outdoors in myopia development compared to time spent on sports (Guggenheim et al., 2012).

A series of clinical trials were conducted to examine whether the increased outdoor time was beneficial for myopia control. A study in Taiwan launched the ROC programme (a recess outside the classroom, in which classrooms were emptied for about 80 minutes per day) among primary school students (aged 7-11 years) reported a 1-year reduction of incident myopia from 17.7% in the control group to 8.4% in the intervention group (Wu et al., 2013). Later, a RCT study in Taiwan implemented ROC711 program in the intervention group which encouraged children to have a total of 11 hours or more outdoor time in a week. The protective effects of outdoor time were significant in both nonmyopic and myopic children compared with control group (Wu et al., 2018). In mainland

China, a RCT among children in grade 1 (aged 6-7 years) also found that an additional 40 minutes of outdoor time per day after school achieved a 23% reduction in the incidence of myopia after three years (30.4% vs. 39.5%) (He et al., 2015).

In contrast, the effect of outdoor time on reducing myopia *progression* was inconsistent across studies, only one study conducted in Taiwan (mean age: 6.34 years old) reported significant reduction in myopia progression (-0.57 D/y vs. -0.79 D/y) and slower axial elongation (0.45 mm/y vs. 0.60 mm/y) in myopes compared to the control group (Wu et al., 2018). A meta-analysis analyzed 2 clinical trials and 4 cohort studies, conducted between 2000 and 2015, found no effect of outdoor time on individuals with existing myopia (Xiong et al., 2017). In contrast, recent cohort studies showed an association between outdoor time and reduced myopia progression (Huang et al., 2020; Read et al., 2015; Saxena et al., 2017).

Several mechanisms were proposed for how outdoor time can have a protective effect against myopia development. First, the light-dopamine hypothesis. Light stimulates the release of dopamine as a neurotransmitter. The increase in retinal dopamine levels due to the exposure to high light levels is proposed as a potential mechanism underlying the protective effect of outdoor activities (Ashby et al., 2009; Ashby et al., 2010). Light intensity can be as high as

100,000 lux or more in sunny days compared to 340 lux indoors (Wu et al., 2018). Animal studies found that normal chicks raised under high light levels (10,000 lux) developed less myopia than those raised under low light levels (50 lux) (Cohen et al., 2011). In addition, a dopamine D2 receptor antagonist can abolish the protective effect of higher intensity light in chicks (Ashby et al., 2010). Notably, higher light levels have been shown to prevent the development of form deprivation myopia and the axial elongation in chicks (40 000 lux) (Ashby et al., 2010; Cohen et al., 2012), rhesus monkeys (28 000 lux) (Smith III et al., 2012), and tree shrews (15 000 lux) (Siegwart et al., 2012). However, elevated light levels cannot prevent the development of lens induced myopia, it can only reduce the rate of progression but full compensation can still be achieved in chick and monkey models (Ashby et al., 2010; Nickla et al., 2011; Smith III et al., 2013). Besides, the rate of compensation to monocular -3 D lenses in infant macaque monkeys was not affected by daily exposure to 25,000 lux for 6 h/d, compared to control lighting conditions (350 lux for 12 h/d) (Smith III et al., 2013).

In Australia, children experiencing high average daily light exposure (1455  $\pm$  317 lux, 0.065 mm/y) had axial elongation reduction by 50% than those experiencing low average daily light exposure (459  $\pm$  117 lux, 0.13 mm/y) in the Role of Outdoor Activity in Myopia (ROAM) study (aged 10 to 15 years) (Read et al., 2015). Further evidence in China found that more midday outdoor time is associated with less myopia (Guan et al., 2019). A RCT study reported the

same protective effect on myopia for shorter duration (125 to 199 minutes) with higher intensity ( $\geq$  10,000 lux) or longer exposure ( $\geq$  200 minutes) with moderate light intensities ( $\geq$  1,000 lux or > 3,000 lux) (Wu et al., 2018).

Second, the light- vitamin D hypothesis. The role of vitamin D has also been suggested because greater exposure to sunlight leads to an increase in its concentration. Studies found lower levels of vitamin D in myopes than nonmyopes (Mutti et al., 2011; Yazar et al., 2014), and proposed possible influence on scleral growth and ciliary muscle enlargement (Mutti et al., 2011). Although myopes were found to have lower vitamin D level compared to nonmyopes, the results suggested that vitamin D level could only be used as a biomarker for outdoor time (Guggenheim et al., 2014; Tang et al., 2019).

The third hypothesis is the interaction between environment and the pattern of retina defocus. In the indoor visual scene, retina is constantly exposed to a dynamic combination of hyperopic and myopic defocus depending on the fixation, accommodative state and the surrounding environment (Zhu, 2013). Compared with the complex indoor retinal defocus pattern, outdoors distance viewing needs lower accommodative demand (0-1 D) and thus the pattern of retinal defocus is relatively uniform and stable (Flitcroft, 2012).

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The protective effect of outdoor time provides evidence and guidance on myopia control measurements. A one-year interventional study in China (aged 6–14 years) of elevating light levels in the classroom (500 lux vs. 100 lux) also found lower myopia incidence (4% vs 10%) and shorter axial growth for both nonmyopes (0.13 vs. 0.18 mm) and myopes (0.20 vs. 0.27 mm), compared with the control group (Hua et al., 2015). A novel classroom designed to increase children's exposure to outdoor light is also conducted in China (Zhou et al., 2017). After all, from public health perspective, encouraging children to have more outdoor activities is a practical and cost-effective way to prevent myopia.

# 1.3.2.5 Socioeconomic Status

Socioeconomic status is more likely to have a mediating effect linking risk factors (e.g. education) with myopia development (Morgan et al., 2021). It covers a wide range of factors including parental educational level, family income and habituation. Children who read > 2 books every week were found to have a higher chance for having high myopia (SER  $\leq$  -3.00 D). It can be explained by higher parental education, which encourages children to read more, or higher family income, which have the ability to purchase books or have easy access to those facilities such as library (Saw et al., 2002). Higher family income (OR = 1.37) was associated with myopia among high school students (Wu et al., 2015). However, in the Generation R study, children from low income family (OR=2.62) and with a low maternal education (OR 2.27) were more often

myopic (Tideman et al., 2018). Therefore, when interpreting socioeconomic information, it might be better to integrate this information with daily activities and living environment.

#### 1.3.2.6 Urbanization

As shown in Table 1.2, a higher myopia prevalence was found in urban than rural area in several studies (He et al., 2007; Ip et al., 2008; Lin et al., 2004; Sapkota et al., 2008; Saw et al., 2001). However, the difference in myopia prevalence cannot simply be attributed to geographic variation. In some studies, there were confounding factors such as the proportion of parental myopia, parents' educational level, socioeconomic status, less outdoor time, and more time spent on near work activities that can contribute to the difference between urban and rural environments. In addition. population density (Ip et al., 2008; Zhang et al., 2010), home size (Choi et al., 2017), home type (Ip et al., 2008) also shows their independent influences on myopia prevalence.

Study	Location	Age	Cycloplegia	Муоріа	Myopia prevalence (urban vs.	OR (urban	Adjustment
		(Yrs)			rural)	vs. rural)	
Saw et al., 2001	Xiamen, China	8-9	Yes	SER < -0.50 D	19.3% vs. 6.6%	N/A	N/A
He et al., 2007	Yangxi, China	13-17	Yes	SER ≤ -0.50 D	50.0% vs. 33.0%	2.64	Gender, grade level, and parental education
Sapkota et al., 2008	Nepal	10–15	Yes	SER ≤ -0.50 D	10.9%-27.3% vs. 0.5%-3.0%	N/A	N/A
lp et al., 2008	Australia	11-14	Yes	SER ≤ -0.50 D	17.8% vs. 6.9%	2.2	Age, sex, ethnicity, near work, outdoor activity, and parental myopia.
Gao et al., 2008	Cambodia	12-14	Yes	SER ≤ -0.50 D	13.7% vs. 2.5%	7.8	Study design
Guo et al., 2016	Beijing,	5-13	No	SER ≤ -1.00 D	Boys: 29.9% vs. 7.9% (grade 1);	0.17	Age, maternal myopia, time
	China				53.2% vs. 18.8% (grade 4)	(compared to	spent on outdoor, indoor
					Girls: 26.6% vs. 2.7% (grade 1);	urban region)	activities
					76.2% vs. 15.6% (grade 4)		

Table 1.2. Studies investigating urbanization on the prevalence of myopia.

#### 1.3.2.7 Occupation

Higher prevalence of myopia was also found in certain occupations which involved close work. Compared with people who did physical work or unskilled, students and office workers had higher rates of myopia (Goldschmidt, 2003; Tscherning, 1882). For examples, around 80% of textile workers without myopia history who were involved in a close working distance of 30 cm developed myopia compared with 0% myopia among age- and education-matched controls who did other jobs (i.e., office, sale, production) in the same factory (Simensen et al., 1994).

In addition, the myopia prevalence of microscopists was found to be 71% compared with 37% of that among unselected population in the UK (Adams et al., 1992). In Hong Kong, 87% of microscopists were myopic compared to 70% myopia prevalence in the general population (Ting et al., 2004).

# 1.3.2.8 School Type

Competitive education system imposing long hours of near work is a potential risk factor for myopia. Cohn found that myopia prevalence was higher in schools with more rigorous teaching than those in village, with only 1% myopia rate when children first entered the school compared to 60% in the highest grade (Cohn, 1886). Similarly, orthodox Jewish boys in Israel who received intensive religious education were much more myopic than their sisters who received much less intensive education and those who received secular

education (Zylbermann et al., 1993). In Hong Kong, less myopia was found in activity schools compared with traditional schools in a two-year longitudinal study (Goldschmidt et al., 2001). In Singapore, students who achieved better grades could enter the express stream. The age and gender adjusted odds ratio of myopia for the express stream was 3.03 and that for the normal academic stream was 1.68, when compared to the normal technical stream (Quek et al., 2004). In the SMS study, children attending selective schools were twice as likely to have myopia as those in comprehensive schools (OR: 2.2) after adjusted for age, sex, ethnicity, parental myopia, near work related parameters, and outdoor activity (Ip et al., 2008). The influence of school type was also shown in several studies in China (Guo et al., 2017; Thorn et al., 2020; You et al., 2012).

#### <u>1.4 Aims of This Study</u>

Education plays an important role in the myopia development. According to the Programme for International Student Assessment (PISA) outcomes, Asian countries such as China and Singapore, as well as Australia and European countries, occupied the top of the ranking list in educational performance. However, these Asian countries are also known to have much higher myopia prevalence compared with other countries. It is suggested that the educational system could be a potential environmental risk factor (Morgan & Rose., 2013). There were two studies investigating myopia risk factors under different educational systems (Rose et al., 2008; Saw et al., 2002). Because they were conducted in different countries, they may suffer from potential confounding factors such as differential living environment and population density, which are known to have an impact on myopia development. Considering Hong Kong is an international city and has multicultural environment, the aims of the current study were: *(1)* to investigate the myopia risk factors under the two different educational systems in Hong Kong; and *(2)* to investigate whether there was a change in myopia proportion after the study at home period due to COVID-19 lockdown.

# Chapter 2: Risk Factors of Myopia in a Local Primary School and an International School in Hong Kong: A Pilot Study

# Introduction

Myopia is the most common refractive error and is associated with excessive axial elongation of the eye (Wolffsohn et al., 2019). Myopia prevalence varies across the world, with a prevalence of myopia in young adults of more than 80% in East and Southeast Asian countries (He et al., 2004; Kim et al., 2013; Lin et al., 2004). Myopia with early onset and fast progression has a high risk of developing into high myopia (Fan et al., 2004; Lin et al., 2004). High myopia is associated with a series of ocular complications including retinal diseases and glaucoma (Morgan et al., 2012), which may further affect quality of life (Jones et al., 2012) and increase the financial burden on both society and the individual (Zheng et al., 2013). It is well known that myopia is a multifactorial disorder. Both genetic and environmental factors play a role in myopia development (Morgan et al., 2012).

Hong Kong is one of the most developed and vibrant cities in Asia. Its important role in global commercial and financial hub has attracted millions to Hong Kong for work. According to the Census in 2016, a total of 584,383 non-Chinese, constituting 8.0% of the whole population in Hong Kong, were living in Hong Kong in 2016 (Census and Statistical Department, 2017). In order to meet the

educational demand for non-local families in Hong Kong and provide a multicultural educational environment, there are currently 44 international primary schools (Education Bureau, 2019). Thus two school educational systems exist in Hong Kong. Such systems also exist in China (e.g. Beijing and Shanghai), Japan, and India (Brummitt et al., 2013). Of the educational systems in Hong Kong, one is local, government-supported schooling in which the curriculum is followed closely across the schools. Based on the primary education results, students are later allocated to different levels of secondary schools (Cheung et al., 2005). Therefore, in order to enter a secondary school with an outstanding reputation, the educational environment among primary local school students is guite intensive and competitive (Ng, 2012). The other type, international schools, has different curriculum from local schooling. Students participate in the International Baccalaureate (IB) program or the curriculum of their home countries, rather than taking the local examinations in Hong Kong. Although it is difficult to directly compare the study intensity between two school systems due to the different curriculums and assessment criteria, it is generally believed that the international school has a less pressured learning environment than the local school. Despite the increasing number of local children attending international schools in Hong Kong (Education Bureau, 2019), local schooling is still the mainstream education mode, due primarily to the high tuition fees in the internationals school sector (Ng, 2012).

According to the international PISA surveys of educational outcomes (www.oced.org/pisa), locations in Asia such as Shanghai, Hong Kong, and Singapore occupied the top of the ranking list but also had highest myopia prevalence. In contrast, western countries, such as Finland and Australia, also achieved top international rankings, but with much lower myopia prevalence (Morgan & Rose, 2013). This suggests that the educational system could be a potential environmental risk factor (Morgan et al., 2018). Although the association between education and myopia has been well-established (Mountjoy et al., 2018), only a few studies have compared myopia risk factors in different educational systems, within the same country or city (Rose et al., 2008; Saw et al., 2002). In this respect, although two studies have shown that Chinese children in the more intensive educational system had higher myopia prevalence, these children were from two different countries (Xia'men versus Singapore, and Singapore versus Sydney), with potential confounding factors such as living environment, population density and income. Another crosssectional study in Hong Kong also found higher myopia prevalence in local schools (n=289) than that in the international schools (n=835). Myopia prevalence was higher among Chinese students than Caucasian students, but myopia prevalence among Caucasian students was higher than that reported in students of similar age in Europe and North America (Lam et al., 2004). On the other hand, no significant difference in myopia prevalence among Chinese students was found between the two school systems. The authors suggested

that the results were an effect of the different genetic backgrounds of the groups of students, and an effect of the Hong Kong environment.

The primary aim of the current study was to investigate whether primary school children in the two different Hong Kong educational systems were exposed to the same set of myopia risk factors known to date. The secondary aim was to assess parents' awareness of myopia risk factors in the two different school systems.

# <u>Methods</u>

# Questionnaire design:

This questionnaire was designed to collect information from parents on (1) myopia risk factors of primary school children, and (2) their awareness of myopia risk factors known to date. Based on a review of current literature and existing validated questionnaires, including the SMS Study (Ojaimi et al., 2005), SCORM study (Saw et al., 1999) and ACES (Li et al., 2015), the questions were grouped under five categories (Table 2.1).

Table 2.1. Items covered in the questionnaire are grouped under five main categories.

	Main category	Items collected
i)	Demographic information	Name, date of birth, gender, grade, ethnicity,
		educational level, family income.
ii)	Family history of myopia	Parents' myopia history.
iii)	Ocular history of child	Previous eye care experience, ocular health,
		current ophthalmic aids, and myopia control
		aids.
iv)	Parents' awareness of myopia	Myopia risk factors.

v)	Environmental/Behavioral risk factors	Non-screen time (reading, writing, etc.), screen
	related to myopia	time (smartphone and tablet), outdoor time,
		viewing distance, near work duration, head tilt.

Classifications for ethnicity, educational level, and income were as defined by referral to the Hong Kong Census (Census and Statistical Department, 2017). Parental myopia history was acquired directly by asking "Does the child's mother/father suffer from myopia (near-/short-sightedness)?". Questions in the child's ocular health history section were taken from questionnaire used in the Sydney Myopia Study (Ojaimi et al., 2005). For myopia control methods, three commercially available products in Hong Kong were listed: Orthokeratology (Ortho-K) (Cho et al., 2019), Defocus Incorporated Multiple Segments (DIMS) lenses (Lam et al., 2020) and multifocal soft contact lenses (Lam et al., 2014). Questions in the "parents' awareness of myopia" category were newly developed. Parents were asked if they were aware of myopia risk factors with scientific evidence reported in the literature. These risk factors included parental myopia (Mutti et al., 2002), continuous near work with few or no breaks (Ip et al., 2008), insufficient outdoor time (Rose et al., 2008) and head tilt (Li et

al., 2015).

Environmental or behavioral risk factors included time spent on non-screen nearwork activities (reading and writing) and handheld digital electronic devices (smartphone and tablet). These were assessed for weekdays and weekends separately (Saw et al., 1999). Information about outdoor time was collected by asking about time spent on outdoor physical activity (playing sports, running, riding a bike, etc.) and leisure activity (walking, having a picnic, etc.), it was similar to the SMS study (Ojaimi et al., 2005). Questions about viewing distance and near work duration were taken from the SMS questionnaire. Viewing distance was estimated by parents' observation of their children.

# Validation of Questionnaire

Figure 2.1. Flowcharts illustrating the steps involved in the two phases of validating the questionnaire.



The validation of questionnaire involved two phases. Phase I aimed to test the comprehensibility of the questionnaire, i.e. whether questions were precise and easy to understand for parents. A face-to-face interview was conducted at the Optometry Research Clinic in the Hong Kong Polytechnic University. A think-out-loud model was applied for the face-to-face validity assessment (Presser et al., 2004). Five parents were invited to complete the questionnaire and encouraged to raise questions related to the content. Corrections were made to improve clarity (e.g., changing "rest" to "look far into the distance") and font size. After these modifications, another three parents were invited to complete

the revised questionnaire, when no further comments were raised.

Phase II of validation was to test the reliability of the questionnaire. Twenty parents from the optometry clinic of the Hong Kong Polytechnic University were invited to complete the revised questionnaire. They were asked to complete the same questionnaire twice, separated by two weeks (Saw et al., 1999).

#### **Population**

One international school and one local school in Hong Kong were selected for vision screenings conducted in September and October 2018. Informed letters of consent were obtained from parents. The study followed the tenets of the Declaration of Helsinki and was approved by the Human Subjects Ethics Committee of The Hong Kong Polytechnic University (HSEARS20180726001). All children were invited to participate in the screening, however, only students who fulfilled the inclusion criteria were analyzed. Inclusion criteria were (1) Chinese school children aged 8-10 years old; and (2) currently not undergoing any myopia control treatment. This age range was selected because it is known to exhibit a high incidence of myopia (Fan et al., 2004). The questionnaire was distributed via school teachers to parents and collected before the vision screening.

#### Examination procedures

The same set of ophthalmic instruments and school settings were adopted in both schools. The vision screenings were conducted between 9 am to 12 pm during normal school days. The school's administrator decided the order for each class and students were guided by teachers to the screening site. Time spent on the whole screening process was less than twenty minutes. All measurements were completed under the natural room lighting (400 lux). An open-field autorefractometer (Shin-Nippon, NVision K5001) was used to measure refraction while students were instructed to look at the Maltese cross at six meters. Five consecutive readings of each eye were obtained and averaged. Ocular axial length was measured using a IOL Master (Carl Zeiss Meditec). Five consecutive measurements with signal - to - noise ratios > 2.0were collected and averaged for analysis. Both devices were calibrated using a model eye on a daily basis. In order not to interfere with classroom learning activities and to increase the participation rate, cycloplegic drugs to relax accommodation were not applied, which may have caused a myopic shift of no more than 0.63 D ± 0.65 D in myopes and hyperopes aged between 4-18 years old (You et al., 2012; Sankaridurg et al., 2017).

#### Statistical Analysis

The reliability of the questionnaire was evaluated by calculating the intraclass correlation coefficient (ICC) for the results collected from Phase II (see above). An ICC of at least 0.75 is considered to have good reliability (Portney & Watkins,

2009). ICC values and their 95% confidence intervals were calculated based on a mean-rating, absolute-agreement, 2-way random-effects model.

The refractive errors were decomposed into spherical-equivalent refraction (SER) and J0 and J45 astigmatic components according to Fourier analysis (Thibos et al., 1997). Only the data from the right eye was used because the refractive and biometric data of the right and left eyes were highly correlated (Pearson correlation, r> +0.87, p< 0.001). Myopia is usually defined as SER  $\leq$  -0.50 D (Flitcroft et al., 2019), but refraction data was obtained without cycloplegia, more conservative criteria were also applied to define myopia, i.e. SER  $\leq$  -1.00 D. Refractive astigmatism was defined as cylindrical error  $\geq$  0.50 DC. Due to the small sample size in both surveys, the term "myopia proportion" instead of "myopia prevalence" is used in the results section (McCullough et al., 2016).

Statistical analyses were performed using SPSS (version 22, IBM Corp., Amonk, NY, US) with the significance level set at  $\alpha$  <0.05. First, a descriptive analysis was performed to compare ocular and non-ocular parameters between the two schools, and myopes and nonmyopes in the same school. To be specific, continuous variables collected in 2018 were compared with either unpaired t-test or Mann-Whitney U test, depending on the normality tested using the Shapiro-Wilk test. Data were presented as mean ( $\pm$  S.D.) or median

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(interquartile range, IQR). Chi-squared test was used to compare categorical variables between groups and reported in percentages. Second, univariate regression models were used to examine the risk factors of myopia on the presence of myopia and axial length under the two different educational systems. Then a multivariate analysis was conducted with the presence of myopia and axial length as dependent variables, and all other parameters significant in the univariate analysis as independent parameters. The backward stepwise method was further used to cater for the small sample size in the regression models, which was to eliminate insignificant variables starting from the one with the highest p value, until the p values of all remaining variables were below 0.05.

#### <u>Results</u>

### 2.1 Test-Retest Reliability of Questionnaire

Table 2.2 shows the ICC for the reliability of each item. In general, all had good repeatability (all ICC  $\geq$  0.60).

Table 2.2. Questionnaire repeatability.

Items	ICC (95% CI)
time spent on printed materials on weekdays	0.94 (0.85, 0.98)
time spent on tablet on weekdays	0.79 (0.53, 0.91)
time spent on smartphone on weekdays	0.74 (0.46, 0.89)
time spent on printed materials on weekends	0.89 (0.74, 0.95)
time spent on tablet on weekends	0.60 (0.14, 0.83)
time spent on smartphone on weekends	0.62 (0.23, 0.83)
outdoor physical activities on weekdays	0.83 (0.63, 0.93)
outdoor leisure activities on weekdays	0.86 (0.68, 0.94)
outdoor physical activities on weekends	0.87 (0.70, 0.95)
outdoor leisure activities on weekends	0.85 (0.66, 0.94)

# 2.2 Subject recruitment

# Figure 2.2. Flowcharts for local and international schools' students participation.



In the local school, 264 students were invited to join the study, and 159 students were included in the current vision screening and 112 school children returned the questionnaire. In the international school, 350 students were invited to join the study, and 223 students were included in the current study for vision screening and 125 school children in the international school returned the questionnaire. The following analyses were only conducted on students who participated in the vision screening and returned their questionnaires (Local school: 112; International school: 125).

In order to evaluate the potential influence of students who participated in the screening but did not return questionnaires on the overall results, Table 2.3 compares the characteristics of those who returned questionnaire and those who did not in two schools. In the local school, no significant differences were found between students who returned questionnaires and those who did not return in age, gender and ocular parameters. However, students in the international school who did not return questionnaire were more likely to be male and myopic.

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	Local School			International School		
-	Responded	Not responded	P value	Responded	Not responded	P value
Age (years old)	9.17±0.82	9.03±0.94	0.44	8.94±0.85	9.01±0.83	0.53
Female (%)	56.3	44.8	0.27	51.5	35.5	0.017
Myopia (%)	37.5	34.5	0.76	13.1	24.7	0.025
SER (IQR)	-0.31 (-1.49,+0.19)	-0.44 (-1.82, +0.06)	0.39	+0.13 (-0.43, +0.44)	-0.19 (-0.94, +0.32)	0.03
J0 (IQR)	+0.18 (0, +0.43)	+0.24 (+0.03, +0.38)	0.88	+0.12 (-0.02, +0.28)	+0.10 (-0.03, +0.24)	0.67
J45 (IQR)	-0.06 (-0.14, +0.02)	0 (-0.10, +0.10)	0.03	0 (-0.09, +0.09)	-0.05(-0.12, +0.08)	0.05
AXL (mm)	23.39±0.89	$23.74 \pm 1.09$	0.072	$23.34{\pm}0.94$	$23.56 \pm 0.98$	0.09

Table 2.3. Comparison of responding and non-responding students.

IQR: interquartile range

#### 2.3.1 Ocular parameters results between two schools

Comparison of the participating students in the local school and international schools (Table 2.4) revealed that, the proportion of myopia (SER  $\leq$  -0.50 D) in the local school was more than twice as high as that in the international school (46.4% vs. 22.4%, Chi-square test,  $\chi^2 = 15.25$ , p<0.001), even if a more conservative definition was used (37.5% vs. 12.8%, Chi-square test,  $\chi^2 = 19.50$ , p<0.001). If children who did not return questionnaires were included, the myopia proportion was still higher in the local school than in the international school (italicized data shown in brackets in the Table 2.4). Similarly, the median SER value was more myopic in the local school than in the international school (Mann-Whitney U test, U=4724.0, p<0.001). There was also a significant difference in the proportion of students with astigmatism (Cyl  $\geq$  1.00 DC) between two schools (Chi-square test,  $\chi^2 = 14.21$ , p<0.001). The J0 (Mann-Whitney U test, U=5492.50, p=0.004) and J45 (Mann-Whitney U test, U=5521.0, p=0.005) astigmatic components were both higher in the local school than in

the international school. However, the axial length did not differ between the two schools (unpaired t-test, t=0.29, p=0.77).

	Local School	International School	P value
Myopia proportion (SER ≤ -0.50 D)	46.4%	22.4%	<0.001
Myopia proportion (SER ≤ -1.00 D)	37.5% (40.0%)	12.8% (23. <i>1%</i> )	<0.001
SER (IQR)	-0.31 (-1.49, +0.19) D	+0.13 (-0.41, +0.44) D	<0.001
Astigmatism proportion (Cyl ≥ 0.50 DC)	57.1%	48.0%	0.16
Astigmatism proportion (Cyl ≥ 1.00 DC)	25.0%	7.2%	<0.001
J0 (IQR)	+0.18 (0, +0.43) D	+0.12 (-0.03, +0.27) D	0.004
J45 (IQR)	-0.06 (-0.14, +0.02) D	0 (-0.10, +0.09) D	0.005
AXL (S.D)	23.39±0.89 mm	23.35±0.95 mm	0.77
	23.56±0.99 mm	23.50±0.97 mm	0.55

Table 2.4. Proportions of ocular parameters between two schools.

IQR: interquartile range

# 2.3.2 Questionnaire results between two schools

Overall, students in the local school were slightly older than those attending the international school (unpaired t-test, t=2.006, p=0.046) (Table 2.5), but there were no significant differences in gender distribution between the two schools. However, the proportions of parental myopia (76.8% vs. 54.5%, Chi-square test,  $\chi 2 = 13.18$ , p<0.001) and high myopia (19.2% vs. 6.3%, Chi-square test,  $\chi 2 = 8.71$ , p=0.003) were both higher in the international school than those in the local school. Furthermore, parents of children in the international school were more likely to have attained a higher educational level (father: 90.4% vs. 15.2%, Chi-square test,  $\chi 2 = 114.94$ , p<0.001) and had considerably higher family income compared

with parents in the local school (2×C Fisher's exact test, p<0.001). Local school students spent about four hours more per week on both non-screen near work (reading, writing, etc.) (Mann-Whitney Test, U=5337.0, p=0.002) and handheld digital devices (Mann-Whitney Test, U=3683.0, p<0.001) than international school students. Specifically, local school students spent longer hours on their smartphone than international school students (Mann-Whitney Test, U=2530.0, p<0.001). In contrast, international school students had more outdoor time than those in the local school (Mann-Whitney Test, U=4975.0, p<0.001). However, no differences between two schools were found on viewing distances under the three conditions (reading/writing, smartphone use and tablet use) (unpaired t-test, p>0.05), visual habits such as head tilt when doing near work and continuous near work for more than 30 minutes (Chi-square test, p>0.05).

	Local School	International School	P value
Age (years old)	9.17±0.82	8.95±0.85	0.046
Female (%)	56.3	52.0	0.51
Parental myopia (%) <sup>†</sup>	54.5	76.8	<0.001
Parental high myopia (%) <sup>‡</sup>	6.3	19.2	0.003
Father's educational level (%)			<0.001
Upper secondary or below	84,8	9.6	
Post-secondary or above	15.2	90.4	
Mother's educational level (%)			<0.001
Upper secondary or below	91.1	21.6	
Post-secondary or above	8.9	78.4	
Monthly family income (%)			<0.001
≤HK\$ 9,999	7.4	0	
НК\$ 10,000-НК\$ 19,999	51.9	0	
HK\$ 20,000-HK\$ 29,999	21.3	0	
НК\$ 30,000-НК\$ 39,999	12.0	3.2	
HK\$ 40,000-HK\$ 49,999	4.6	4.8	
≥HK\$ 50,000	2.8	92.0	
Near work time			
Non-screen time (IQR)	10.8 (5.3, 16.4) h/wk	7.0 (4.5, 12.0) h/wk	0.002
Total handheld digital screen time (IQR)	9.5 (4.2, 14.4) h/wk	5.2 (2.0, 9.0) h/wk	<0.001
Smartphone use time	4.5 (1.6, 10.4) h/wk	0 (0, 3.9) h/wk	<0.001
Tablet use time	0 (0, 7.0) h/wk	2.0 (0, 6.5) h/wk	0.16
Viewing distance			
Reading/writing distance	25.34±10.82 cm	26.65±9.56 cm	0.38
Smartphone viewing distance	23.42±10.94 cm	24.96±8.96 cm	0.36
Tablet viewing distance	31.67±15.41 cm	27.90±9.79 cm	0.49
Outdoor time (IQR)	5.0 (3.0, 7.5) h/wk	7.5 (5.0, 10.5) h/wk	<0.001
Proportion of head tilt	56.3%	50.0%	0.34
Proportion of continuous near work	46.4%	44.4%	0.75

Table 2.5. Comparison of questionnaire results between two schools.

 †, ‡: Parental myopia and parental high myopia (SER ≤ -6.00 D) scored positive if at least one parent has myopia/ high myopia.

IQR: interquartile range

# 2.4 Questionnaire results among myopes between two schools

A descriptive analysis was then performed to compare characteristics of myopes (SER  $\leq$  -1.00 D) between two schools to determine whether there was
any difference in myopia risk factors (Table 2.6). There were no differences in age (unpaired t-test, p>0.05) or gender distribution (Chi-square test, p>0.05) between myopes in the two schools and did not differ from results of overall demographic comparison of the two schools. Myopes in the local school were likely to have parents, who had an upper secondary or below education level than those in the international school (Chi-square test,  $\chi^2 > 19.95$ , all p<0.001). There was no difference in the proportion of parental myopia and high myopia between two schools (Chi-square test, p>0.05). Monthly family income in myopes in the international school was also significantly higher than those in the local school (2×C Fisher's exact test, p<0.001). However, in terms of nonocular parameters, myopes in the international school had more non-screen (Mann-Whitney Test, U=211.5, p=0.03) and outdoor time (Mann-Whitney Test, U=184.5, p=0.008) than those in the local school. Visual habits such as viewing distance (unpaired t-test, p>0.05), head tilt proportion (Chi-square test, p>0.05), and proportion of continuous near work (Chi-square test, p>0.05) did not differ among myopes between the two schools.

	Local School (41)	International School (16)	P value
Age	9.17±0.79	9.25±0.86	0.73
Female	75.0%	25.0%	0.63
Father's educational level			<0.001
Upper secondary or below	90.0%	10.0%	
Post-secondary or above	33.3%	66.7%	
Mother's educational level			<0.001
Upper secondary or below	86.7%	13.3%	
Post-secondary or above	23.1%	76.9%	
Parental myopia <sup>†</sup>	69.6%	30.4%	0.34
Parental high myopia <sup>‡</sup>	60.0%	40.0%	0.33
Monthly family income			<0.001
≤HK\$ 9,999	5.0%	0	
HK\$ 10,000-HK\$ 19,999	57.5%	0	
HK\$ 20,000-HK\$ 29,999	22.5%	0	
HK\$ 30,000-HK\$ 39,999	10.0%	6.3%	
HK\$ 40,000-HK\$ 49,999	5.0%	12.5%	
≥HK\$ 50,000	0	81.2%	
Near work time			
Non-screen time (IQR)	11.0 (6.0, 15.0) h/wk	12.3 (6.8, 16.1) h/wk	0.030
Total handheld digital screen time	7.3 (4.5, 13.4) h/wk	6.8 (4.0, 11.9) h/wk	0.59
(IQR)			
Smartphone use time	5.5 (2.0, 9.9) h/wk	5.5 (2.0, 11.0) h/wk	0.24
Tablet use time	0 (0, 7.0) h/wk	0 (0, 7.0) h/wk	0.64
Viewing distance			
Reading/writing distance	24.58±10.94 cm	$25.14 \pm 12.38$ cm	0.88
Smartphone viewing distance	$24.10 \pm 12.17 \text{ cm}$	22.69±10.76 cm	0.72
Tablet viewing distance	$35.00 \pm 18.03 \text{ cm}$	31.88±12.23 cm	0.74
Outdoor time (IQR)	5.0 (3.0, 7.5) h/wk	8.0 (5.5, 13.3) h/wk	0.008
Proportion of head tilt	73.5%	26.5%	0.82
Proportion of continuous near work	78.8%	21.2%	0.21

Table 2.6. Comparisons of myopes between two schools.

†, ‡: Parental myopia and parental high myopia (SER  $\leq$  -6.00 D) refers the proportion with at

least one parent with myopia/ high myopia.

IQR: interquartile range

#### 2.5.1 Comparisons of non-ocular parameters in each school

In the local school, no significant differences were found between myopes and non-myopes in age, gender, parental educational level and monthly family income (Table 2.7, Chi-square test, all p>0.05). However, the proportions of parental myopia (76.2% vs. 41.4%, Chi-square test,  $\chi^2 = 12.79$ , p<0.001) and high myopia (14.3% vs. 1.4%, Chi-square test,  $\chi^2 = 7.41$ , p=0.007) were significantly higher in myopes compared with non-myopes. In addition, myopes tended to spend longer time on near work before taking breaks than non-myopes (Chi-square test,  $\chi^2 = 6.47$ , p=0.011). No differences were found for other parameters.

In the international school, no significant differences were found between myopes and non-myopes in age, gender, maternal educational level and monthly family income (Chi-square test, all p>0.05). However, the proportion of father with post-secondary or above education in myopes was less than that of non-myopes (Chi-square test,  $\chi^2$  =5.01, p=0.025). The proportions of parental myopia and high myopia were both higher in myopes and non-myopes in the international school (Chi-square test, p>0.05). Myopes also spent more time on smartphone use than that of non-myopes (Mann-Whitney Test, U=233.5, p=0.02). No differences were found for other parameters.

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Local School	Муоре	Non-myope	P value
Age	9.17±0.79	9.17±0.83	0.98
Female	57.1%	55.7%	0.88
Father's educational level			0.84
Upper secondary or below	85.7%	84.3%	
Post-secondary or above	14.3%	15.7%	
Mother's educational level			0.61
Upper secondary or below	92.9%	90.0%	
Post-secondary or above	7.1%	10.0%	
Parental myopia <sup>†</sup>	76.2%	41.4%	<0.001
Parental high myopia <sup>‡</sup>	14.3%	1.4%	0.007
Monthly family income			0.71
≤HK\$ 9,999	5.0%	8.8%	
HK\$ 10,000-HK\$ 19,999	57.5%	48.5%	
HK\$ 20,000-HK\$ 29,999	22.5%	20.6%	
HK\$ 30,000-HK\$ 39,999	10.0%	13.2%	
HK\$ 40,000-HK\$ 49,999	5.0%	4.4%	
≥HK\$ 50,000	0	4.5%	
Near work time			
Non-screen time (IQR)	12.3 (6.8, 16.1) h/wk	10.0 (4.9, 16.9) h/wk	0.21
Total handheld digital screen time (IQR)	6.8 (4.0, 11.9) h/wk	11.0 (4.5, 16.0) h/wk	0.16
Smartphone use time	5.5 (2.0, 11.0) h/wk	4.1 (0, 10.1) h/wk	0.28
Tablet use time	0 (0, 7.0) h/wk	0.5 (0, 5.1) h/wk	0.72
Outdoor time (IQR)	5.0 (3.0, 7.5) h/wk	5.0 (3.0, 7.5) h/wk	0.68
Viewing distance			
Reading/writing distance	24.58±10.94 cm	$25.78 \pm 10.82 \text{ cm}$	0.63
Smartphone viewing distance	24.10±12.17 cm	$23.00 \pm 10.21 \text{ cm}$	0.67
Tablet viewing distance	35.00±18.03 cm	$30.00 \pm 15.49 \text{ cm}$	0.68
Proportion of head tilt	59.5%	54.3%	0.59
Proportion of continuous near work	61.9%	37.1%	0.011

Table 2.7. Comparison of non-ocular parameters of students in the two schools.

International School	Муоре	Non-myope	P value
Age	9.25±0.86	8.90±0.84	0.13
Female	50.0%	52.3%	0.86
Father's educational level			0.025
Upper secondary or below	25.0%	7.3%	
Post-secondary or above	75.0%	92.7%	
Mother's educational level			0.98
Upper secondary or below	37.5%	19.3%	
Post-secondary or above	62.5%	80.7%	
Parental myopia <sup>†</sup>	87.5%	75.2%	0.28
Parental high myopia <sup>‡</sup>	25.0%	18.3%	0.53
Monthly family income			0.22
≤HK\$ 9,999	0	0	
HK\$ 10,000-HK\$ 19,999	0	0	
HK\$ 20,000-HK\$ 29,999	0	0	
HK\$ 30,000-HK\$ 39,999	6.3%	2.8%	
HK\$ 40,000-HK\$ 49,999	12.5%%	3.7%	
≥HK\$ 50,000	81.2%	93.5%	
Near work time			
Non-screen time (IQR)	7.0 (2.8, 13.3) h/wk	7.0 (4.5, 12.0) h/wk	0.66
Total handheld digital screen time (IQR)	6.0 (2.8, 10.0) h/wk	5.0 (2.0, 9.0) h/wk	0.82
Smartphone use time	4.5 (0, 7.8) h/wk	0 (0, 2.6) h/wk	0.02
Tablet use time	1.0 (0, 7.0) h/wk	2.2 (0, 6.2) h/wk	0.60
Viewing distance			
Reading/writing distance	25.14±12.38 cm	26.89±9.10 cm	0.53
Smartphone viewing distance	22.69±10.76 cm	25.49±8.50 cm	0.32
Tablet viewing distance	31.88±12.23 cm	27.38±9.43 cm	0.22
Outdoor time (IQR)	8.0 (5.5, 13.3) h/wk	7.5 (5.0, 9.0) h/wk	0.29
Proportion of head tilt	56.3%	49.1%	0.59
Proportion of continuous near work	43.8%	44.4%	0.96

 $\uparrow$ ,  $\ddagger$ : Parental myopia and parental high myopia (SER ≤ -6.00 D) refers the proportion with at least one parent with myopia/ high myopia.

IQR: interquartile range

2.5.2 Factors associated with myopia in the two schools

In univariate analysis (Table 2.8), myopia in students attending the local school was associated with parental myopia (OR: 4.52, 95% CI: 1.93-10.63, p=0.001), parental high myopia (OR: 11.50, 95% CI: 1.33-99.22, p=0.026) and continuous near work time (OR: 2.75, 95% CI: 1.25-6.06, p=0.012). Other factors were not associated with myopia in the local school. In the international school, myopia in students were associated with a father who had upper secondary or below education background (OR: 4.21, 95% CI: 1.10-16.90, p=0.036) and smartphone use time (OR: 1.18, 95% CI: 1.01-1.39, p=0.037). Other factors were not associated with myopia in the international school.

	Local School		International So	chool
	OR (95% CI)	P value	OR (95% CI)	P value
Father's educational level				
Upper secondary or below			4.21 (1.10, 16.09)	0.036
Parental myopia <sup>†</sup>	4.52 (1.93, 10.63)	0.001		
Parental high myopia <sup>‡</sup>	11.50 (1.33, 99.22)	0.026		
Near work time				
Smartphone use time			1.18 (1.01, 1.39)	0.037
Tablet use time				
Proportion of continuous near work	2.75 (1.25, 6.06)	0.012		

Table 2.8. Univariate analysis of risk factors and myopia in two school students.

†, ‡: Parental myopia and parental high myopia (SER ≤ -6.00 D) refers the proportion with at

least one parent with myopia/ high myopia.

The multivariate regression analysis included myopia as the dependent parameter and all variables which were significant (p<0.05) in the univariate analysis as independent parameters (Table 2.9). In the local school, parental myopia (OR: 3.67, 95% CI: 1.50-9.02, p=0.005) and continuous near work time (OR: 2.92, 95% CI: 1.23-6.92, p=0.015), but not parental high myopia (OR: 7.89, 95% CI: 0.85-73.41, p=0.069), were significantly associated with myopia. In the international school, only father's educational level (OR: 6.55, 95% CI: 1.39-30.92, p=0.018) was associated with myopia.

Table 2.9. Multivariate regression analysis of risk factors and myopia in two school students.

	Local School		International Sc	hool
	OR (95% CI)	P value	OR (95% CI)	P value
Father's educational level				
Upper secondary or below			6.55 (1.39, 30.92)	0.018
Parental myopia <sup>†</sup>	3.67 (1.50, 9.02)	0.005		
Parental high myopia <sup>‡</sup>	7.89 (0.85, 73.41)	0.069		
Near work time				
Smartphone use time			1.16 (0.98, 1.38)	0.078
Tablet use time				
Proportion of continuous near work	2.92 (1.23, 6.92)	0.015		

†, ‡: Parental myopia and parental high myopia (SER ≤ -6.00 D) refers the proportion with at least one parent with myopia/ high myopia.

We also did a similar analysis on risk factors of myopia on axial length (Table 2.10). In univariate analysis, axial length in the local school were associated

with parental myopia (unstandardized coefficient  $\beta$ =0.33, 95% CI: 0.16-0.50, p<0.001), parental high myopia (unstandardized coefficient  $\beta$ =0.51, 95% CI: 0.15, 0.88, p=0.006), and continuous near work (unstandardized coefficient  $\beta$ =0.23, 95% CI: 0.06-0.41, p=0.011). Other factors were not significantly associated with axial length in the local school. Axial length in the international school were associated with father's educational level (unstandardized coefficient  $\beta$ =0.23, 95% CI: 0.03-0.43, p=0.025) and smartphone use time (unstandardized coefficient  $\beta$ =0.023, 95% CI: 0.003-0.043, p=0.022). Other factors were not significantly associated with axial length associated with axial length associated with axial school.

Table 2.10. Univariate analysis of risk factors and axial length in two school students.

	Local School		International Scl	nool
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Father's educational level				
Upper secondary or below			0.23 (0.03, 0.43)	0.025
Parental myopia <sup>†</sup>	0.33 (0.16, 0.50)	<0.001		
Parental high myopia <sup>‡</sup>	0.51 (0.15, 0.88)	0.006		
Near work time				
Smartphone use time			0.023 (0.003, 0.043)	0.037
Tablet use time				
Proportion of continuous near work	0.23 (0.06, 0.41)	0.011		

†, ‡: Parental myopia and parental high myopia (SER ≤ -6.00 D) refers the proportion with at least one parent with myopia/ high myopia.

In the multivariate regression analysis, axial length was the dependent

parameter and all those variables which were significant (p<0.05) in the univariate analysis as well as age and gender (Table 2.11) were independent parameters. In the local school (adjusted R<sup>2</sup>=3.0%), axial length was associated with parental myopia (unstandardized coefficient  $\beta$ =0.35, 95% CI: 0.021-0.68, p=0.037). In the international school (adjusted R<sup>2</sup>=2.9%), only father's educational level was remained in the model, but it was not significant (unstandardized coefficient  $\beta$ =0.61, 95% CI: -0.03-1.26, p=0.063).

Table 2.11. Multivariate linear regression of risk factors and axial length in two school students.

	Local School		International Sc	hool
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Father's educational level				
Upper secondary or below			0.61 (-0.03, 1.26)	0.063
Parental myopia <sup>†</sup>	0.35 (0.021, 0.68)	0.037		

†: Parental myopia refers the proportion with at least one parent with myopia.

#### 2.6 Parents' awareness of myopia risk factors in the two schools

Descriptive analysis was used to compare parents' awareness of myopia complications and its risk factors between two schools. Nearly 75% of parents from both schools agreed that myopia is a health risk, which may lead to eye diseases or vision loss and more than 90% agreed it is necessary to take children for eye examinations regularly (Chi-square test, p>0.05). Furthermore, more than 80% of parents in both schools agreed that near-work related parameters, such as long working hours on near work without breaks, improper

posture, and dim lighting conditions were related to myopia. Compared to parents from the local school, more parents in the international school thought genetic factors (75.4% vs 56.9%, Chi-square test,  $\chi^2$  =8.89, p=0.003) and little outdoor time (41.8% vs 25.7%, Chi-square test,  $\chi^2$  =6.64, p=0.010) were associated with myopia (Table 2.12).

Table 2.12. Parents' awareness of myopia risk factor in two schools.

	Local School (%)	International School (%)	P value
Do you consider myopia as a health risk ?			0.99
Yes	74.8%	74.8%	
Is it necessary to bring your child to do eye			
examination regularly?			
Yes	92.8%	97.6%	0.085
Myopia risk factors			
Long period of near work without a break	90.8%	94.3%	0.32
Improper postures for reading and writing	83.5%	89.3%	0.19
Dim lighting condition	82.6%	87.7%	0.27
Hereditary factor	56.9%	75.4%	0.003
Little outdoor time	25.7%	41.8%	0.010
Unbalanced diet	12.8%	20.5%	0.12

#### **Discussion**

In the current study, the myopia proportion among 8-10 years old school children in the local school was more than twice as high as that in the international school (46.4% vs. 22.4%, SER ≤ -0.50 D), even if a more conservative definition was used (37.5% vs. 12.8%, SER ≤ -1.00 D). Although there was no difference in axial length between the two schools, the astigmatism proportion in the local school was much higher than that in the international school (25.0% vs. 7.2%, Cyl ≥ 1.00 DC), which may be part of the reasons for the different myopia proportions in two schools. The myopia proportion in the local school was consistent with those in previous studies of Hong Kong children (Fan et al., 2004; Lam et al., 2012; Choy et al., 2021). In an earlier study which recruited older Hong Kong Chinese students than the current study (13-15 years vs 8-10 years), no difference in myopia prevalence was found among students attending the international school and the local school (Lam et al., 2004). These results suggest different incident or progression rates in the two school systems, or that the students in the two school systems were exposed to different risk factors.

Using a validated questionnaire, it was found that the students from the two schools were exposed to different risk factors. First, significantly more parents in the international school (90.4% & 78.4%) received education at post-

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secondary level or above compared with parents in the local school (15.2% & 8.9%) (Table 2.5). Second, there were significantly higher proportions of parental myopia (76.8% vs. 54.5%) and high myopia (19.2% vs. 6.3%) in the international school compared with those in the local school (Table 2.5). Third, local school students spent nearly 4 h/wk or more on both non-screen near work activities (reading, writing, drawing, etc.) and handheld digital devices than those in the international school (Table 2.5). Fourth, international school students spent more time outdoors than the local school students (7.5 h/wk vs. 5 h/wk) (Table 2.5). Further multiple regression analysis showed that the myopic students in the local school were exposed to the combination of parental myopia history and continuous near work time without breaks, whereas in the international school, myopia in students was associated with their father's educational level (Table 2.9).

Why would a risk factor have more impact on the prevalence of myopia in one school system than the other? It should be noted that the multiple regression analyses were performed on myopic students of the two schools separately, but no common risk factors were found. Under the local school system, parental myopia proportion was associated with the presence of myopia and axial length. The impact of parental myopia on children's myopia development has been consistently reported (Jones et al., 2007; Liao et al., 2019; Mutti et al., 2002). Parental myopia is usually regarded as a hereditary factor transmitted from

parents to children and affects axial length and corneal curvature (Goldschmidt et al., 2014). However, parental myopia as a risk factor can also be considered as myopic parents passing on their own academic standards or reading habits to their children rather than passing on myopia itself (Li et al., 2015, Saw et al., 2002). In this study, despite the much higher proportions of parental myopia and high myopia in the international school, the myopia proportion among the students is lower in this school than in the local school, suggesting that factors other than genetics might have a stronger protective effect in this school population. Although the father's educational level was associated with myopia in the international school system, educational level is a complex issue and closely associated with socioeconomic status. In this respect, findings about the association between socioeconomic status and myopia remain controversial. For example, myopic children were found to have myopic parents with higher parental level of education, higher income, and white collar or professional occupations in a Chinese study (Xiang et al., 2012). However, in the Generation R study, a higher myopia proportion was found in children from families with low income, low maternal education and non-European ethnicity (Tideman et al., 2018). Socioeconomic status, such as education and income, may act as a mediating effect in myopia development and represent certain living conditions and habits (e.g. near work activity and outdoor time) that are more directly involved in the pathogenesis of myopia (Tideman et al., 2018).

In addition, smartphone use time in the international school was found to be associated with myopia and a longer axial length in the univariate analysis. The increasing usage of digital devices in recent ten years has increased people's concern about its impact on the children's refractive development. Previous studies have shown that people tended to work with a closer working distance when using digital screens than printed hardcopies even when the texts were adjusted to a similar size (Bababekova et al., 2011; Panke et al., 2019). We speculated that children might have adapted to a close working distance because of the increased digital screen usage. No association was found between working distance and myopia, but this could be due to the inaccurate estimation made by parents. Objective devices are therefore needed for measuring working distance to confirm this speculation. In addition, digital devices differed from typical paper work in brightness, contrast, and resolution, whether and how these factors alter the working distance need further studies. In this study, the association between screen time and myopia was inconsistent. Myopia prevalence in Asian countries such as Singapore, Korea or Japan was already high several decades ago even before digital devices were introduced. Thus, further studies are also needed to investigate the influence of digital devices on refractive development.

The majority of Hong Kong parents were aware of the risk of myopia and the necessity of regular eye examinations. Parents in both schools agreed that near

work related parameters, such as continuous near work and improper postures for reading and writing are myopia risk factors. A survey among Singapore parents also showed similar results (Dirani et al., 2019). Although the role of outdoor time in preventing myopia has received much attention in recent years, less than half of the Hong Kong parents were aware of it. In contrast, 87.7% Singapore parents were aware of the importance of outdoor activity as an intervention to slow the progression of myopia (Dirani et al., 2019), probably because outdoor time as a preventive measure had been integrated into their school education system (Board, 2010). In contrast, positive parental attitudes and behaviors towards their children's vision, such as monitoring device usage has been associated with a delayed onset and reduced progression of myopia (Zhou et al., 2017). Thus, public education including myopia risk factors and treatment options should be enhanced.

There are several limitations in the current study. First, as cycloplegic drugs to relax accommodation were not used, this may have affected the absolute value of refraction, but the relative comparison between the two schools should not have been affected. Second, as keratometry was not performed, it could not be confirmed if the increased astigmatism percentage was due to corneal astigmatism. Third, only the time spent on tablet and smartphones was evaluated in the questionnaire, other screen time, such as computer usage and TV watching time was not considered, which could be the reason for the lack

of association between screen time and myopia. Fourth, as only two schools were included and the response rates were not high, whether the current study results can be generalized to all schools still needs to be confirmed.

To conclude, it was found that the myopia proportion differed between different educational systems in Hong Kong, the myopia proportion was higher in the local school compared with that in the international school. Furthermore, students under different educational systems were exposed to different myopia risk factors. Therefore, when formulating public health policy for myopia control, different strategies should be adopted according to individual risk factors.

# Chapter 3: Proportion of Myopia and Axial Length in Hong Kong Children after Study at Home during COVID-19 Lockdown

## **Introduction**

Due to the COVID-19 pandemic, majority of governments worldwide closed schools in an attempt to contain the spread of infection, which is estimated to have affected over 80% of the global student population ("UNESCO: COVID-19 Impact on Education,"). These closures have led to increasing concern about their impact on myopia incidence in school age children due to increased time spent on near work and possibly a reduction in outdoor activities (Guan et al., 2020; Wong et al., 2020). The association between time spent on near work and myopia has been investigated for many years. A meta-analysis, involving 12 cohort studies and 15 cross-sectional studies conducted between 1989 and 2014 and including children aged 6 to 18 years old, found that more time spent on near work activities was associated with an increased risk of myopia (odds ratio=1.14; 95% confidence intervals 1.08-1.20) (Huang et al., 2015). Other visual habits such as continuous reading for more than 30 (Ip et al., 2008) or 45 (Li et al., 2015) minutes were found to be associated with increased risk of having myopia. Similarly, increased myopia risk was also associated with close reading distance (< 30 cm (Ip et al., 2008; Hsu et al., 2017) or < 20 cm (Guo et al., 2016; Li et al., 2015)) and with tilting the head while reading and writing. In

contrast, increased outdoor time was shown to reduce myopia incidence in school-based clinical trials (He et al., 2015; Wu et al., 2018). However, its role in retarding myopia progression is still not clear (Wu et al., 2017) with only one study showing significantly less myopic shift in myopes (Wu et al., 2018). The effect of increased usage of handheld devices was recently reported by a study in Ireland that objectively measured smartphone data usage and observed an association with myopia (McCrann et al., 2020). Increased screen time on smartphones and computers was also found to be related to more myopic refraction and longer axial length in children aged 6–14 years in the urban area of Tianjin (Liu et al., 2019). Given the evidence on the association between risk factors and myopia, it has been suggested in the literature that the evaluation of myopia prevalence after home confinement period (Pellegrini et al., 2020) or post pandemic (Navel et al., 2020) is needed to provide timely information to better control myopia progression.

During the school closures to contain the spread of COVID-19 in Hong Kong, all schools were encouraged to integrate e learning platforms with online resources for students to study at home from February 2020 to June 2020. To date, little is known about whether there is indeed an increased prevalence of myopia among school children during home confinement. To determine the proportion of myopia in the same age group immediately after the home confinement period, we conducted a vision screening in Jun 2020 for the same age group in the same primary school and collected questionnaire data related to visual habits for comparisons between 2018 cohort.

## **Methods**

The same screening as described in Chapter 2 was conducted in the same local school in June 2020. The second survey was conducted on children of the same age group two weeks after the reopening of the school. Inclusion and exclusion were the same with study 1. We modified questions about time spent on different activities during school close down period rather than typical school days to capture differences in life styles compared with normal school days. A questionnaire was distributed via the school teachers to parents of participants and collected before the eye examination.

In both surveys, the same ophthalmic instruments and school settings were adopted. In brief, the eye examination was conducted on school campus during school days in the morning, The non-cycloplegic refractive state was measured using an open-field autorefractometer (Shin-Nippon, NVision K5001). Children were instructed to fixate at a target (Maltese cross) at six meters under natural viewing conditions (approximately 400 lux), and five consecutive readings of each eye were obtained and averaged. The measurement was performed without the administration of cycloplegia to avoid interfering with classroom learning activities during the school day and to increase the participation rate. Ocular axial length was measured using an IOL Master (Carl Zeiss Meditec). The averaged value of five consecutive measurements with signal - to - noise ratios > 2.0 was used for analysis. Both devices were calibrated using a model eye on a daily basis.

#### Statistical Analysis

The refractive errors were decomposed into spherical-equivalent refraction (SER) and J0 and J45 astigmatic components according to the Fourier analysis (Thibos et al., 1997). Only the data from the right eye was used because the refractive and biometric data of the right and left eyes were highly correlated (Pearson's correlations, r>+0.87, p<0.001). Myopia was defined as SER  $\leq$  -0.50 D (Flitcroft et al., 2019). Because refraction data was obtained without cycloplegia, a more conservative criteria was applied to define myopia, SER  $\leq$  -1.00 D. Refractive astigmatism was defined as cylindrical error  $\geq$  0.50 DC. Because of the relatively small sample sizes in both surveys, the term "myopia proportion" rather than "myopia prevalence" was used in the result section (McCullough et al., 2016).

Statistical analyses were performed using the Statistical Package for Social Science (version 22, IBM Corp., Amonk, NY, US) with the significance level set at  $\alpha$  <0.05. Continuous variables collected in 2018 and 2020 were compared

with either unpaired t-test or Mann-Whitney U test, depending on the normality tested by the Shapiro-Wilk test. Data were presented as mean ( $\pm$ S.D.) or median (interquartile range, IQR). Chi-squared test was used to compare categorical variables between groups and reported in percentages.

#### <u>Results</u>

#### <u>3.1 Subject recruitment</u>

In the 2018 survey, of the 264 students who were invited to join the study, 179 students agreed to participate (67.8% response rate). Of these, ten students exceeded the age limit and four were not of Chinese ethnicity. Another six respondents were excluded from the analysis because they had received myopia control interventions (Ortho-K, n = 4; Defocus-Incorporated-Multiple-Segments lens, n = 2). As a result, 159 students were included in the 2018 survey. In the 2020 survey, 236 students were invited to join the study, and 207 students agreed to participate (87.7% response rate). Eighteen students exceeded the age limit and five were not Chinese. In addition, data of five respondents receiving myopia control interventions (Defocus-Incorporated-Multiple-Segments lens, n = 1; Atropine, n = 2; Progressive addition lens, n = 2) were excluded from further analysis, leaving 179 students in the 2020 survey. All children included in both surveys were from 8 to 10 years old. Of the eligible schoolchildren (2018: n= 159; 2020: n= 179), 112 (70.4%) and 173 (96.6%)

children participated in vision screenings and returned the questionnaire in 2018 and 2020, respectively. None had self-reported ocular diseases. There were no significant differences in age, gender, family income, and parental myopia or high myopia (SER  $\leq$  -6.00 D) between schoolchildren participating in the 2018 and 2020 surveys (Table 3.1).

	2018	2020	P value
Sample size	112	173	
Mean age (S.D.)	9.17±0.82	$9.15 \pm 1.06$	0.86
Male (%)	43.8	54.2	0.088
Monthly family income (%)			0.72
≤ HK\$19,999	59.6	57.4	
> HK\$19,999	40.4	42.6	
Parental myopia (%) <sup>†</sup>	54.5	57.1	0.66
Parental high myopia (%) <sup>†</sup>	6.3	7.1	0.77

Table 3.1 Demographic information.

† refers to at least one parent with myopia / high myopia.

#### 3.2.1 Proportion of refractive errors

Overall, proportions of schoolchildren with myopia and astigmatism were significantly higher in the 2020 cross-sectional survey than that in 2018 (Figure 3.1). In 2020, 95.8% of schoolchildren were myopic using the lower criterion (SER  $\leq$  -0.50 D), which was twice as high the proportion of myopia in 2018 (46.4%, Chi-square test,  $\chi 2 = 90.11$ , p<0.001). The significant difference remained even after using the more stringent criterion to define myopia (SER  $\leq$  -1.00 D) (75.6% in 2020 vs. 37.5% in 2020; Chi-square test,  $\chi 2 = 40.76$ , p<0.001). The proportion of astigmatism (Cyl  $\geq$  0.50 DC) was also higher in

2020 than in 2018 (79.2% vs. 57.1%, Chi-square test,  $\chi^2$  = 15.63, p<0.001). Because some students participated in both vision screenings, we also analyzed refractive errors by age. Proportions of schoolchildren with myopia (SER  $\leq$  -1.00 D) and astigmatism were significantly higher in the 2020 crosssectional survey than that in 2018, across all age groups (Figure 3.2). In 2020, myopia proportion was twice as high as in 2018 across all age groups (8-yearold: 31.0% vs. 69.8%, Chi-square test,  $\chi^2 = 10.47$ , p=0.001; 9-year-old: 42.9% vs. 79.6%, Chi-square test,  $\chi^2 = 12.65$ , p<0.001; 10-year-old: 35.4% vs. 76.3%, Chi-square test,  $\chi 2 = 20.59$ , p<0.001). Significant increase in the astigmatism proportion (Cyl ≥ 0.50 DC) was also found (9-year-old: 51.4% vs. 77.8%, Chisquare test,  $\gamma 2 = 6.71$ , p=0.01; 10-year-old group: 60.4% vs. 82.9%, Chi-square test,  $\chi^2$  = 7.76, p=0.005) except in 8-year-old group (58.6% vs. 74.4%, Chisquare test,  $\chi 2 = 1.99$ , p= 0.16). When refractive astigmatism was defined as  $Cyl \ge 1.00$  DC, no difference was found across all age groups (Chi-square test, p ≥ 0.43).



Figure 3.1 Percentage of refractive errors in 2018 and 2020 cohorts. Percentages of myopia (defined as either  $\leq$  -0.50 D or  $\leq$  -1.00 D) and astigmatism ( $\geq$  0.50 DC) increased significantly for students in the 2020 cohort. Note that the 2020 survey was conducted 2 weeks after the ending of schoolfrom-home period. Comparisons of percentages of the same age group (8-10 years) were made by Chi-square tests. \*\*\*p<0.001.



Figure 3.2 Percentage of refractive errors by age in 2018 and 2020 cohorts. (A) Percentages of myopia (defined as  $\leq$  -1.00 D) increased significantly for students in the 2020 cohort in all age groups. (B) Significant increase in astigmatism ( $\geq$  0.50 DC) was not found in the 8-year-old group in the 2020 cohort. Note that the 2020 survey was conducted 2 weeks after the ending of school-from-home period. Comparisons of percentages of the same age group (8-10 years) were made by Chi-square tests. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001.

#### 3.2.2 Refractive error components and axial length

Table 3.2 presents the results of refractive components and axial length in the two cross-sectional surveys by age. Compared to data collected in 2018, on average, the median SER in 2020 was approximately 1.00 D more myopic (Mann-Whitney U test, U > 906,  $p \le 0.001$ ). In addition, the averaged axial length was longer in 2020 than in 2018, but both of them failed to reach statistical significance (unpaired t-test,  $p \ge 0.05$ ). As expected, the axial length was inversely correlated with the SER (2018, Pearson r=-0.61, p<0.001; 2020, Pearson r= -0.67, p<0.001). Compared to the 2018 survey, schoolchildren who participated in the 2020 survey also had a higher cylindrical power except in 8-year-old group (Mann-Whitney U tests, U = 1180 & 2309, p < 0.05), more positive J0 astigmatic component only in the 10-year-old (Mann-Whitney U tests, U = 1255, p = 0.004), and less negative J45 astigmatic component in the 8 year-old group (Mann-Whitney U tests, U = 319, p < 0.001).

8-year-old	2018	2020	P value
SER (IQR)	-0.31 (-1.16, 0.16)	-1.19 (-1.81, -0.93)	0.001
Axial length (mm)	23.15±0.87	23.47±0.94	0.15
Cylinder power (IQR)	0.62 (0.31, 0.81)	0.62 (0.37, 0.87)	0.37
J0 (IQR)	+0.20 (+0.12, +0.40)	+0.25 (+0.17, +0.42)	0.37
J45 (IQR)	-0.08 (-0.15, 0)	+0.03 (-0.04, +0.15)	<0.001
9-year-old	2018	2020	P value
SER (IQR)	-0.31 (-1.50, +0.12)	-1.47 (-2.21, -1.06)	0.001
Axial length (mm)	23.43±0.96	23.62±0.84	0.34
Cylinder power (IQR)	0.50 (0.25, 1.00)	0.62 (0.50, 0.87)	0.047
J0 (IQR)	+0.17 (0, +0.47)	+0.28 (+0.18, +0.40)	0.060
J45 (IQR)	-0.01 (-0.14, +0.05)	0.00 (-0.09, +0.09)	0.36
10-year-old	2018	2020	P value
SER (IQR)	-0.23 (-1.56, +0.19)	-1.53 (-2.53, -1.00)	<0.001
Axial length (mm)	23.48±0.83	23.81±1.02	0.059
Cylinder power (IQR)	0.50 (0.28, 0.97)	0.75 (0.53, 1.09)	0.013
J0 (IQR)	+0.16 (0, +0.43)	+0.36 (+0.17, +0.53)	0.004
J45 (IQR)	-0.05 (-0.12, +0.03)	-0.03 (-0.14, +0.06)	0.49

Table 3.2 Results of refractive-error components and axial length for the crosssectional survey data..

IQR: interquartile range

Table 3.3 below shows the refractive change of 38 children (Female: Male = 17:21) who participated in both vision screenings. The change in refractive errors of this subgroup shows the similar trend observed in the cross-sectional data. Myopia and axial length were both increased significantly, by  $1.63\pm0.61$  D and  $0.53\pm0.30$  mm, respectively (paired t-test, *t* = -16.40 & 11.00, both *p* <

0.001). The cylindrical power was on average increased by  $0.35\pm0.40$  D (paired t-test, t = 5.53, p < 0.001) and J0 astigmatism became more positive by  $0.21\pm0.25$  D (t = 5.01, p < 0.001). In contrast, the J45 astigmatism became less negative, by  $0.05\pm0.19$  D (t = 1.79, p = 0.08), but the change did not reach statistical significance.

Table 3.3. Results of refractive-error components and axial length for 38 children who participated in both 2018 and 2020 surveys.

	2018	2020	P value <sup>#</sup>
SER (D)	-0.57±1.57	-2.21±1.56	< 0.001
Axial length (mm)	23.16±1.00	23.69±1.09	< 0.001
Cylinder power (D)	0.77±1.00	1.13±0.87	< 0.001
J0 (D)	+0.31±0.53	+0.51±0.47	< 0.001
J45 (D)	-0.09±0.12	-0.03±0.16	0.08

<sup>#</sup> All data followed the normal distribution (Shapiro-Wilk test, all p > 0.20). Paired t-tests were performed to compare data collected in 2018 and 2020.

IQR: interquartile range

## 3.2.3 Time spent on different kinds of activities

Overall, schoolchildren in the 2020 cohort on average spent more time on handheld digital devices, but less time on non-screen work compared to those in 2018 (Table 3.4). The time spent on handheld digital devices, including time spent on smartphones and tablets, was 1 h/day and 0.75 h/day longer in 2020 than in 2018 for weekdays (Mann-Whitney U test, U = 4933.0, p<0.001) and weekends (Mann-Whitney U test, U = 7209.0, p=0.001), respectively. In

contrast, schoolchildren spent 0.5 h/day less on non-screen work in 2020 than in 2018, but the difference was significant only for weekdays (Mann-Whitney U test, U = 7232.0, p=0.001). Schoolchildren in the 2020 cohort also spent 0.5 h/day more time on outdoor activities during weekdays than those in 2018 (Mann-Whitney U test, U = 7378.0, p=0.001). No significant difference in time spent outdoors was found for weekends (Mann-Whitney U test, U = 8299.0, p=0.091). Consequently, on average, no significant difference was found in time spent outdoors between the two cohorts.

Besides, more students in 2020 cohort tilted their heads when performing near work activities (82.7% versus 56.3%, chi-square test, p<0.001) and more students in 2020 performed continuous near work for 30 minutes or longer before having breaks (77.4% versus 46.4%, chi-square test, p<0.001).

Time (h/day)	2018	2020	P value
	2010	2020	1 Value
Non-screen time (IQR)			
Average	1.55 (0.73, 2.38)	1.0 (0.53, 1.98)	0.002
Weekday	1.50 (1.00, 2.50)	1.00 (0.50, 2.00)	0.001
Weekend	1.30 (0.00, 2.00)	1.00 (0.50, 2.00)	0.22
Handheld digital screen time (IQR)			
Average	1.40 (0.60, 2.18)	1.60 (1.10, 2.10)	0.013
Weekday	1.00 (0.50, 2.00)	2.00 (1.00, 3.00)	<0.001
Weekend	2.00 (1.00, 3.00)	2.75 (2.00, 4.00)	0.001
Outdoor time (IQR)			
Average	0.70 (0.40, 1.10)	0.90 (0.50, 1.48)	0.11
Weekday	0.50 (0.00, 0.50)	1.00 (0.00, 1.00)	0.001
Weekend	1.50 (0.50, 2.50)	1.50 (1.00, 2.00)	0.091
Head tilt	56.3%	82.7%	<0.001
>30 min continuous near work	46.4%	77.4%	<0.001

Table 3.4 Non-ocular parameter between two cohorts.

Average time was calculated as (5×average weekday time + 2×average weekend time) /7. IQR: interquartile range

# **Discussion**

This was a cross-sectional study in the same school setting comparing results of two vision screenings conducted in 2018 and 2020 separately. It should be noted that the "study from home" period only lasted for 4 months before the second vision screening, a direct impact due to this short interval on refraction and axial length in young school children must therefore be interpreted cautiously. Nevertheless, the myopia proportion in 2020 was twice as high as in 2018 (95.8% vs 46.4%, SER  $\leq$  -0.50 D), even if a more conservative criterion to define myopia was used (75.7% vs 37.5%, SER  $\leq$  -1.00 D) (see also Figure 3.1). There was on average a 1-D increase in myopia between the two surveys. The finding was further confirmed increase in axial length when comparing the 2020 survey with the 2018 survey separated by only 18 months. Likewise, longitudinal data collected from 38 schoolchildren who participated in both vision screenings also showed an increased myopia and a longer axial length, respectively over the two-year follow-up period.

In both surveys, we used the same ophthalmic instruments and school settings to conduct the examination. This minimized the possibility that the difference in the myopia proportion between the two surveys was due to the examination procedure. In order to avoid affecting classroom activities during the normal school day and to encourage participation of school children, cycloplegia was not used in both surveys. However, even though an open-field autorefractor was used and the participant was instructed to fixate at distant visual target during the non-cycloplegic refraction, this procedure cannot exclude the possibility that the refractive state we measured was affected by ocular accommodation. Nevertheless, because both surveys used the same procedures of non-cycloplegic refractions for children from the same age group, the impacts of accommodation on refractions might be similar in both cohorts.

Both surveys shared similar demographic characteristics with subtle differences in participation rate and sex ratio. While age, family income and parental myopia were not significantly different between the two cohorts (Table 3.1), the participation rate in 2020 survey was about 20% higher than that in 2018 survey (87.7% vs 67.8%). This could be due to the parents' awareness of increasing near work activities during the 'study from home' period and/or the demands for eye examination to prepare for school re-opening.

The significant increase in myopia proportion in the 2020 cohort is in strong contrast to those reported in previous studies also focusing on Hong Kong Chinese students (Figure 3.3). The similar results were also found in a recent study where the prevalence of myopia appeared to be approximately 3 times higher in 2020 than in other years for children aged 6 years (21.5% vs 5.7%), 2 times higher for children aged 7 years (26.2% vs 16.2%), and 1.4 times higher for those aged 8 years (37.2% vs 27.7%) in the rural region of China (Wang et al., 2021). Despite the difference in methodology, including the use of cycloplegic auto-refraction in different studies, the prevalence of myopia at different ages varied at most in the range of 20-30% (Lam et al., 2012), the proportion of myopia in 2020 after school closures being much higher than any of these previous studies, including two published in 2020. In this regard, a study comparing myopia prevalence in Hong Kong Chinese schoolchildren over two decades (1990s to 2010s) found no significant increase (Lam et al., 2004). Results from these studies are shown in Fig 3.3.



Figure 3.3 Percentage of myopia in Hong Kong Chinese school children (4-12

years) across studies. Percentage of myopia (either  $\leq$  -0.50 D or < -0.50 D) is plotted as a function of age for studies focusing on Hong Kong Chinese school children. Note that only data of school children <13 years old from these studies are used for comparison purposes. Symbols with cross-hair (+) represent studies using cycloplegic refraction. Data of the two cohorts in the current studies are highlighted in blue (2018) and red (2020) symbols. [O: (Edwards MH, 1999);  $\Box$ : (Lam et al, 1991);  $\mathbb{A}$ : (Goldshmidt et al, 2001);  $\oplus$ : (Fan et al, 2004a);  $\boxplus$ : (Fan et al, 2004b);  $\triangle$ : (Lam et al, 2012);  $\nabla$ : (Choy et al, 2020);  $\overline{*}$ : (Yam et al, 2020)].

In the current study, we received confirmation from school teachers that the classroom activities and curriculum had not changed in the last two years, except for the integration of e-learning platforms for students to study at home during the school closure. In addition, there were no differences in family incomes and parental myopia (normal and high myopia) between the two cohorts (Table 3.1). These results suggest minimal influences of school environment, social economic status, and genetic variances on the increased myopia proportion in this study. However, we observed a significantly longer handheld digital screen time but a shorter non-screen time in the 2020 survey when compared to the 2018 survey. We speculate that a possible reason for the significant increase in myopia proportion in the current study is the increased screen time. Due to the change in study mode during the lockdown period, more school assignments were done online instead of traditional written

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assignments after communicating with school teachers. The relationship between screen time and myopia has been investigated in previous studies. In a recent meta-analysis involving 15 studies using data collected between 1990 to 2010, no consistent relationship was found between screen time and myopia (Lanca et al., 2019). However, unlike the current study, which only measured screen time spent on smartphones or tablets in the questionnaire, many studies included in the meta-analysis evaluated screen time involving computer use and video game play, which may involve a longer working distance than handheld digital devices. Furthermore, the data analyzed in these studies were collected during a period (1990-2010) that may not reflect the immense increase in use of handheld digital devices, which commenced in the last decade (Boulos et al., 2011). Of note, the "screen time" in this study did not include the time spent on desktop computers; thus, we cannot exclude the possibility that increased computer usage might have contributed to the increased myopia proportion. Further studies are strongly warranted to consider all kinds of screen time when investigating the potential influence of screen time on myopia development.

Another possible contributing factor to the surge in myopia proportion is the short time spent outdoors in this study, even though the average time outdoors increased from 0.7 h/day to 0.9 h/day over the lockdown period. In the previous survey, students were asked about outdoor time outside school, however, their

travelling time and outdoor time inside school (e.g. class break and outside physical education) was not considered. Therefore, the average total outdoor time (inside and outside school) in 2018 should be more than 0.7 h/day. Since schools were closed during the lockdown period, the outdoor time recorded was their total outdoor time. In this regard, outdoor time could be reduced in 2020 compared with typical school days. Outdoor time has been shown to have a protective effect against myopia onset (He et al., 2015; Wu et al., 2018; Wu et al., 2013; Xiong et al., 2017). In the CLEER study, a total outdoor time >14 h/week (2 h/day) significantly reduced the risk of a child becoming myopic, despite parental myopia (Jones et al., 2007), but a recent study on Hong Kong primary school children failed to find a protective effect of outdoor time on myopia prevalence (Choy et al., 2020). It is recommended by WHO that schoolchildren in East Asian countries should have 2-3 hours outdoor time each day (Ang et al., 2020). In the current study, both cohorts failed to reach this daily dosage of 2 h/day, with only 4.5% in 2018 and 14.9% in 2020 spending  $\geq$  2 h/day outdoors. Considering the intensive classroom curriculum in the local school system, frequently augmented with further after-school tutorial classes, whether increasing time outdoors could help protect school children in Hong Kong from developing myopia awaits further studies.

Hong Kong is one of the most densely populated cities in East Asia and people generally live in relatively small flats due to the high housing costs (Census and Statistical Department, 2017). A survey in 2019 showed that the average living space per person in public housing was 13.3 m<sup>2</sup> (Authority, 2019). A smaller home size was associated with longer axial length and more myopic refraction (Choi et al., 2017). Because the children had to stay at home during the pandemic, the small home size might have exposed them to more hyperopic defocus in the peripheral visual field, which is hypothesized to trigger myopia development (Flitcroft, 2012; Smith III et al., 2009; Smith III et al., 2005). Further analyses of questionnaire data on visual habits related to near work showed two differences between the cohorts, which may accentuate this environmental risk factor (see Results section for details): First, more students in 2020 cohort tilted their heads when performing near work activities; second, more students in 2020 performed continuous near work for 30 minutes or longer before having eye breaks. Further studies are needed to determine whether the unequal amount of hyperopic defocus on the retina caused by head tilt (Charman, 2011; Logan et al., 2021) and/or the constant hyperopic defocus due to continuous near work (Ip et al., 2008) contribute to the dramatic increase of myopia proportion in this study.

There are several limitations in the current study. First, this was a crosssectional study comparing results from two separate vision screenings targeted at different cohorts. We did not have ocular parameters on the same group of schoolchildren before and after school closure, thus a causal relationship
cannot be determined from the current study. Further studies are needed to confirm the influence of school closure on the children's refractive development. Second, cycloplegic refractions were not used in either screening, in order to avoid affecting classroom activities during the normal school day and to encourage participation, thus the possibility that measurement of the refractive state may have been affected by accommodation could not be excluded. Nevertheless, the proportion of myopia after school closures remained nearly twice as high as that observed in the earlier screening, even if a more conservative criterion to define myopia (SER  $\leq$  -1.00 D) was employed (Figure 1). Third, the sample sizes of both cohorts were not large. At the time of writing, all schools in Hong Kong are once again closed due to the surge of COVID-19 infections (from 13<sup>th</sup> July, 2020). Because uncorrected refractive errors in children can affect their academic performance (Harvey et al., 2016) and increase the rate of myopia progression, more vision screenings are urgently needed to confirm whether the results of this study are generalizable to other ages and to effectively identify children at high risk of developing myopia to receive a comprehensive eye examination. Finally, although a questionnaire is the most convenient and efficient way to collect general information from a large group of participants, it is subject to recall bias. Objective methods such as use of a clouclip are needed to capture parameters related to time spent on near work (Wen et al., 2019).

To conclude, vision screenings conducted in the same school separated by 2 years on different cohorts showed that the proportion of myopia in 8-10 years old children had doubled accompanied by increased axial length. These results underscore the importance of health service planning to cope with the possible increasing demand of vision care after the pandemic. Future research is warranted to determine the effect of home confinement and online learning on refractive error development. Guardians are advised to focus on their children's visual habits occasioned by the significant changes in their study pattern.

# **Chapter 4: Conclusions**

## 4.1 Conclusions

The findings from this thesis suggest that: (1) myopia proportion differed between different educational systems in Hong Kong, i.e. myopia proportion was higher in the local school compared with that in the international school; (2) students under different educational systems were exposed to different myopia risk factors; and (3) the proportion of myopia was double accompanied with increased axial length after home confinement in the same school, environmental factors may contribute to such increase.

Considering the demographic differences existed in the two schools such as the higher family income and higher proportion of parental myopia history in the international school, as well as non-demographic differences such as more time on non-screen activities and handheld digital devices, less outdoor time in the local school, our results showed that both genetic and environmental factors contributed to the myopia development with different weights among different individuals. Therefore, when making public polices on myopia prevention or intervention, attention should be paid to assess risk factors in different educational systems.

During the school closure due to COVID-19 epidemic, students had to stay at

home. We found that myopia proportion was double accompanied by increased axial length. There were no differences in demographic information and parental myopia history, environmental factors including screen time and outdoor time in the same school. Thus, public health care sector may need to cope with the potential increasing demand of vision care after the pandemic.

### 4.2 Future study

Considering the fact that environmental factors are easier to modify compared to genetic factors, further studies on environmental risk factors for myopia development are needed since students spend a significant amount of time on campus and 70% of the learning process is via vision (Narayanasamy et al., 2016; Ritty et al., 1993). These factors may include room lighting condition, seating arrangements, font size, and contrast sensitivity of multi-media equipment involved in the learning activities. Longitudinal studies are also needed to investigate the potential influence of home confinement during COVID-19 on children's visual development.

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# References

- Abbott, M. L., Schmid, K. L., & Strang, N. C. (1998). Differences in the accommodation stimulus response curves of adult myopes and emmetropes. *Ophthalmic and Physiological Optics*, *18*, 13-20.
- ADAMS, D. W., & McBRIEN, N. A. (1992). Prevalence of myopia and myopic progression in a population of clinical microscopists. *Optometry and Vision Science, 69*, 467-473.
- Al-Bdour, M., Odat, T., & Tahat, A. (2001). Myopia and level of education. *European journal of ophthalmology*, *11*, 1-5.
- Ang, M., Flanagan, J. L., Wong, C. W., Müller, A., Davis, A., Keys, D., et al. (2020). Myopia control strategies recommendations from the 2018 WHO/IAPB/BHVI Meeting on Myopia. *British Journal of Ophthalmology.*
- Ashby, R., Ohlendorf, A., & Schaeffel, F. (2009). The effect of ambient illuminance on the development of deprivation myopia in chicks. *Investigative Ophthalmology & Visual Science, 50*, 5348-5354.
- Ashby, R. S., & Schaeffel, F. (2010). The effect of bright light on lens compensation in chicks. *Investigative Ophthalmology & Visual Science, 51*, 5247-5253.
- Authority, H. K. H. (2019). *Housing in Figures 2019: The Government of The Hong Kong Special Administrative Region*.
- Bababekova, Y., Rosenfield, M., Hue, J. E., & Huang, R. R. (2011). Font size and viewing distance of handheld smart phones. *Optometry and vision science, 88*, 795-797.
- Bao, J., Yang, A., Huang, Y., Li, X., Pan, Y., Ding, C., et al. (2021). One-year myopia control efficacy of spectacle lenses with aspherical lenslets. *British Journal of Ophthalmology*.
- Benavente-Perez, A., Nour, A., & Troilo, D. (2012). The effect of simultaneous negative and positive defocus on eye growth and development of refractive state in marmosets. *Investigative Ophthalmology & Visual Science, 53*, 6479-6487.
- Board, H. P. (2010). Health Promotion Board Annual Report 2009/2010.
- Boulos, M. N. K., Wheeler, S., Tavares, C., & Jones, R. (2011). How smartphones are changing the face of mobile and participatory healthcare: an overview, with example from eCAALYX. *Biomedical engineering online, 10*, 24.
- Brown, N. P., Koretz, J. F., & Bron, A. J. (1999). The development and maintenance of emmetropia. *Eye, 13*, 83-92.
- Brummitt, N., & Keeling, A. (2013). Charting the growth of international schools. *International education and schools: Moving beyond the first, 40*, 25-36.
- Buehren, T., Collins, M. J., & Carney, L. (2003). Corneal aberrations and reading. *Optometry and Vision Science, 80*, 159-166.
- Buehren, T., Collins, M. J., & Carney, L. G. (2005). Near work induced wavefront aberrations in myopia. *Vision research*, 45, 1297-1312.
- Census and Statistical Department, H. (2017). 2016 Population By-census-Main Results.
- Chakraborty, R., Read, S. A., & Collins, M. J. (2012). Monocular myopic defocus and daily changes in axial length and choroidal thickness of human eyes. *Experimental eye research, 103*, 47-54.

- Chakraborty, R., Read, S. A., & Collins, M. J. (2013). Hyperopic defocus and diurnal changes in human choroid and axial length. *Optometry and Vision Science, 90*, 1187-1198.
- Chamberlain, P., Peixoto-de-Matos, S. C., Logan, N. S., Ngo, C., Jones, D., & Young, G. (2019). A 3-year randomized clinical trial of MiSight lenses for myopia control. *Optometry and Vision Science, 96*, 556-567.
- Chassiakos, Y. L. R., Radesky, J., Christakis, D., Moreno, M. A., & Cross, C. (2016). Children and adolescents and digital media. *Pediatrics, 138*, e20162593.
- Chen, C. Y.-C., Scurrah, K. J., Stankovich, J., Garoufalis, P., Dirani, M., Pertile, K. K., et al. (2007). Heritability and shared environment estimates for myopia and associated ocular biometric traits: the Genes in Myopia (GEM) family study. Human genetics, 121, 511-520.
- Chen, Y.-P., Hocking, P. M., Wang, L., Považay, B., Prashar, A., To, C.-H., et al. (2011). Selective breeding for susceptibility to myopia reveals a gene–environment interaction. *Investigative Ophthalmology & Visual Science, 52*, 4003-4011.
- Chen, Y., Wang, W., Han, X., Yan, W., & He, M. (2016). What twin studies have taught us about myopia. *The Asia-Pacific Journal of Ophthalmology, 5*, 411-414.
- Cheng, H., Barnett, J. K., Vilupuru, A. S., Marsack, J. D., Kasthurirangan, S., Applegate, R. A., et al. (2004). A population study on changes in wave aberrations with accomodation. *Journal* of Vision, 4, 3-3.
- Cheung, A. C., Randall, E. V., & Tam, M.-K. (2005). Expanding the Private School Sector: Government Policy and Private Secondary Schools in Hong Kong, 1988-2001. *International Journal of Educational Policy, Research, and Practice: Reconceptualizing Childhood Studies, 6*, 139-172.
- Cho, P., & Cheung, S.-W. (2017). Protective role of orthokeratology in reducing risk of rapid axial elongation: a reanalysis of data from the ROMIO and TO-SEE studies. *Investigative Ophthalmology & Visual Science, 58*, 1411-1416.
- Cho, P., & Tan, Q. (2019). Myopia and orthokeratology for myopia control. *Clinical and Experimental Optometry, 102*, 364-377.
- Choi, K. Y., Yu, W. Y., Lam, C. H. I., Li, Z. C., Chin, M. P., Lakshmanan, Y., et al. (2017). Childhood exposure to constricted living space: a possible environmental threat for myopia development. *Ophthalmic and Physiological Optics*, 37, 568-575.
- Choy, B. N. K., You, Q., Zhu, M. M., Lai, J. S. M., Ng, A. L. K., & Wong, I. Y. H. (2020). Prevalence and associations of myopia in Hong Kong primary school students. *Japanese Journal of Ophthalmology*, 1-13.
- Chua, S. Y. L., Ikram, M. K., Tan, C. S., Lee, Y. S., Ni, Y., Shirong, C., et al. (2015). Relative contribution of risk factors for early-onset myopia in young Asian children. *Investigative Ophthalmology & Visual Science, 56*, 8101-8107.
- Chua, S. Y.L., Sabanayagam, C., Cheung, Y. B., Chia, A., Valenzuela, R. K., Tan, D., et al. (2016). Age of onset of myopia predicts risk of high myopia in later childhood in myopic Singapore children. *Ophthalmic and Physiological Optics, 36*, 388-394.
- Ciuffreda, K. J., & Lee, M. (2002). Differential refractive susceptibility to sustained nearwork. *Ophthalmic and Physiological Optics, 22*, 372-379.
- Ciuffreda, K. J., & Ordonez, X. (1998). Vision therapy to reduce abnormal nearwork-induced transient myopia. *Optometry and vision science: official publication of the American Academy of Optometry, 75*, 311-315.

- Ciuffreda, K. J., & Wallis, D. M. (1998). Myopes show increased susceptibility to nearwork aftereffects. *Investigative Ophthalmology & Visual Science, 39*, 1797-1803.
- Cohen, Y., Belkin, M., Yehezkel, O., Solomon, A. S., & Polat, U. (2011). Dependency between light intensity and refractive development under light–dark cycles. *Experimental eye research, 92*, 40-46.
- Cohen, Y., Peleg, E., Belkin, M., Polat, U., & Solomon, A. S. (2012). Ambient illuminance, retinal dopamine release and refractive development in chicks. *Experimental eye research, 103*, 33-40.
- Cohn, H. L. (1886). The hygiene of the eye in schools. Simpkin, Marshall.
- Coleman, D. J. (1970). Unified model for accommodative mechanism. *American journal of ophthalmology, 69*, 1063-1079.
- Collins, M. J., Buehren, T., Bece, A., & Voetz, S. C. (2006). Corneal optics after reading, microscopy and computer work. *Acta Ophthalmologica Scandinavica, 84*, 216-224.
- Collins, M. J., Wildsoet, C. F., & Atchison, D. A. (1995). Monochromatic aberrations and myopia. *Vision research*, *35*, 1157-1163.
- Curtin, B. J. (1985). The myopias. Basic science and clinical management.
- Curtin, B. J., & Karlin, D. B. (1971). Axial length measurements and fundus changes of the myopic eye. *American journal of ophthalmology, 71*, 42-53.
- Dennis, Y. T., Lam, C. S., Guggenheim, J. A., Lam, C., Li, K.-k., Liu, Q., et al. (2007). Simultaneous defocus integration during refractive development. *Investigative Ophthalmology & Visual Science, 48*, 5352-5359.
- Delshad, S., Collins, M. J., Read, S. A., & Vincent, S. J. (2020). The human axial length and choroidal thickness responses to continuous and alternating episodes of myopic and hyperopic blur. Plos One, 15, e0243076.
- Dirani, M., Salim, A., Keel, S., & Foreman, J. (2019). Awareness of Myopia: A Survey Among Parents Residing in Singapore.
- Donders, F. C., & Moore, W. D. (1864). *On the anomalies of accommodation and refraction of the eye: With a preliminary essay on physiological dioptrics* (Vol. 22): New Sydenham Society.
- Drexler, W., Findl, O., Schmetterer, L., Hitzenberger, C. K., & Fercher, A. F. (1998). Eye elongation during accommodation in humans: differences between emmetropes and myopes. *Investigative Ophthalmology & Visual Science, 39*, 2140-2147.
- Education Bureau, H. (2019). Student Enrolment Statistics, 2019/20.
- Education Bureau, H. (2020). Education System and Policy.
- Edwards, M. H. (1999). The development of myopia in Hong Kong children between the ages of 7 and 12 years: a five-year longitudinal study. *Ophthalmic and Physiological Optics, 19*, 286-294.
- Enthoven, C. A., Tideman, J. W. L., Polling, J. R., Tedja, M. S., Raat, H., Iglesias, A. I., et al. (2019). Interaction between lifestyle and genetic susceptibility in myopia: the Generation R study. *European journal of epidemiology, 34*, 777-784.
- Enthoven, C. A., Tideman, J. W. L., Polling, J. R., Yang-Huang, J., Raat, H., & Klaver, C. C. (2020). The impact of computer use on myopia development in childhood: The Generation R study. *Preventive Medicine*, *132*, 105988.
- Fan, D., Rao, S., Cheung, E., Islam, M., Chew, S., & Lam, D. (2004). Astigmatism in Chinese preschool children: prevalence, change, and effect on refractive development. *British Journal of*

Ophthalmology, 88, 938-941.

- Fan, D. S. P., Cheung, E. Y. Y., Lai, R. Y. K., Kwok, A. K. H., & Lam, D. S. C. (2004). Myopia progression among preschool Chinese children in Hong Kong. *Annals-Academy of Medicine Singapore, 33*, 39-43.
- Fan, D. S. P., Lam, D. S. C., Lam, R. F., Lau, J. T. F., Chong, K. S., Cheung, E. Y. Y., et al. (2004). Prevalence, incidence, and progression of myopia of school children in Hong Kong. *Investigative Ophthalmology & Visual Science, 45*, 1071-1075.
- Fan, Q., Verhoeven, V. J., Wojciechowski, R., Barathi, V. A., Hysi, P. G., Guggenheim, J. A., et al. (2016). Meta-analysis of gene–environment-wide association scans accounting for education level identifies additional loci for refractive error. *Nature communications, 7*, 1-12.
- Fledelius, H. C., & Christensen, A. C. (1996). Reappraisal of the human ocular growth curve in fetal life, infancy, and early childhood. *British Journal of Ophthalmology, 80*, 918-921.
- Flitcroft, D. (2014). Emmetropisation and the aetiology of refractive errors. Eye, 28, 169-179.
- Flitcroft, D. I. (2012). The complex interactions of retinal, optical and environmental factors in myopia aetiology. *Progress in Retinal and Eye Research, 31*, 622-660.
- Flitcroft, D. I., He, M., Jonas, J. B., Jong, M., Naidoo, K., Ohno-Matsui, K., et al. (2019). IMI Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies. *Investigative Ophthalmology & Visual Science, 60*, M20-M30.
- Fotedar, R., Rochtchina, E., Morgan, I., Wang, J. J., Mitchell, P., & Rose, K. A. (2007). Necessity of cycloplegia for assessing refractive error in 12-year-old children: a population-based study. *American journal of ophthalmology*, 144, 307-309.
- French, A. N., Morgan, I. G., Mitchell, P., & Rose, K. A. (2013). Risk Factors for Incident Myopia in Australian Schoolchildren The Sydney Adolescent Vascular and Eye Study. *Ophthalmology*, *120*, 2100-2108.
- Garner, L. F., & Yap, M. K. (1997). Changes in ocular dimensions and refraction with accommodation. *Ophthalmic and Physiological Optics*, *17*, 12-17.
- Gee, S. S., & Tabbara, K. F. (1988). Increase in ocular axial length in patients with corneal opacification. *Ophthalmology*, *95*, 1276-1278.
- Ghorbani Mojarrad, N., Williams, C., & Guggenheim, J. A. (2018). A genetic risk score and number of myopic parents independently predict myopia. *Ophthalmic and Physiological Optics*, *38*, 492-502.
- Ghosh, A., Collins, M. J., Read, S. A., & Davis, B. A. (2012). Axial length changes with shifts of gaze direction in myopes and emmetropes. *Investigative Ophthalmology & Visual Science*, 53, 6465-6471.
- Ghosh, A., Collins, M. J., Read, S. A., Davis, B. A., & Chatterjee, P. (2014). Axial elongation associated with biomechanical factors during near work. *Optometry and Vision Science*, *91*, 322-329.

Goldschmidt, E. (2003). The mystery of myopia. Acta Ophthalmologica Scandinavica, 81, 431-436.

- Goldschmidt, E., & Jacobsen, N. (2014). Genetic and environmental effects on myopia development and progression. *Eye, 28,* 126-133.
- Goldschmidt, E., Lam, C. S. Y., & Opper, S. (2001). The development of myopia in Hong Kong children. *Acta Ophthalmologica Scandinavica, 79*, 228-232.
- Goss, D. A. (1991). Clinical accommodation and heterophoria findings preceding juvenile onset of myopia. *Optometry and vision science: 68*, 110-116.

- Grosvenor, T. (1987). A review and a suggested classification system for myopia on the basis of age-related prevalence and age of onset. *American journal of optometry and physiological optics, 64*, 545-554.
- Grosvenor, T. (1988). High axial length/corneal radius ratio as a risk factor in the development of myopia. *American journal of optometry and physiological optics, 65*, 689-696.
- Guan, H., Okely, A. D., Aguilar-Farias, N., del Pozo Cruz, B., Draper, C. E., El Hamdouchi, A., et al. (2020). Promoting healthy movement behaviours among children during the COVID-19 pandemic. *Lancet Child Adolesc. Health*, *4*, 416-418.
- Guggenheim, J. A., Northstone, K., McMahon, G., Ness, A. R., Deere, K., Mattocks, C., et al. (2012). Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. *Investigative Ophthalmology & Visual Science, 53*, 2856-2865.
- Guggenheim, J. A., Northstone, K., McMahon, G., Ness, A. R., Deere, K., Mattocks, C., et al. (2012). Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. *Investigative Ophthalmology & Visual Science, 53*, 2856-2865.
- Guggenheim, J. A., Williams, C., Northstone, K., Howe, L. D., Tilling, K., St Pourcain, B., et al. (2014).
   Does vitamin D mediate the protective effects of time outdoors on myopia? Findings from a prospective birth cohort. Investigative Ophthalmology & Visual Science, 55, 8550-8558.
- Guo, L., Yang, J., Mai, J., Du, X., Guo, Y., Li, P., et al. (2016). Prevalence and associated factors of myopia among primary and middle school-aged students: a school-based study in Guangzhou. *Eye, 30*, 796-804.
- Guo, Y., Duan, J. L., Liu, L. J., Sun, Y., Tang, P., Lv, Y. Y., et al. (2017). High myopia in greater Beijing school children in 2016. *Plos One, 12*, e0187396.
- Guo, Y., Liu, L. J., Tang, P., Lv, Y. Y., Feng, Y., Xu, L., et al. (2017). Outdoor activity and myopia progression in 4-year follow-up of Chinese primary school children: The Beijing Children Eye Study. *Plos One, 12*, e0175921.
- Gusek-Schneider, G. C., & Martus, P. (2001). Stimulus deprivation myopia in human congenital ptosis: a study of 95 patients. *Journal of pediatric ophthalmology and strabismus, 38*, 340-348.
- Gwiazda, J., Grice, K., Held, R., McLellan, J., & Thorn, F. (2000). Astigmatism and the development of myopia in children. *Vision research, 40*, 1019-1026.
- Gwiazda, J., Hyman, L., Hussein, M., Everett, D., Norton, T. T., Kurtz, D., et al. (2003). A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Investigative Ophthalmology & Visual Science, 44*, 1492-1500.
- Gwiazda, J., Thorn, F., Bauer, J., & Held, R. (1993). Myopic children show insufficient accommodative response to blur. *Investigative Ophthalmology & Visual Science, 34*, 690-694.
- Harb, E., Thorn, F., & Troilo, D. (2006). Characteristics of accommodative behavior during sustained reading in emmetropes and myopes. *Vision research, 46*, 2581-2592.
- Harvey, E. M., Miller, J. M., Twelker, J. D., & Davis, A. L. (2016). Reading Fluency in School-Age Children with Bilateral Astigmatism. *Optometry and vision science, 93*, 118.
- He, J. C., Sun, P., Held, R., Thorn, F., Sun, X., & Gwiazda, J. E. (2002). Wavefront aberrations in eyes of emmetropic and moderately myopic school children and young adults. *Vision research*, 42, 1063-1070.
- He, M., Huang, W., Zheng, Y., Huang, L., & Ellwein, L. B. (2007). Refractive error and visual

impairment in school children in rural southern China. *Ophthalmology, 114*, 374-382. e371.

- He, M., Zeng, J., Liu, Y., Xu, J., Pokharel, G. P., & Ellwein, L. B. (2004). Refractive error and visual impairment in urban children in southern China. *Investigative Ophthalmology & Visual Science*, *45*, 793-799.
- He, M., Zeng, J., Liu, Y., Xu, J., Pokharel, G. P., & Ellwein, L. B. (2004). Refractive error and visual impairment in urban children in southern China. *Investigative Ophthalmology & Visual Science*, *45*, 793-799.
- He, M., Zheng, Y., & Xiang, F. (2009). Prevalence of myopia in urban and rural children in mainland China. *Optometry and Vision Science, 86*, 40-44.
- He, M. G., Xiang, F., Zeng, Y. F., Mai, J. C., Chen, Q. Y., Zhang, J., et al. (2015). Effect of Time Spent Outdoors at School on the Development of Myopia Among Children in China A Randomized Clinical Trial. *Jama, 314*, 1142-1148.
- He, X., Zou, H., Lu, L., Zhao, R., Zhao, H., Li, Q., et al. (2015). Axial length/corneal radius ratio: association with refractive state and role on myopia detection combined with visual acuity in Chinese schoolchildren. *Plos One, 10*, e0111766.
- He, X., Sankaridurg, P., Xiong, S., Li, W., Zhang, B., Weng, R., et al. (2019). Shanghai time outside to reduce myopia trial: design and baseline data. *Clinical & experimental ophthalmology*, 47, 171-178.
- Hepsen, I. F., Evereklioglu, C., & Bayramlar, H. (2001). The effect of reading and near-work on the development of myopia in emmetropic boys: a prospective, controlled, three-year follow-up study. *Vision research, 41*, 2511-2520.
- Hiraoka, T., Kotsuka, J., Kakita, T., Okamoto, F., & Oshika, T. (2017). Relationship between higherorder wavefront aberrations and natural progression of myopia in schoolchildren. *Scientific Reports, 7*, 1-9.
- Holden, B. A., Fricke, T. R., Wilson, D. A., & al, e. (2016). Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. *Ophthalmology*, *123*, 1036-1042.
- Hoseini-Yazdi, H., Vincent, S. J., Read, S. A., & Collins, M. J. (2020). Astigmatic Defocus Leads to Short-Term Changes in Human Choroidal Thickness. *Investigative Ophthalmology & Visual Science, 61*, 48-48.
- Hsu, C.-C., Huang, N., Lin, P.-Y., Fang, S.-Y., Tsai, D.-C., Chen, S.-Y., et al. (2017). Risk factors for myopia progression in second-grade primary school children in Taipei: a population-based cohort study. *British Journal of Ophthalmology, 101*, 1611-1617.
- Hu, Y., Ding, X., Guo, X., Chen, Y., Zhang, J., & He, M. (2020). Association of age at myopia onset with risk of high myopia in adulthood in a 12-year follow-up of a Chinese cohort. *JAMA* ophthalmology, 138, 1129-1134.
- Hua, W. J., Jin, J. X., Wu, X. Y., Yang, J. W., Jiang, X., Gao, G. P., et al. (2015). Elevated light levels in schools have a protective effect on myopia. *Ophthalmic and Physiological Optics*, 35, 252– 262.
- Huang, J., Hung, L.-F., Ramamirtham, R., Blasdel, T. L., Humbird, T. L., Bockhorst, K. H., et al. (2009). Effects of form deprivation on peripheral refractions and ocular shape in infant rhesus monkeys (Macaca mulatta). Investigative Ophthalmology & Visual Science, 50, 4033-4044.
- Huang, J., Hung, L.-F., & Smith, E. L. (2011). Effects of foveal ablation on the pattern of peripheral refractive errors in normal and form-deprived infant rhesus monkeys (Macaca mulatta).

Investigative Ophthalmology & Visual Science, 52, 6428-6434.

- Huang, H. M., Chang, D. S. T., & Wu, P. C. (2015). The Association between Near Work Activities and Myopia in Children-A Systematic Review and Meta-Analysis. *Plos One, 10*.
- Huang, J., Wen, D., Wang, Q., McAlinden, C., Flitcroft, I., Chen, H., et al. (2016). Efficacy comparison of 16 interventions for myopia control in children: a network meta-analysis. *Ophthalmology*, *123*, 697-708.
- Huang, P.-C., Hsiao, Y.-C., Tsai, C.-Y., Tsai, D.-C., Chen, C.-W., Hsu, C.-C., et al. (2020). Protective behaviours of near work and time outdoors in myopia prevalence and progression in myopic children: a 2-year prospective population study. *British Journal of Ophthalmology*, 104, 956-961.
- Hung, L.-F., Crawford, M. L., & Smith, E. L. (1995). Spectacle lenses alter eye growth and the refractive status of young monkeys. *Nature medicine*, *1*, 761-765.
- Inagaki, Y. (1986). The rapid change of corneal curvature in the neonatal period and infancy. *Archives of Ophthalmology, 104*, 1026-1027.
- Ip, J. M., Huynh, S. C., Robaei, D., Kifley, A., Rose, K. A., Morgan, I. G., et al. (2008). Ethnic differences in refraction and ocular biometry in a population-based sample of 11-15-year-old Australian children. *Eye, 22*, 649-656.
- Ip, J. M., Rose, K. A., Morgan, I. G., Burlutsky, G., & Mitchell, P. (2008). Myopia and the urban environment: findings in a sample of 12-year-old Australian school children. *Investigative Ophthalmology & Visual Science, 49*, 3858-3863.
- Ip, J. M., Saw, S. M., Rose, K. A., Morgan, I. G., Kifley, A., Wang, J. J., et al. (2008). Role of near work in myopia: Findings in a sample of Australian school children. *Investigative Ophthalmology & Visual Science*, 49, 2903-2910.
- Irving, E., Sivak, J., & Callender, M. (1992). Refractive plasticity of the developing chick eye. *Ophthalmic and Physiological Optics, 12*, 448-456.
- Jonas, J. B., Xu, L., Wang, Y. X., Bi, H. S., Wu, J. F., Jiang, W. J., et al. (2016). Education-related parameters in high myopia: adults versus school children. *Plos One, 11*, e0154554.
- Jones-Jordan, L. A., Mitchell, G. L., Cotter, S. A., Kleinstein, R. N., Manny, R. E., Mutti, D. O., et al. (2011). Visual activity before and after the onset of juvenile myopia. *Investigative Ophthalmology & Visual Science*, *52*, 1841-1850.
- Jones-Jordan, L. A., Sinnott, L. T., Cotter, S. A., Kleinstein, R. N., Manny, R. E., Mutti, D. O., et al. (2012). Time outdoors, visual activity, and myopia progression in juvenile-onset myopes. *Investigative Ophthalmology & Visual Science, 53*, 7169-7175.
- Jones, D., & Luensmann, D. (2012). The prevalence and impact of high myopia. *Eye & Contact Lens, 38*, 188-196.
- Jones, L. A., Sinnott, L. T., Mutti, D. O., Mitchell, G. L., Moeschberger, M. L., & Zadnik, K. (2007). Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci, 48*, 3524-3532.
- Jung, S.-K., Lee, J. H., Kakizaki, H., & Jee, D. (2012). Prevalence of myopia and its association with body stature and educational level in 19-year-old male conscripts in Seoul, South Korea. *Investigative Ophthalmology & Visual Science, 53*, 5579-5583.
- Kee, C.-s., Hung, L.-F., Qiao-Grider, Y., Ramamirtham, R., Winawer, J., Wallman, J., et al. (2007). Temporal constraints on experimental emmetropization in infant monkeys. Investigative Ophthalmology & Visual Science, 48, 957-962.

- Kleinstein, R. N., Jones, L. A., Hullett, S., Kwon, S., Lee, R. J., Friedman, N. E., et al. (2003). Refractive error and ethnicity in children. *Archives of Ophthalmology*, *121*, 1141-1147.
- Kang, P., & Swarbrick, H. (2011). Peripheral refraction in myopic children wearing orthokeratology and gas-permeable lenses. *Optometry and Vision Science, 88*, 476-482.
- Kim, E. C., Morgan, I. G., Kakizaki, H., Kang, S., & Jee, D. (2013). Prevalence and Risk Factors for Refractive Errors: Korean National Health and Nutrition Examination Survey 2008-2011. *Plos One, 8.*
- Kinge, B., Midelfart, A., Jacobsen, G., & Rystad, J. (2000). The influence of near-work on development of myopia among university students. A three-year longitudinal study among engineering students in Norway. *Acta Ophthalmologica Scandinavica, 78*, 26-29.
- Koo, T. K., & Li, M. Y. (2016). A guideline of selecting and reporting intraclass correlation coefficients for reliability research. *Journal of chiropractic medicine*, 15, 155-163.
- Ku, P. W., Steptoe, A., Lai, Y. J., Hu, H. Y., Chu, D. C., Yen, Y. F., et al. (2019). The Associations between Near Visual Activity and Incident Myopia in Children A Nationwide 4-Year Follow-up Study. *Ophthalmology*, *126*, 214-220.
- Kubota, T., Miyake, K., & Hirasawa, T. (2012). Epigenetic understanding of gene-environment interactions in psychiatric disorders: a new concept of clinical genetics. *Clinical epigenetics*, *4*, 1-8.
- Kurtz, D., Hyman, L., Gwiazda, J. E., Manny, R., Dong, L. M., Wang, Y., et al. (2007). Role of parental myopia in the progression of myopia and its interaction with treatment in COMET children. *Investigative Ophthalmology & Visual Science, 48*, 562-570.
- Lam, C. S., & Goh, W. S. (1991). The incidence of refractive errors among school children in Hong Kong and its relationship with the optical components. *Clinical and Experimental Optometry*, 74, 97-103.
- Lam, C. S. Y., Edwards, M., Millodot, M., & Goh, W. S. H. (1999). A 2-year longitudinal study of myopia progression and optical component changes among Hong Kong schoolchildren. *Optometry and Vision Science, 76*, 370-380.
- Lam, C. S. Y., Goldschmidt, E., & Edwards, M. H. (2004). Prevalence of myopia in local and international schools in Hong Kong. *Optometry and Vision Science, 81*, 317-322.
- Lam, C. S. Y., Lam, C. H., Cheng, S. C. K., & Chan, L. Y. L. (2012). Prevalence of myopia among Hong Kong Chinese schoolchildren: changes over two decades. *Ophthalmic and Physiological Optics*, 32, 17-24.
- Lam, C. S. Y., Tang, W. C., Tse, D. Y.-y., Lee, R. P. K., Chun, R. K. M., Hasegawa, K., et al. (2020). Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. *British Journal of Ophthalmology, 104*, 363-368.
- Lam, C. S. Y., Tang, W. C., Tse, D. Y. Y., Tang, Y. Y., & To, C. H. (2014). Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2year randomised clinical trial. *British Journal of Ophthalmology*, *98*, 40-45.
- Lam, D. S., Fan, D. S., Chan, W.-M., Tam, B. S., Kwok, A. K., Leung, A. T., et al. (2005). Prevalence and characteristics of peripheral retinal degeneration in Chinese adults with high myopia: a cross-sectional prevalence survey. *Optometry and Vision Science*, *82*, 235-238.
- Lam, D. S., Fan, D. S., Lam, R. F., Rao, S. K., Chong, K. S., Lau, J. T., et al. (2008). The effect of parental history of myopia on children's eye size and growth: results of a longitudinal study.

Investigative Ophthalmology & Visual Science, 49, 873-876.

- Lanca, C., & Saw, S. M. (2019). The association between digital screen time and myopia: A systematic review. *Ophthalmic and Physiological Optics*.
- Lau, J. K., Vincent, S. J., Cheung, S.-W., & Cho, P. (2020). Higher-order aberrations and axial elongation in myopic children treated with orthokeratology. *Investigative Ophthalmology* & Visual Science, 61, 22-22.
- Lau, J. K., Vincent, S. J., Collins, M. J., Cheung, S.-W., & Cho, P. (2018). Ocular higher-order aberrations and axial eye growth in young Hong Kong children. *Scientific Reports, 8*, 1-10.
- Li, S.-M., Li, S.-Y., Kang, M.-T., Zhou, Y., Liu, L.-R., Li, H., et al. (2015). Near work related parameters and myopia in Chinese children: the Anyang Childhood Eye Study. *Plos One, 10*, e0134514.
- Li, S. M., Li, S. Y., Kang, M. T., Zhou, Y., Liu, L. R., Li, H., et al. (2015). Near Work Related Parameters and Myopia in Chinese Children: the Anyang Childhood Eye Study. *Plos One, 10*, e0134514.
- Liang, C.-L., Yen, E., Su, J.-Y., Liu, C., Chang, T.-Y., Park, N., et al. (2004). Impact of family history of high myopia on level and onset of myopia. *Investigative Ophthalmology & Visual Science*, *45*, 3446-3452.
- Liang, J., & Williams, D. R. (1997). Aberrations and retinal image quality of the normal human eye. JOSA A, 14, 2873-2883.
- Liao, C., Ding, X., Han, X., Jiang, Y., Zhang, J., Scheetz, J., et al. (2019). Role of Parental Refractive Status in Myopia Progression: 12-Year Annual Observation From the Guangzhou Twin Eye Study. *Investigative Ophthalmology & Visual Science, 60*, 3499-3506.
- Lin, L. L., Shih, Y. F., Hsiao, C. K., & Chen, C. J. (2004). Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. *Annals-Academy of Medicine Singapore, 33*, 27-33.
- Lin, Z., Vasudevan, B., Ciuffreda, K. J., Wang, N. L., Zhang, Y. C., Rong, S. S., et al. (2013). Nearworkinduced transient myopia and parental refractive error. *Optometry and Vision Science*, 90, 507-516.
- Lin, Z., Vasudevan, B., Mao, G. Y., Ciuffreda, K. J., Jhanji, V., Li, X. X., et al. (2016). The influence of near work on myopic refractive change in urban students in Beijing: a three-year followup report. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 254, 2247-2255.
- Liu, S., Ye, S., Xi, W., & Zhang, X. (2019). Electronic devices and myopic refraction among children aged 6-14 years in urban areas of Tianjin, China. *Ophthalmic and Physiological Optics, 39*, 282-293.
- Logan, N. S., Radhakrishnan, H., Cruickshank, F. E., Allen, P. M., Bandela, P. K., Davies, L. N., et al. (2021). IMI Accommodation and binocular vision in myopia development and progression. *Investigative ophthalmology & visual science*, 62, 4-4.
- Long, J., Cheung, R., Duong, S., Paynter, R., & Asper, L. (2017). Viewing distance and eyestrain symptoms with prolonged viewing of smartphones. *Clinical and Experimental Optometry*, *100*, 133-137.
- Lopes, M. C., Andrew, T., Carbonaro, F., Spector, T. D., & Hammond, C. J. (2009). Estimating heritability and shared environmental effects for refractive error in twin and family studies. *Investigative Ophthalmology & Visual Science, 50*, 126-131.
- Low, W., Dirani, M., Gazzard, G., Chan, Y.-H., Zhou, H.-J., Selvaraj, P., et al. (2010). Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. *British*

Journal of Ophthalmology, 94, 1012-1016.

- Lu, F., Zhou, X., Jiang, L., Fu, Y., Lai, X., Xie, R., et al. (2009). Axial myopia induced by hyperopic defocus in guinea pigs: A detailed assessment on susceptibility and recovery. *Experimental eye research*, *89*, 101-108.
- Mallen, E. A., Kashyap, P., & Hampson, K. M. (2006). Transient axial length change during the accommodation response in young adults. *Investigative Ophthalmology & Visual Science*, *47*, 1251-1254.
- Mark, H. H. (1971). Johannes Kepler on the eye and vision. *American journal of ophthalmology, 72*, 869-878.
- Matsumura, H., & Hirai, H. (1999). Prevalence of myopia and refractive changes in students from 3 to 17 years of age. *Survey of Ophthalmology, 44*, S109-S115.
- McCrann, S., Loughman, J., Butler, J. S., Paudel, N., & Flitcroft, D. I. (2020). Smartphone use as a possible risk factor for myopia. *Clinical and Experimental Optometry*.
- McCullough, S. J., O'Donoghue, L., & Saunders, K. J. (2016). Six Year Refractive Change among White Children and Young Adults: Evidence for Significant Increase in Myopia among White UK Children. *Plos One, 11*.
- McCullough, S. J., O'Donoghue, L., & Saunders, K. J. (2016). Six Year Refractive Change among White Children and Young Adults: Evidence for Significant Increase in Myopia among White UK Children. *Plos One, 11*.
- Mirshahi, A., Ponto, K. A., Hoehn, R., Zwiener, I., Zeller, T., Lackner, K., et al. (2014). Myopia and level of education: results from the Gutenberg Health Study. *Ophthalmology*, *121*, 2047-2052.
- Mohney, B. G. (2002). Axial myopia associated with dense vitreous hemorrhage of the neonate. *Journal of American Association for Pediatric Ophthalmology and Strabismus, 6*, 348-353.
- Momeni-Moghaddam, H., Maddah, N., Wolffsohn, J. S., Etezad-Razavi, M., Zarei-Ghanavati, S., Rezayat, A. A., et al. (2019). The Effect of Cycloplegia on the Ocular Biometric and Anterior Segment Parameters: A Cross-Sectional Study. *Ophthalmology and therapy*, *8*, 387-395.
- Morgan, I., & Rose, K. (2005). How genetic is school myopia? *Progress in Retinal and Eye Research, 24*, 1-38.
- Morgan, I.G., Rose K., Ellwein L.B. (2010). Is emmetropia the natural endpoint for human refractive development? An analysis of population-based data from the refractive error study in children (RESC). Acta Ophthalmologica, 88, 877–884.
- Morgan, I. G., Ashby, R. S., & Nickla, D. L. (2013). Form deprivation and lens-induced myopia: are they different? *Ophthalmic and Physiological Optics*, *33*, 355-361.
- Morgan, I. G., French, A. N., & Rose, K. A. (2018). Intense schooling linked to myopia. *British Medical Journal*.
- Morgan, I. G., Ohno-Matsui, K., & Saw, S. M. (2012). Myopia. Lancet, 379, 1739-1748.
- Morgan, I. G., & Rose, K. A. (2013). Myopia and international educational performance. *Ophthalmic* and *Physiological Optics, 33*, 329-338.
- Morgan, R., & Munro, M. (1973). Refractive problems in Northern natives. *Canadian journal of ophthalmology. Journal canadien d'ophtalmologie, 8*, 226.
- Morgan, I. G., Wu, P.-C., Ostrin, L. A., Tideman, J. W. L., Yam, J. C., Lan, W., et al. (2021). IMI risk factors for myopia. *Investigative ophthalmology & visual science, 62*, 3-3.
- Mountjoy, E., Davies, N. M., Plotnikov, D., Smith, G. D., Rodriguez, S., Williams, C. E., et al. (2018).

Education and myopia: assessing the direction of causality by mendelian randomisation. *British Medical Journal, 361*, k2022.

- Mutti, D. O., & Marks, A. R. (2011). Blood levels of vitamin D in teens and young adults with myopia. *Optometry and vision science, 88*, 377.
- Mutti, D. O., Mitchell, G. L., Hayes, J. R., Jones, L. A., Moeschberger, M. L., Cotter, S. A., et al. (2006). Accommodative lag before and after the onset of myopia. *Investigative Ophthalmology* & Visual Science, 47, 837-846.
- Mutti, D. O., Mitchell, G. L., Jones, L. A., Friedman, N. E., Frane, S. L., Lin, W. K., et al. (2005). Axial growth and changes in lenticular and corneal power during emmetropization in infants. *Investigative Ophthalmology & Visual Science, 46*, 3074-3080.
- Mutti, D. O., Mitchell, G. L., Moeschberger, M. L., Jones, L. A., & Zadnik, K. (2002). Parental myopia, near work, school achievement, and children's refractive error. *Investigative Ophthalmology & Visual Science, 43*, 3633-3640.
- Narayanasamy, S., Vincent, S. J., Sampson, G. P., & Wood, J. M. (2016). Visual demands in modern Australian primary school classrooms. *Clinical and Experimental Optometry, 99*, 233-240.
- Navel, V., Beze, S., & Dutheil, F. (2020). COVID-19, sweat, tears… and myopia? *Clinical and Experimental Optometry*.
- Neil Charman, W. (2011). Myopia, posture and the visual environment. *Ophthalmic and Physiological Optics, 31*, 494-501.
- Ng, V. (2012). The decision to send local children to international schools in Hong Kong: local parents' perspectives. *Asia Pacific Education Review, 13*, 121-136.
- Nickla, D. L., & Totonelly, K. (2011). Dopamine antagonists and brief vision distinguish lensinduced-and form-deprivation-induced myopia. *Experimental eye research, 93*, 782-785.
- Nickla, D. L., & Wallman, J. (2010). The multifunctional choroid. *Progress in Retinal and Eye Research, 29*, 144-168.
- Norton, T. T. (1990). Experimental myopia in tree shrews. *Myopia and the control of eye growth, 155*, 178-194.
- Ohno-Matsui, K., Kawasaki, R., Jonas, J. B., Cheung, C. M. G., Saw, S.-M., Verhoeven, V. J., et al. (2015). International photographic classification and grading system for myopic maculopathy. *American journal of ophthalmology*, *159*, 877-883. e877.
- Ojaimi, E., Rose, K. A., Morgan, I. G., Smith, W., Martin, F. J., Kifley, A., et al. (2005). Distribution of ocular biometric parameters and refraction in a population-based study of Australian children. *Investigative Ophthalmology & Visual Science, 46*, 2748-2754.
- Ojaimi, E., Rose, K. A., Smith, W., Morgan, I. G., Martin, F. J., & Mitchell, P. (2005). Methods for a population-based study of myopia and other eye conditions in school children: the Sydney Myopia Study. *Ophthalmic epidemiology, 12*, 59-69.
- Panke, K., Jakobsone, L., Svede, A., & Krumina, G. (2019). Smartphone viewing distance during active or passive tasks and relation to heterophoria. Paper presented at the Fourth International Conference on Applications of Optics and Photonics.
- Pararajasegaram, R. (1999). VISION 2020 The Right to Sight: from strategies to action. *American Journal of Ophthalmology, 128*, 359-360.
- Parssinen, O., & Lyyra, A. L. (1993). Myopia and Myopic Progression among Schoolchildren a 3-Year Follow-up-Study. *Investigative Ophthalmology & Visual Science, 34*, 2794-2802.
- Pellegrini, M., Bernabei, F., Scorcia, V., & Giannaccare, G. (2020). May home confinement during

the COVID-19 outbreak worsen the global burden of myopia? *Graefe's Archive for Clinical* and *Experimental Ophthalmology*, 1-2.

- Philip, K., Sankaridurg, P., Holden, B., Ho, A., & Mitchell, P. (2014). Influence of higher order aberrations and retinal image quality in myopisation of emmetropic eyes. *Vision research*, 105, 233-243.
- Portney, L. G., & Watkins, M. P. (2009). *Foundations of clinical research: applications to practice* (Vol. 892): Pearson/Prentice Hall Upper Saddle River, NJ.
- Presser, S., Couper, M. P., Lessler, J. T., Martin, E., Martin, J., Rothgeb, J. M., et al. (2004). Methods for testing and evaluating survey questions. *Public opinion quarterly, 68*, 109-130.
- Qian, D. J., Zhong, H., Li, J., Niu, Z., Yuan, Y., & Pan, C. W. (2016). Myopia among school students in rural China (Yunnan). *Ophthalmic and Physiological Optics, 36*, 381-387.
- Quek, T. P., Chua, C. G., Chong, C. S., Chong, J. H., Hey, H. W., Lee, J., et al. (2004). Prevalence of refractive errors in teenage high school students in Singapore. *Ophthalmic and Physiological Optics*, 24, 47-55.
- Ramos, R. G., & Olden, K. (2008). Gene-environment interactions in the development of complex disease phenotypes. *International journal of environmental research and public health*, 5, 4-11.
- Read, S. A., Collins, M. J., & Sander, B. P. (2010). Human optical axial length and defocus. *Investigative Ophthalmology & Visual Science, 51*, 6262-6269.
- Read, S. A., Collins, M. J., & Vincent, S. J. (2015). Light exposure and eye growth in childhood. *Investigative Ophthalmology & Visual Science, 56*, 6779-6787.
- Read, S. A., Collins, M. J., Woodman, E. C., & Cheong, S.-H. (2010). Axial length changes during accommodation in myopes and emmetropes. *Optometry and Vision Science*, 87, 656-662.
- Ritty, J. M., Solan, H. A., & Cool, S. J. (1993). Visual and sensory-motor functioning in the classroom: A preliminary report of ergonomic demands. *Journal of the American Optometric Association*.
- Rose, K. A., Morgan, I. G., Ip, J., Kifley, A., Huynh, S., Smith, W., et al. (2008). Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology*, *115*, 1279-1285.
- Rose, K. A., Morgan, I. G., Ip, J., Kifley, A., Huynh, S., Smith, W., et al. (2008). Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology*, *115*, 1279-1285.
- Rose, K. A., Morgan, I. G., Smith, W., Burlutsky, G., Mitchell, P., & Saw, S.-M. (2008). Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney. *Archives of Ophthalmology*, *126*, 527-530.
- Rosenfield, M., & Ciuffreda, K. J. (1994). Cognitive Demand and Transient Nearwork-Induced Myopia. *Optometry and Vision Science, 71*, 381-385.
- Rosenfield, M., & Gilmartin, B. (1998). Myopia and nearwork: Elsevier Health Sciences.
- Rudnicka, A. R., Kapetanakis, V. V., Wathern, A. K., Logan, N. S., Gilmartin, B., Whincup, P. H., et al. (2016). Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: implications for aetiology and early prevention. *British Journal of Ophthalmology, 100*, 882-890.
- Sankaridurg, P., He, X., Naduvilath, T., Lv, M., Ho, A., Smith III, E., et al. (2017). Comparison of noncycloplegic and cycloplegic autorefraction in categorizing refractive error data in children. *Acta Ophthalmologica*, *95*, e633-e640.

- Sapkota, Y. D., Adhikari, B. N., Pokharel, G. P., Poudyal, B. K., & Ellwein, L. B. (2008). The prevalence of visual impairment in school children of upper-middle socioeconomic status in Kathmandu. *Ophthalmic epidemiology*, 15, 17-23.
- Saw, S.-M., Katz, J., Schein, O. D., Chew, S.-J., & Chan, T.-K. (1996). Epidemiology of myopia. *Epidemiologic reviews, 18*, 175-187.
- Saw, S.-M., Nieto, F. J., Katz, J., & Chew, S.-J. (1999). Estimating the magnitude of close-up work in school-age children: a comparison of questionnaire and diary instruments. *Ophthalmic epidemiology*, *6*, 291-301.
- Saw, S.-M., Shankar, A., Tan, S.-B., Taylor, H., Tan, D. T., Stone, R. A., et al. (2006). A cohort study of incident myopia in Singaporean children. *Investigative Ophthalmology & Visual Science*, *47*, 1839-1844.
- Saw, S.-M., Tong, L., Chua, W.-H., Chia, K.-S., Koh, D., Tan, D. T., et al. (2005). Incidence and progression of myopia in Singaporean school children. *Investigative Ophthalmology & Visual Science*, 46, 51-57.
- Saw, S.-M., Wu, H.-M., Seet, B., Wong, T.-Y., Yap, E., Chia, K.-S., et al. (2001). Academic achievement, close up work parameters, and myopia in Singapore military conscripts. *British Journal of Ophthalmology, 85*, 855-860.
- Saw, S. M., Carkeet, A., Chia, K. S., Stone, R. A., & Tan, D. T. H. (2002). Component dependent risk factors for ocular parameters in Singapore Chinese children. *Ophthalmology*, *109*, 2065-2071.
- Saw, S. M., Carkeet, A., Chia, K. S., Stone, R. A., & Tan, D. T. H. (2002). Component dependent risk factors for ocular parameters in Singapore Chinese children. *Ophthalmology*, 109, 2065-2071.
- Saw, S. M., Chua, W. H., Hong, C. Y., Wu, H. M., Chan, W. Y., Chia, K. S., et al. (2002). Nearwork in early-onset myopia. *Investigative Ophthalmology & Visual Science*, *43*, 332-339.
- Saw, S. M., Hong, R. Z., Zhang, M. Z., Fu, Z. F., Ye, M., Tan, D., et al. (2001). Near-work activity and myopia in rural and urban schoolchildren in China. *Journal of pediatric ophthalmology and strabismus, 38*, 149-155.
- Saw, S. M., Zhang, M. Z., Hong, R. Z., Fu, Z. F., Pang, M. H., & Tan, D. T. H. (2002). Near-work activity, night-lights, and myopia in the Singapore-China study. *Archives of Ophthalmology*, *120*, 620-627.
- Saxena, R., Vashist, P., Tandon, R., Pandey, R., Bhardawaj, A., Menon, V., et al. (2015). Prevalence of myopia and its risk factors in urban school children in Delhi: the North India Myopia Study (NIM Study). *Plos One, 10*.
- Saxena, R., Vashist, P., Tandon, R., Pandey, R. M., Bhardawaj, A., Gupta, V., et al. (2017). Incidence and progression of myopia and associated factors in urban school children in Delhi: The North India Myopia Study (NIM Study). *Plos One, 12*.
- Schaeffel, F., Glasser, A., & Howland, H. C. (1988). Accommodation, refractive error and eye growth in chickens. *Vision research, 28*, 639-657.
- Schaeffel, F., Troilo, D., Wallman, J., & Howland, H. C. (1990). Developing eyes that lack accommodation grow to compensate for imposed defocus. *Visual neuroscience, 4*, 177-183.
- Scheiman, M., Zhang, Q., Gwiazda, J., Hyman, L., Harb, E., Weissberg, E., et al. (2014). Visual activity and its association with myopia stabilisation. *Ophthalmic and Physiological Optics, 34*,

353-361.

- Schwahn, H. N., & Schaeffel, F. (1994). Chick eyes under cycloplegia compensate for spectacle lenses despite six-hydroxy dopamine treatment. *Investigative Ophthalmology & Visual Science, 35*, 3516-3524.
- Shen, L., Melles, R. B., Metlapally, R., Barcellos, L., Schaefer, C., Risch, N., et al. (2016). The association of refractive error with glaucoma in a multiethnic population. *Ophthalmology*, *123*, 92-101.
- Shen, W., & Sivak, J. G. (2007). Eyes of a lower vertebrate are susceptible to the visual environment. *Investigative Ophthalmology & Visual Science, 48*, 4829-4837.
- Shen, W., Vijayan, M., & Sivak, J. G. (2005). Inducing form-deprivation myopia in fish. *Investigative Ophthalmology & Visual Science, 46*, 1797-1803.
- Siegwart Jr, J. T., Ward, A. H., & Norton, T. T. (2012). Moderately elevated fluorescent light levels slow form deprivation and minus lens-induced myopia development in tree shrews. *Investigative Ophthalmology & Visual Science*, 53, 3457-3457.
- Simensen, B., & Thorud, L. O. (1994). Adult-onset myopia and occupation. *Acta Ophthalmologica*, *72*, 469-471.
- Smith III, E. L., & Hung, L.-F. (2000). Form-deprivation myopia in monkeys is a graded phenomenon. *Vision research, 40*, 371-381.
- Smith, E. L., Hung, L.-F., Kee, C.-s., & Qiao, Y. (2002). Effects of brief periods of unrestricted vision on the development of form-deprivation myopia in monkeys. Investigative Ophthalmology & Visual Science, 43, 291-299.
- Smith, E. L., Kee, C.-s., Ramamirtham, R., Qiao-Grider, Y., & Hung, L.-F. (2005). Peripheral vision can influence eye growth and refractive development in infant monkeys. *Investigative Ophthalmology & Visual Science, 46*, 3965-3972.
- Smith, E. L., Ramamirtham, R., Qiao-Grider, Y., Hung, L.-F., Huang, J., Kee, C.-s., et al. (2007). Effects of foveal ablation on emmetropization and form-deprivation myopia. *Investigative Ophthalmology & Visual Science, 48*, 3914-3922.
- Smith III, E. L., Hung, L.-F., & Huang, J. (2009). Relative peripheral hyperopic defocus alters central refractive development in infant monkeys. *Vision research, 49*, 2386-2392.
- Smith III, E. L., Hung, L.-F., Huang, J., Blasdel, T. L., Humbird, T. L., & Bockhorst, K. H. (2010). Effects of optical defocus on refractive development in monkeys: evidence for local, regionally selective mechanisms. *Investigative ophthalmology & visual science*, *51*, 3864-3873.
- Smith, E. L., Hung, L.-F., & Huang, J. (2012). Protective effects of high ambient lighting on the development of form-deprivation myopia in rhesus monkeys. *Investigative Ophthalmology & Visual Science*, *53*, 421-428.
- Smith, E. L., Hung, L.-F., Arumugam, B., & Huang, J. (2013). Negative lens–induced myopia in infant monkeys: effects of high ambient lighting. *Investigative Ophthalmology & Visual Science*, 54, 2959-2969.
- Smith III, E. L., Arumugam, B., Hung, L.-F., She, Z., Beach, K., & Sankaridurg, P. (2020). Eccentricitydependent effects of simultaneous competing defocus on emmetropization in infant rhesus monkeys. *Vision Research*, *177*, 32-40.
- Stone, R. A., Pendrak, K., Sugimoto, R., Lin, T., Gill, A. S., Capehart, C., et al. (2006). Local patterns of image degradation differentially affect refraction and eye shape in chick. *Current eye research*, *31*, 91-105.

- Sun, J., Zhou, J., Zhao, P., Lian, J., Zhu, H., Zhou, Y., et al. (2012). High prevalence of myopia and high myopia in 5060 Chinese university students in Shanghai. *Investigative Ophthalmology & Visual Science*, *53*, 7504-7509.
- Tan, G., Ng, Y., Lim, Y., Ong, P., Snodgrass, A., & Saw, S. (2000). Cross-sectional study of nearwork and myopia in kindergarten children in Singapore. *Annals of the Academy of Medicine, Singapore, 29*, 740-744.
- Tan, Q., Ng, A. L., Choy, B. N., Cheng, G. P., Woo, V. C., & Cho, P. One-year results of 0.01% atropine with orthokeratology (AOK) study: a randomised clinical trial. *Ophthalmic and Physiological Optics*.
- Tang, S. M., Lau, T., Rong, S. S., Yazar, S., Chen, L. J., Mackey, D. A., et al. (2019). Vitamin D and its pathway genes in myopia: systematic review and meta-analysis. *British Journal of Ophthalmology*, 103, 8-17.
- Tedja, M. S., Wojciechowski, R., Hysi, P. G., Eriksson, N., Furlotte, N. A., Verhoeven, V. J., et al. (2018). Genome-wide association meta-analysis highlights light-induced signaling as a driver for refractive error. *Nature genetics*, *50*, 834-848.
- Thibos, L. N., Wheeler, W., & Horner, D. (1997). Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optometry and vision science*,, *74*, 367-375.
- Thorn, F., Chen, J., Li, C., Jiang, D., Chen, W., Lin, Y., et al. (2020). Refractive status and prevalence of myopia among Chinese primary school students. *Clinical and Experimental Optometry*, *103*, 177-183.
- Tideman, J. W. L., Polling, J. R., Hofman, A., Jaddoe, V. W., Mackenbach, J. P., & Klaver, C. C. (2018). Environmental factors explain socioeconomic prevalence differences in myopia in 6-yearold children. *British Journal of Ophthalmology*, *102*, 243-247.
- Tideman, J. W. L., Polling, J. R., Jaddoe, V. W., Vingerling, J. R., & Klaver, C. C. (2019). Environmental risk factors can reduce axial length elongation and myopia incidence in 6-to 9-year-old children. *Ophthalmology*, *126*, 127-136.
- Ting, P. W., Lam, C. S., Edwards, M. H., & Schmid, K. L. (2004). Prevalence of myopia in a group of Hong Kong microscopists. *Optometry and Vision Science*, *81*, 88-93.
- Troilo, D., & Judge, S. J. (1993). Ocular development and visual deprivation myopia in the common marmoset (Callithrix jacchus). *Vision research, 33*, 1311-1324.
- Troilo, D., Smith, E. L., Nickla, D. L., Ashby, R., Tkatchenko, A. V., Ostrin, L. A., et al. (2019). IMI– Report on experimental models of emmetropization and myopia. Investigative Ophthalmology & Visual Science, 60, M31-M88.
- Tscherning, M. (1882). Studier over Myopiens Aetiologi, af M. Tscherning: . Myhre.
- Twelker, J. D., Mitchell, G. L., Messer, D. H., Bhakta, R., Jones, L. A., Mutti, D. O., et al. (2009). Children's ocular components and age, gender, and ethnicity. *Optometry and vision science*, *86*, 918.
- Vasudevan, B., Ciuffreda, K. J., & Ludlam, D. P. (2009). Accommodative training to reduce nearwork-induced transient myopia. *Optometry and Vision Science, 86*, 1287-1294.
- Vera-Díaz, F. A., Strang, N. C., & Winn, B. (2002). Nearwork induced transient myopia during myopia progression. *Current eye research, 24*, 289-295.
- von Noorden, G. K., & Lewis, R. A. (1987). Ocular axial length in unilateral congenital cataracts and blepharoptosis. *Investigative Ophthalmology & Visual Science, 28*, 750-752.

- Wallman, J., & Adams, J. I. (1987). Developmental aspects of experimental myopia in chicks: susceptibility, recovery and relation to emmetropization. *Vision research, 27*, 1139-1163.
- Wallman, J., Turkel, J., & Trachtman, J. (1978). Extreme myopia produced by modest change in early visual experience. *Science, 201*, 1249-1251.
- Wallman, J., & Winawer, J. (2004). Homeostasis of eye growth and the question of myopia. *Neuron, 43*, 447-468.
- Wang, J., Li, Y., Musch, D. C., Wei, N., Qi, X., Ding, G., et al. (2021.). Progression of Myopia in School-Aged Children After COVID-19 Home Confinement. Jama Ophthalmology.
- Weizhong, L., Zhikuan, Y., Wen, L., Xiang, C., & Jian, G. (2008). A longitudinal study on the relationship between myopia development and near accommodation lag in myopic children. *Ophthalmic and Physiological Optics, 28*, 57-61.
- Wen, L., Cheng, Q., Lan, W., Cao, Y., Li, X., Lu, Y., et al. (2019). An Objective Comparison of Light Intensity and Near-Visual Tasks Between Rural and Urban School Children in China by a Wearable Device Clouclip. *Translational vision science & technology, 8*, 15-15.
- Wenbo, L., Congxia, B., & Hui, L. (2017). Genetic and environmental-genetic interaction rules for the myopia based on a family exposed to risk from a myopic environment. *Gene, 626*, 305-308.
- Wiesel, T. N., & Raviola, E. (1977). Myopia and eye enlargement after neonatal lid fusion in monkeys. *Nature, 266*, 66-68.
- Wildsoet, C. F. (2003). Neural pathways subserving negative lens-induced emmetropization in chicks–insights from selective lesions of the optic nerve and ciliary nerve. *Current eye research*, *27*, 371-385.
- Williams, C., Miller, L., Gazzard, G., & Saw, S.-M. (2008). A comparison of measures of reading and intelligence as risk factors for the development of myopia in a UK cohort of children. *British Journal of Ophthalmology*, *92*, 1117-1121.
- Williams, K. M., Bertelsen, G., Cumberland, P., Wolfram, C., Verhoeven, V. J., Anastasopoulos, E., et al. (2015). Increasing Prevalence of Myopia in Europe and the Impact of Education. *Ophthalmology*, *122*, 1489-1497.
- Winawer, J., & Wallman, J. (2002). Temporal constraints on lens compensation in chicks. *Vision Research, 42*, 2651-2668.
- Wojciechowski, R. (2011). Nature and nurture: the complex genetics of myopia and refractive error. *Clinical Genetics, 79*, 301-320.
- Wolffsohn, J. S., Flitcroft, D. I., Gifford, K. L., Jong, M., Jones, L., Klaver, C. C., et al. (2019). IMI– myopia control reports overview and introduction. *Investigative Ophthalmology & Visual Science, 60*, M1-M19.
- Wong, C. W., Andrew, T., Jonas, J. B., Ohno-Matsui, K., James, C., Marcus, A., et al. (2020). Digital Screen Time During COVID-19 Pandemic: Risk for a Further Myopia Boom? *American journal of ophthalmology*.
- Wong, T., Foster, P., Johnson, G., & Seah, S. (2002). Education, socioeconomic status, and ocular dimensions in Chinese adults: the Tanjong Pagar Survey. *British Journal of Ophthalmology*, *86*, 963-968.
- Wu, L. J., You, Q. S., Duan, J. L., Luo, Y. X., Liu, L. J., Li, X., et al. (2015). Prevalence and associated factors of myopia in high-school students in Beijing. *Plos One*, *10*.
- Wu, M. M.-m., & Edwards, M. H. (1999). The effect of having myopic parents: an analysis of myopia

in three generations. Optometry and vision science, 76, 387-392.

- Wu, P. C., Chen, C. T., Lin, K. K., Sun, C. C., Kuo, C. N., Huang, H. M., et al. (2018). Myopia Prevention and Outdoor Light Intensity in a School-Based Cluster Randomized Trial. *Ophthalmology*, *125*, 1239-1250.
- Wu, P. C., Tsai, C. L., Wu, H. L., Yang, Y. H., & Kuo, H. K. (2013). Outdoor Activity during Class Recess Reduces Myopia Onset and Progression in School Children. *Ophthalmology*, *120*, 1080-1085.
- Xiang, F., He, M., & Morgan, I. G. (2012). The impact of severity of parental myopia on myopia in Chinese children. *Optometry and Vision Science, 89*, 884-891.
- Xiong, S., Sankaridurg, P., Naduvilath, T., Zang, J., Zou, H., Zhu, J., et al. (2017). Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. *Acta Ophthalmologica, 95*, 551-566.
- Yam, J. C., Li, F. F., Zhang, X., Tang, S. M., Yip, B. H., Kam, K. W., et al. (2020). Two-year clinical trial of the low-concentration atropine for myopia progression (lamp) study: phase 2 report. *Ophthalmology*, *127*, 910-919.
- Yam, J. C., Tang, S. M., Kam, K. W., Chen, L. J., Yu, M., Law, A. K., et al. (2020). High prevalence of myopia in children and their parents in Hong Kong Chinese Population: the Hong Kong Children Eye Study. *Acta Ophthalmologica*.
- Yang, G.-Y., Huang, L.-H., Schmid, K. L., Li, C.-G., Chen, J.-Y., He, G.-H., et al. (2020). Associations between screen exposure in early life and myopia amongst Chinese preschoolers. *International journal of environmental research and public health*, *17*, 1056.
- Yazar, S., Hewitt, A. W., Black, L. J., McKnight, C. M., Mountain, J. A., Sherwin, J. C., et al. (2014). Myopia is associated with lower vitamin D status in young adults. *Investigative Ophthalmology & Visual Science*, 55, 4552-4559.
- You, Q. S., Wu, L. J., Duan, J. L., Luo, Y. X., Liu, L. J., Li, X., et al. (2012). Factors associated with myopia in school children in China: the Beijing childhood eye study. *Plos One, 7*.
- You, X., Wang, L., Tan, H., He, X., Qu, X., Shi, H., et al. (2016). Near work related behaviors associated with myopic shifts among primary school students in the Jiading District of Shanghai: a school-based one-year cohort study. *Plos One*, *11*, e0154671.
- Young, F. A., Leary, G. A., Baldwin, W. R., West, D. C., Box, R. A., Harris, E., et al. (1969). The transmission of refractive errors within Eskimo families. *Optometry and Vision Science*, 46, 676-685.
- Zadnik, K., Satariano, W. A., Mutti, D. O., Sholtz, R. I., & Adams, A. J. (1994). The effect of parental history of myopia on children's eye size. *Jama, 271*, 1323-1327.
- Zhang, M., Li, L., Chen, L., Lee, J., Wu, J., Yang, A., et al. (2010). Population density and refractive error among Chinese children. *Investigative Ophthalmology & Visual Science, 51*, 4969-4976.
- Zhang, X., Qu, X., & Zhou, X. (2015). Association between parental myopia and the risk of myopia in a child. *Experimental and therapeutic medicine*, *9*, 2420–2428.
- Zhao, J., Mao, J., Luo, R., Li, F., Pokharel, G. P., & Ellwein, L. B. (2004). Accuracy of noncycloplegic autorefraction in school-age children in China. Optometry and vision science, 81, 49-55.
- Zheng, Y.-F., Pan, C.-W., Chay, J., Wong, T. Y., Finkelstein, E., & Saw, S.-M. (2013). The economic cost of myopia in adults aged over 40 years in Singapore. *Investigative Ophthalmology & Visual Science*, *54*, 7532-7537.

- Zhou, R., Zhang, W., Yang, Y., Li, Y., Zhang, J., & Wang, W. (2014). Analysis of myopia prevalence and influencing factors among primary school students in the urban area of Lanzhou city. *International Eye Science*, 14, 903-907.
- Zhou, S., Yang, L., Lu, B., Wang, H., Xu, T., Du, D., et al. (2017). Association between parents' attitudes and behaviors toward children's visual care and myopia risk in school-aged children. *Medicine*, *96*.
- Zhou, Z., Chen, T., Wang, M., Jin, L., Zhao, Y., Chen, S., et al. (2017). Pilot study of a novel classroom designed to prevent myopia by increasing children's exposure to outdoor light. *Plos One, 12*, e0181772.
- Zhu, X. (2013). Temporal integration of visual signals in lens compensation (a review). *Experimental* eye research, 114, 69-76.
- Zhu, X., Winawer, J. A., & Wallman, J. (2003). Potency of myopic defocus in spectacle lens compensation. *Investigative Ophthalmology & Visual Science, 44*, 2818-2827.
- Zylbermann, R., Landau, D., & Berson, D. (1993). The Influence of Study Habits on Myopia in Jewish Teenagers. *Journal of Pediatric Ophthalmology & Strabismus, 30*, 319-322.

# Appendices





# Questionnaire on School Children's Eye Health and Near Work Habits

The myopia rate of primary school students aged 7 to 11 in Hong Kong is close to 40%. This study aims to investigate the risk factors promoting myopia development. The information is collected by the questionnaire.

Our research team has principal Investigator: Dr. Chea-su Kee and two co-Investigators: Dr. Tszwing Leung, Ms. Yuanyuan Liang.

This questionnaire will be completed by **PARENTS** and provide important information about you and your child on the risk factors associated with myopia development. It will take **10 minutes** to complete. **Please confirm with your child in places where you are not sure.** Please make a tick "v" in the applicable boxes or follow the instructions. When you finished, please let your child take it back to school and return to the teacher.

Your participation in this study is voluntary. You may decline to participate or withdraw from the study, at any time. All the information obtained will be used in the academic research and your participation in this study will be kept confidential. All raw data will be destroyed after 7 years upon the completion of the study.

If you have difficulty with the question, please feel free to connect Ms. LIANG for assistance (yyuan.liang@).

## Personal Information about Your Child

- 1. Your child's name: \_\_\_\_\_ (in English)
- 2. Gender (please circle): Male / Female
- 3. Date of birth: \_\_\_\_\_ (DD/MM/YYYY)
- 4. Ethnicity (Please circle): Asian/Other (Please specify)
- 5. Your child's grade is (Please circle): 3 / 4 / 5 / 6

#### Personal Information about Parents (Please make a tick "v" in the applicable boxes)

6a. Is the child's father myopic?

Yes (Go to Q6b)

🗌 No (Go to Q7a)

6b. If yes, what is father's myopic degree of the severe eye?

$\square$	< 3.00 D	3.00 D-5.99 D	□ ≥6.0 D	Not sure
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7a. Is the child's mother myopic?

Yes (Go to Q7b)

🗌 No (Go to Q8)

7b. If yes, what is mother's myopic degree of the severe eye?

8. The highest level of education completed by the father.

Primary school or below

Junior secondary school

Senior secondary school

Post-secondary or above

9. The highest level of education completed by the mother.

Primary school or below

Junior secondary school

Senior secondary school

Post-secondary or above

10. The total monthly family income is

□ ≤\$9,999	☐ \$10,000 - \$14,999	🗌 \$15,000 - \$19,999
☐ \$20,000 - \$24,999	☐ \$25,000 - \$29,999	\$30,000 - \$34,999
🗌 \$35,000 - \$39,999	☐ \$40,000 - \$44,999	\$45,000 - \$49,999
☐ \$50,000 - \$59,999	☐ \$60,000 - \$79,999	□ ≥\$80,000

#### Eye Care for Your Child (Please make a tick "v" in the applicable boxes)

11. When was the last time your child had an eye examination?

Less than 1 year 1 – less than 2 years

2 – less than 3 years 3 years or above Never						
12a. Does your child have myopia?						
Yes (Go to Q12b)						
🗌 No (Go to Q13)						
Don't know (Go to Q13)						
12b. If Yes, does your child take any treatments to control myopia? ("control" means decreasing						
myopia progression)						
□ No						
Yes, please specify:						
Bifocals (have two discrete powers, one for distance viewing and the other for reading)						
Progressive lenses (PAL, have multiple powers, designed for all working distances)						
DIMS lenses (MiyoSmart)						
Ortho-K (a kind of contact lens worn at night)						
Medicine (e.g. Atropine eye drops)						
Other (Please describe)						
Parents' Knowledge about Myopia and Near Work						
Parents' Knowledge about Myopia and Near Work 13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?						
Parents' Knowledge about Myopia and Near Work 13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)? Yes No						
Parents' Knowledge about Myopia and Near Work         13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?         Yes       No         14. Do you think it is necessary to bring your child to do eye examination regularly?						
Parents' Knowledge about Myopia and Near Work         13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?         Yes       No         14. Do you think it is necessary to bring your child to do eye examination regularly?         Yes       No						
Parents' Knowledge about Myopia and Near Work   13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?   Yes No   14. Do you think it is necessary to bring your child to do eye examination regularly?   Yes No   15. Which factors do you think are related to myopia (You can choose more than one)?						
Parents' Knowledge about Myopia and Near Work   13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?   Yes No   14. Do you think it is necessary to bring your child to do eye examination regularly?   Yes No   15. Which factors do you think are related to myopia (You can choose more than one)?   Hereditary factor Long period of near work without a break						
Parents' Knowledge about Myopia and Near Work   13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?   Yes   No   14. Do you think it is necessary to bring your child to do eye examination regularly?   Yes   No   15. Which factors do you think are related to myopia (You can choose more than one)?   Hereditary factor   Long period of near work without a break   Dim lighting condition   Improper postures for reading and writing						
Parents' Knowledge about Myopia and Near Work         13. Do you consider myopia as a health risk (i.e. eye diseases or vision loss)?         Yes       No         14. Do you think it is necessary to bring your child to do eye examination regularly?         Yes       No         15. Which factors do you think are related to myopia (You can choose more than one)?         Hereditary factor       Long period of near work without a break       Dim lighting condition         Improper postures for reading and writing       Unbalanced diet         Little outdoor activities       Other (Please describe)						

# About Near work (Please make a tick "v" in the applicable boxes)

Near work ( < 50cm) includes doing homework, reading for pleasure, drawing, playing the piano,

screen-viewing activities (e.g. smart phones, hand-held computers, etc.)

	Please recall these items over the past two weeks			
	Average time per day during weekdays	Average time per day during	Average distance of	
Near work activity		weekends or holidays	your child's eyes to the	
			working plane	
16. Non-digital work		□No		
outside school hours		Yes, hrs mins/day	cm	
(reading, writing, etc.)	Yes, hrs mins/day			
17. Using smartphone	□No	□No		
outside school hours	Yes, hrs mins/day	Yes, hrs mins/day	cm	
18. Using tablet	No	□No		
outside school hours	Yes, hrs mins/day	Yes, hrs mins/day	cm	
19. Other, please	□No	□No		
specify:	Yes, hrs mins/day	Yes, hrs mins/day	cm	



20. Does your child tilt his/her head when writing (beyond 45 angle degree)?

🗌 Yes 🗌 No

21. For how long does your child continuously do close work (reading, using tablet, etc.) before

taking visual breaks (i.e. look far into the distance)?

Never

Every 15 minutes

Every 30 minutes

Every 60 minutes

O More than 60 minutes

#### About Outdoor activities

Outdoor activities included general activities (being on the playground, walking, or riding a bike),

leisure activities (a picnic, spending time at the beach, hiking), and outdoor sports.

22. How long does your child spend on outdoor activities every day outside school hours during

#### weekdays?

Not at all □≤1 hour □ 1.01-1.99 hours □ ≥2 hours
23. How long does your child spend on outdoor activities every day during weekends?
Not at all □≤1 hour □ 1.01-1.99 hours □ ≥2 hours

### Thanks for your patience and cooperation, the questionnaire is complete!