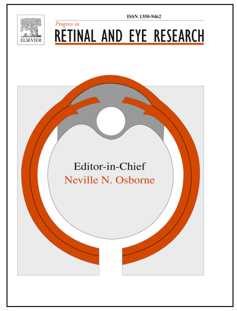
Accepted Manuscript



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PII: S1350-9462(17)30039-3

DOI: 10.1016/j.preteyeres.2017.09.004

Reference: JPRR 687

To appear in: *Progress in Retinal and Eye Research*

Received Date: 21 May 2017

Revised Date: 11 September 2017

Accepted Date: 20 September 2017

Please cite this article as: Morgan, I.G., French, A.N., Ashby, R.S., Guo, X., Ding, X., He, M., Rose, K.A., The epidemics of myopia: Aetiology and prevention, *Progress in Retinal and Eye Research* (2017), doi: 10.1016/j.preteyeres.2017.09.004.

THE EPIDEMICS OF MYOPIA: AETIOLOGY AND PREVENTION

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ABSTRACT

There is an epidemic of myopia in East and Southeast Asia, with the prevalence of myopia in young adults around 80-90%, and an accompanying high prevalence of high myopia in young adults (10-20%). This may foreshadow an increase in low vision and blindness due to pathological myopia. These two epidemics are linked, since the increasingly early onset of myopia, combined with high progression rates, naturally generates an epidemic of high myopia, with high prevalences of “acquired” high myopia appearing around the age of 11-13. The major risk factors identified are intensive education, and limited time outdoors. The localization of the epidemic appears to be due to the high educational pressures and limited time outdoors in the region, rather than to genetically elevated sensitivity to these factors. Causality has been demonstrated in the case of time outdoors through randomized clinical trials in which increased time outdoors in schools has prevented the onset of myopia. In the case of educational pressures, evidence of causality comes from the high prevalence of myopia and high myopia in Jewish boys attending Orthodox schools in Israel compared to their sisters attending religious schools, and boys and girls attending secular schools. Combining increased time outdoors in schools, to slow the onset of myopia, with clinical methods for slowing myopic progression, should lead to the control of this epidemic, which would otherwise pose a major health challenge. Reforms to the organization of school systems to reduce intense early competition for accelerated learning pathways may also be important.

KEYWORDS: myopia; high myopia; pathological myopia; prevention n; control;education; schools; time outdoors; dopamine; atropine; orthokeratology; optical devices

Contents

1. Introduction

As a recent report in Nature, entitled "The Myopia Boom" demonstrated, it is now widely accepted that there is an epidemic of myopia in the developed countries of East and Southeast Asia, paralleled by an epidemic of high myopia (Dolgin, 2015). Recent meta-analyses have suggested that close to half of the world's population may be myopic by 2050, with as much as 10% highly myopic (Holden et al., 2016a). Because of the links of high myopia to pathological myopia (Spaide et al., 2014), in which changes in the choroid, retina and sclera can lead to uncorrectable vision loss, and because correction of the underlying refractive error does not prevent the appearance of pathology, prevention of myopia and particularly high myopia has become an important international public health priority (Morgan et al., 2012; Holden et al., 2016b).

These epidemics have been extensively reviewed from a variety of perspectives (Foster and Jiang 2014; French et al., 2013a; Holden et al., 2014; Holden et al. 2016a,b; Hysi et al. 2014; Morgan, 2003; Morgan and Rose, 2005, 2013; Morgan et al., 2012; Ohno-Matsui et al., 2016; Pan et al., 2012; Rose et al., 2016; Sankaridurg and Holden, 2014; Wallman and Winawer, 2004; Wojciechowski, 2011; Wojciechowski and Hysi, 2013), which can be consulted for more details. The specific aim of this review is to bring together the evidence that there is an epidemic of myopia in the developed countries of East and Southeast Asia, to compare it to an epidemic of myopia in Jewish boys attending Orthodox schools in Israel, to analyse the conditons in which the epidemics of myopia have emerged, and to link broad changes in society to specific changes in education and specific environmental exposures such as near work and time outdoors, through to biological pathways. We will not deal extensively with genetic factors, because it is now generally accepted that genetic change is too slow to explain the rapid changes in prevalence that have taken place in East and Southeast Asia (Hysi et al., 2014; Morgan and Rose 2005; Wojciechowski 2011, Wojciechowski and Hysi, 2013). For the purpose of this review, we will simply note that genetic factors impose a level of baseline risk of myopia, and concentrate on the associations of myopia with environmental risk factors which have led to the epidemic of myopia in the developed countries of East and Southeast Asia. We conclude that changes in education and the time that children spend outdoors have played a major causal role in the emergence of the myopia epidemics, and that these factors can be modified to achieve prevention.

2. An epidemic of myopia

2.1 The evidence for an epidemic

In the developed countries of East and Southeast Asia, the prevalence of myopia is now 80-90% in children completing secondary schooling at the age of 17-18 (Morgan et al., 2012), compared to the prevalences of 20-40% seen in many developed western countries (Cumberland et al., 2015; Morgan et al., 2012; Pan et al., 2012; Vitale et al., 2008, 2009; Williams et al., 2015a). In contrast, in less developed parts of the world, with less developed education systems, the prevalence of myopia in young adults is often less than 5-10% (Anera et al., 2009; Casson et al., 2012; Dandona et al., 2002a,b; Gao et al., 2012; Jimenez et al., 2004, 2012; Khandekar and Abdu-Helmi, 2004; Lewallen et al., 1995; Lindquist et al., 2011; Lithander, 1999; Pokharel et al., 2000; Soler et al., 2015).

2.2 The geographical localization of the epidemic

The countries reporting high prevalences of myopia are clustered in East and Southeast Asia. Many have populations of Chinese ancestry, but the prevalence of myopia is also high in South Korea (Jung et al., 2012; Kim et al., 2014) and Japan (Ding et al., 2017; Matsumura and Hirai, 1999), where the population is not of Chinese ancestry, and it is high in those of Indian and Malay origin in Singapore (Koh et al., 2014). A high prevalence of myopia is not found in most countries in Asia (Morgan and Rose, 2005; Pan et al., 2015). Despite this, myopia has often been described as a Chinese or Asian problem, when, in fact, the epidemic crosses ethnic boundaries, but is quite tightly localized geographically.

It is important to use correct geographical terminology for regions, in order to accurately identify where the epidemic is taking place. It is then possible to look for common factors in these regions, and within these regions, in affected countries, which contrast with conditions in other countries and regions which are not affected. Asia is a large continent, extending east of the Ural Mountains and River, south of the Black Sea, and East of the Dardanelles and Red Sea (Figure 1). It is diverse in terms of the continental genetic ancestry of its populations, and diverse in terms of culture and levels of economic development. It is therefore unlikely to be a coherent unit in relation to any complex disease, and in the case of myopia, it is not.

Asia includes East Asia, and Southeast Asia, where the most prominent myopia epidemic is located, as well as Central, South and West Asia. East Asia is defined as consisting of China, including Hong Kong and Macao, Taiwan, Japan, North Korea, South Korea, and Mongolia. The prevalence of myopia is high in most parts of East Asia (Morgan et al., 2012; Pan et al., 2012), but there is no data available on North Korea and Macao, and the prevalence appears to be low in Mongolia (Morgan et al., 2006; Wickremasinghe et al., 2004). Macao's close affinities to mainland China and Hong Kong, and its high educational outcomes, suggest that its prevalence of myopia will be high. In most parts of East Asia, the prevalence of myopia is therefore high.

Southeast Asia consists of Vietnam, Cambodia, Laos, Singapore, Indonesia, Malaysia, Brunei, Thailand, Myanmar, Philippines and Timor Leste. Singapore, which stands out for economic development and high educational standards in the region, is the only country in the region where the prevalence of myopia is known to be high (Morgan et al., 2012, Pan et al., 2012). It is known to be low in children in Cambodia (Casson, et al., 2012), Laos (Gao et al., 2012) and Thailand (Yingyong, 2010). The myopia epidemics are therefore localized to the developed countries of East and Southeast Asia, and causal factors are likely to be common to them, and distinct from other countries in the region.

2.3 The origins of the epidemic of myopia

Elucidating the origins of the epidemics has been problematic, since many older studies, and even some more recent ones, have used unrepresentative sampling procedures and ignored the need for cycloplegia. The best approach to documenting secular changes in prevalence is to have regular population-based surveys of the prevalence of myopia based on cycloplegic refraction, enabling comparison of the prevalence of myopia in different birth cohorts of children (or adults) at the same age. Young adults around the age when secondary schooling finishes in developed societies, and when myopia tends to stabilize, provide a useful standard sample.

Only a series of surveys from Taiwan meet these exacting standards (Ding et al., 2017; Lin et al., 2004; Shih et al., 2009). The first survey in 1983 showed that the prevalence of myopia in 18 year-olds was already over 70%. Subsequent surveys in 1986, 1990, 1995, 2000 and 2006 demonstrated a peak prevalence of over 80%. There were more marked increases in the prevalence of myopia at younger ages, indicating an increasingly early age of onset, but in these seminal studies, there was little analysis of risk factors.

Singapore has provided a less systematic set of data. Initially, unaided visual acuity was measured on males in the age range 15 to 25 in military service examinations (Au Eong et al., 1993a,b; Chew et al., 1988; Tay et al., 1992). Those with uncorrectable low vision were excluded from the analysis, and with this exclusion, low visual acuity (VA) in children is predominantly caused by myopia refractive errors. For the 1974-1984 and 1987-1992 cohorts, low VA, using a VA cut-off of 6/18 or worse, increased from 26.3% in the 1974-1984 cohort, to 44.2% in the 1987-1992 cohort. Recent work suggests that a more appropriate cut-off for defining myopia is around 6/9 or 6/9.5 (Leone et al., 2010; Tong et al., 2004; Xiang et al., 2013). Data on non-cycloplegic refractions, which tend to over-estimate the prevalence of myopia, is available for selected cohorts, with the prevalence of myopia (<-0.5D) in the 1996-1997 cohort, namely 79.3%. rising only slightly to 81.6% in the 2009-2010 cohort (Koh et al., 2014; Wu et al., 2001). Looking at all this data, there can be no doubt that both Taiwan and Singapore have seen a substantial increase in the prevalence of myopia over the past 60 years.

2.4 A more comprehensive review of the evidence

To obtain a more comprehensive picture requires making a compromise between epidemiological purity and effective analysis. We have attempted to estimate the prevalence of myopia in young adults using data obtained using a variety of techniques, accepting that the figures will not be precise, but in the right range, and arguably sufficient to identify an epidemic. The RESC studies provide one of the most consistent sets of data, but the oldest children examined were 15 years-old (Dandona et al., 2002b; Goh et al., 2005; He et al., 2004, 2007; Maul et al., 2000; Murthy et al., 2002; Naidoo et al., 2003; Pokharel et al., 2000; Zhao et al., 2000). In general, we have accepted estimates from ages 15-25 as approximating those of young adults, since onset and progression of myopia are limited in this age group.

We have also used data on non-cycloplegic refractions which will tend to over-estimate the prevalence of myopia in adults, as well as data on visual acuity, which will also tend to over-estimate the prevalence unless those with uncorrectable low visual acuity have been excluded. The visual acuity cut-off is, naturally, crucial. In addition, some data are based on estimates of parental myopia, generally assessed by questionnaire, which will tend to under-estimate the prevalence, since parents with low myopia may not be aware of their condition.

Crucially, to obtain estimates for early birth cohorts, we have assumed that the prevalence of myopia in older people in cross-sectional studies will give an indication of the prevalence of myopia when they were young adults. This assumption has rightly been questioned (Mutti and Zadnik, 2000), because of the known longitudinal hyperopic shifts in refraction in adults due to loss of lens power (Iribarren, 2015). However, since that time, two recent studies have shown that the longitudinal shifts in refraction primarily effect those with emmetropic and hyperopic refractions (Han et al., 2017; Hashemi et al., 2016), and thus the prevalence of myopia remains relatively stable during aging, until myopic shifts take place in association with the development of cataracts. However, the hyperopic shifts in refraction seen for emmetropes and hyperopes mean that while the prevalence of myopia tends to be stable, mean SER will show hyperopic shifts. Cautiously used, we believe that this approach has considerable value in filling gaps in our knowledge, as discussed below.

The argument that substantial cross-sectional differences in the prevalence of myopia, of the kind seen in many of the countries in East and Southeast Asia, can be explained by longitudinal shifts in refraction is vulnerable to a *reductio ad absurdum* argument; in other words that it leads to absurd conclusions. For example, in South Korea, the prevalence of myopia is over 80% in recent birth cohorts and low (10-20%) in older cohorts, in cross-sectional studies (Kim et al., 2013). The recent high prevalence rates have been confirmed using cycloplegic refraction (Jung et al., 2012), but there is no published data on the older birth cohorts when they were young adults. However, the argument that longitudinal hyperopic shifts could explain the difference implies that the earlier birth cohorts have gone through a cycle of high prevalence of myopia and high myopia, followed by a decline to very low levels, and that the current generation may do the same. The emergence of considerable moderate to high myopia is highly unlikely to have been missed in the older cohorts, even without formal studies, since, without correction, moderate to high myopia leads to substantial visual impairment. This argument is clearly not conclusive, but direct evidence is impossible to obtain. It is, however, worth noting that the level of education has markedly increased in this population, from only 6.0% with university education in the oldest cohort to 45.7% in the youngest (Kim et al., 2013), consistent with the general link between education and myopia. It is also worth noting that follow-up of the current generations affected by high prevalences of myopia and high myopia will provide more definitive evidence, since the hypothesis that cross-sectional differences in the prevalence of myopia can be explained by longitudinal hyperopic shifts implies that the current highly myopic cohorts should gradually lose their myopia. It is further worth noting that if this were to happen, the risks of developing pathological myopia might still be high, because the hyperopic shifts in refraction are due to changes in lens power, and not to reductions in excessive axial elongation.

In the case of European populations, the validity of the assumption about older cohorts can be more directly tested. A moderate increase in the prevalence of myopia in Europe, based on non-cycloplegic refractions has been reported (Williams et al., 2015b). As in Korea, education levels have increased in more recent birth cohorts, in parallel with a change in educational exposures from under 5% to close to 50% with tertiary education. The prevalence of myopia in the older European cohorts, which ranges from 15-20%, can be directly compared to the prevalence of myopia in male military recruits in the UK around 1960, using cycloplegic refraction (Sorsby et al., 1960), which was around 10%. The ball-park agreement suggests that cautious extrapolation of this kind is valid.

2.5 Distinct patterns of development of the epidemic of myopia

Bearing all the qualifications in mind, the data collected in Figure 2A on South Korea, Singapore, Taiwan and Hong Kong show a consistent picture of a slow increase in the prevalence of myopia from 20-40% after the Second World War to 70-90% today. Data from Japan have not been included, but there is some evidence that the prevalence of myopia increased prior to the Second World War, dropped for those born just before or after the war, and then started to rise again (Ding et al., 2017; Sato, 1965). Some of the data used in this Figure were also used by Nature for a graph of the myopia boom (Dolgin, 2015).

Figure 2B shows data from several studies in Guangzhou. Some have been published (He et al., 2004; He et al., 2009; Xiang et al., 2013), others are not yet published. Again, the overall picture is quite consistent, but importantly, different to that seen in the other countries in the region. In Guangzhou, the increase in myopia appears to be delayed by around 10-20 years compared to Taiwan, Singapore, Hong Kong and South Korea. Then, for those born after 1970, the prevalence increased extremely rapidly, achieving parity with other developed countries in the region within one generation. The pattern is probably due to the limited expansion of higher education in the early years of the People's Republic of China, followed by rapid expansion after the end of the Cultural Revolution in 1976. The dependence of the prevalence of myopia on educational opportunities, and how rapid change can be, is striking. An erlier epidemic of myopia in North American Eskimo and Canadian Inuit populations also reported marked changes in prevalence of myopia in one generation (Young et al., 1969; Morgan et al., 1973). It should also be noted that in many countries in East and Southeast Asia, the prevalence of myopia is still low.

2.6 Is there an epidemic of myopia in populations of European ancestry?

In populations of European ancestry, there is uncertainty about the prevalence of myopia in more recent birth cohorts, because of the paucity of data based on cycloplegic refractions. Using cycloplegia, a prevalence of myopia of 18.6% in 18-20 year-olds was measured in 2012-2014 in Northern Ireland (McCullough et al., 2016), while follow-up in the Sydney Myopia Study reported a prevalence of 17.8% in those of European ancestry (French et al., 2013b) at a similar age. An earlier Polish study reported a prevalence of 30-36% for 18-20 year-olds (Czepita et al., 2007), and a much higher prevalence (49.7%) was reported in 12 year-old children from Sweden (Villarreal et al., 2000). For comparison, without cycloplegia, a recent NHANES study reported a prevalence of myopia of 52.2% for those aged 20-39 (Vitale et al., 2008), and similar values were reported for the youngest cohorts from Europe in the Gutenberg Health Survey (Wolfram et al., 2014) and from a meta-analysis of predominantly American studies (Kempen et al., 2004). A follow-up NHANES study provided good evidence for an upward trend in the prevalence of myopia (Vitale et al., 2009), but the estimates in this paper are bound to be over-estimates, as the authors emphasise, due to an imprecise definition of myopia. The often cited prevalence of 41.6% from this paper needs to be compared to the more accurate prevalence of myopia of 33.1% reported in Vitale et al., 2008). Somewhat lower values were reported in the UK Biobank Study (Cumberland et al. 2016). There is thus a significant gap between the limited data available on cycloplegic refractions and the estimates obtained without cycloplegia in studies on populations of European ancestry. More data on young adults measured with cycloplegia, or from visual acuity with the use of a pinhole and an appropriate cut-off, are required. But even without this data, it is clear that the prevalence of myopia in young adults of European ancestry in Europe, North America and Australia is much lower than in East and Southeast Asia.

3. An epidemic of high myopia

3.1 The evidence for an epidemic of high myopia

In parallel with the epidemic of school myopia, an epidemic of high myopia (more than 5 or 6D of myopia) has appeared. This epidemic was clear in the first studies from Taiwan (Ding, et al., 2017; Lin et al., 2004). Figure 3 shows current data on myopia and high myopia from East and Southeast Asia. The prevalence of high myopia has increased by as much as 10-fold, more than the proportional increase in total myopia, meaning that the percentage of myopes who become highly myopic has increased (Morgan et al., 2017). The reported prevalence of myopia and high myopia in young adults is much higher than in older adults (Asakuma et al., 2012; He et al., 2009; Liang et al., 2009; Liu et al., 2010; Sawada et al., 2008; Wong et al., 2000).

Two features of the evidence provide a simple explanation of this additional epidemic. As the prevalence of myopia has increased, the age of onset of myopia has decreased, which gives myopia more time to progress before it stabilizes. This hypothesis is supported by evidence that early onset of myopia is associated with higher final myopia (Chua et al., 2016; Iribarren et al. 2009). The rate of progression of myopia in East and Southeast Asia also seems to be higher than in other parts of the world, and particularly high at younger ages (Donovan et al., 2012b). Sankaridurg and Holden (2014) have provided estimates of mean progression by age up to the age of 15. While there will be some progression after that age, it will be limited. Assuming that a child becomes myopic at the age of 6, at the progression rates reported, the child will exceed the threshold for high myopia in 5 to 6 years, at about the age of 11 or 12, consistent with the age of onset of increasing high myopia in the data from Taiwan (Lin et al., 2004), and with more recent data from China (Guo et al., 2015; Wu et al., 2013). When myopia appears at age of 12 or later, the chances of progression to high myopia are much lower, and increasing age of onset further lowers the risk. This is an important indication that prevention needs to begin in primary schools or even preschools, and may not be as crucial in high schools. However, it is important to note that these arguments are based on averages, and personalized prediction regimes will need to be developed.

This pattern of development suggests that the epidemic of high myopia is simply a natural consequence of an epidemic of myopia, characterized by earlier onset and high progression rates. This “acquired” high myopia adds to low levels of high myopia in older populations. The shared origins of the epidemics of myopia and high myopia suggest that they will share epidemiological risk factors, and indeed high myopia in recent birth cohorts shows similar associations with education to those seen for school myopia, whereas this is not seen in some cohorts of older adults with a lower prevalence of high myopia (Jonas et al., 2016). It should be noted that associations of high myopia with education have been reported in some older cohorts (Wong et al., 2000; Wong et al., 2002), suggesting that, even when the prevalence of myopia is relatively low, acquired high myopia can occur in some, perhaps well-educated, people. This finding poses considerable challenges for genetic studies, since in studies on recent samples, genetic contributions may be swamped by large environmental effects. Age of onset of high myopia may help to distinguish genetic from acquired forms (Morgan et al., 2017).

3.2 The implications for pathological myopia

Most of what we know about the links between high myopia and pathological myopia comes from studies on older cohorts (Asakuma et al., 2012; Flitcroft, 2012; Liu et al., 2010; Vongphanit et al., 2002), when high myopia was arguably more genetic in aetiology. Recent developments in the definition of pathological myopia (Ohno-Matsui, 2016) and in the systematic classification of myopic maculopathy (Ohno-Matsui et al., 2015) need to be taken into account, but in general, pathology becomes more severe with more severe myopic refractive error (or greater axial length) and with age. However, how similar the pathology associated with genetic high myopic is to that associated with acquired high myopia is an open question. It is simply too early to have definitive answers, but it would not be wise to assume that “acquired” high myopia has no pathological consequences. If the emergence of pathology in association with high myopia depends purely on the distortions associated with increased axial length in high myopia, then considerable pathology would be expected.

4. Comparison with other social environments

4.1 Comparison with societies with little formal education

There are few studies with good methodology in societies with little formal education, but the prevalence of myopia, determined with cycloplegia, was only 0.4% in a large sample of illiterate African adults in Gabon (Holm, 1937), and the prevalence of myopia under cycloplegia in uneducated adult Inuit was only 1.2% (Skeller, 1954). Only 20 years later, several papers using cycloplegia reported low prevalences of myopia in older Inuit, with much higher prevalences in the younger adults (Alsbirk, 1979; Morgan and Munro, 1973; Morgan et al., 1975; Young et al., 1969), suggesting that there had been a marked inter-generational increase in myopia, attributed to the establishment of settled communities and provision of rudimentary formal education.

The methodologically strong RESC series, which used systematic cycloplegia and population enumeration reported that by the age of 15, the prevalence of myopia in children was less than

3% in rural Nepal (Pokharel et al., 2000). Low prevalences at age 15 were also reported from RESC studies in rural India (6.72%) (Dandona et al., 2002), Durban, South Africa (9.0 to 9.6%) (Naidoo et al., 2003), and urban India (10.8%) (Murthy et al., 2002), consistent with the relatively limited development of their school systems (UNESCO Global Education Monitoring Report, en.unesco.org/statistics, accessed May 3, 2017). Low prevalences of myopia using cycloplegia, but with school-based samples, have also been reported from Laos at .6% at the age of 11) (Gao et al., 2012) and Cambodia (6% at the age of 12) (Casson et al., 2012) These reports are particularly interesting, because they suggest that childhood myopia remains very low unless children are exposed to education, contrasting with a wide-spread belief that children naturally become more myopic with age, as part of the process of physical development.

4.2 Historical changes in western societies developing modern education systems

We can get some insight into historical changes in the prevalence of myopia from two papers on populations of European ancestry, where the birth cohorts go back to the beginning of the previous century. The Beaver Dam Eye Study reported 42.9% myopia in its youngest age cohort (43-54 years old) compared to 14.4% in the oldest, based on non-cycloplegic refraction (Wang et al., 1994). The cohorts were then followed for 10 years (Lee et al., 2002). There were clear myopic shifts in mean SER in more recent birth cohorts, with mean SER for cohorts born before 1922 around 1.0D, and negative mean SER values for those born after 1933 (see Figure 2 of Lee et al., 2002). Because longitudinal hyperopic shift in refraction are likely to affect mean SER, data expressed as percentage of myopia would be more meaningful for our purposes. Similar data were obtained from Europe, expressed as myopia prevalence (see Figure 1 of Williams et al., 2015a). In this case, the prevalence of myopia was low for cohorts born before 1940, but in more recent cohorts, there was a considerable increase in prevalence of myopia when measured at the same age.

Overall, these data suggest that increases in the prevalence of myopia can be traced back as far as early 1900s in Europe and North America. This was a period in which education expanded to meet the needs of modern industry. For example, in the US, only 10% of young people had a high school diploma in 1910, but by 1940, nearly 50% had one (120 Years of American Education. A Statistical Portrait, available at *https://nces.ed.gov/pubs93/93442.pdf*.). Similar levels of education were not seen in East and Southeast Asia until after the Second World War, and in many parts of the world, they have still not appeared. This pattern of development is summarized in Figure 4, showing the increasing prevalence of myopia in young adults as school systems have progressively developed. The major increase from prevalence rates normal in western school systems to those found in East Asian school systems is clear.

5. Environmental risk factors

While the systematic association of myopia prevalence with educational experiences is striking, as with all associations, it could be confounded by parallel changes. As societies have developed, there have been systematic increases in education, but there have been parallel changes in a number of other parameters such as family income, living environments, including changes in population density, style of housing, pollution, diet, and lifestyle, and some associations with factors of this kind have been reported. Recently, it has also become common to argue that computers, smart phones and tablets have played a role, although the early data on high prevalences of myopia from Taiwan and Singapore were collected on cohorts with little to no exposure to these devices.

We have recently dealt with these risk factors in some detail. Overall, we concluded that none of these factors provide good explanations for the development of the myopia epidemics, whereas educational change does. Given the evidence for strong associations between myopia and education, reported risk factors for myopia now need to be rigorously assessed for confounding with education. The detailed arguments are given in another paper (Rose et al., 2016).

5.1 Education is a key causal factor

The link between education and myopia is strong and consistent, and shows up in the association between myopia and years of schooling in adults (Au Eong et al., 1993a; Mirshahi et al., 2014), and during development, in the associations between prevalence of myopia, accelerated learning streams and academic grades (French et al., 2013a; Ip et al., 2008; Quek et al. 2004; Rosner and Belkin, 1987; Saw et al., 2007). In almost all studies which have addressed the issue, in populations of a range of ethnic backgrounds, more educated people are found to be more myopic. In reviewing this issue previously (Morgan and Rose, 2005), we argued that the tendency for schooling to lead to increased myopia had been documented in almost all major population groups, and we suggested that it constituted a common human characteristic. Nothing published since has invalidated this conclusion.

5.2 The epidemic of myopia in Orthodox Jewish boys

In young adult Jewish boys attending Orthodox schools in Israel, the prevalences of myopia (81.3%) and high myopia (20.4%) are as high as those seen in young adults in East and Southeast Asia (Zylbermann et al., 1993), and much higher than in girls attending girls-only Orthodox schools, and boys and girls attending secular schools. Moreover, the extremely distorted distribution of refraction (Figure 5) in Jewish boys attending Orthodox schools, not seen in the other population sub-groups, is very similar to that seen in both boys and girls as young adults in East and Southeast Asia (unpublished data from the Guangzhou Twin Eye Study). Similar distributions of refraction has also been reported for recent cohorts of young adults in Singapore (Koh et al., 2014) and South Korea (Jee et al., 2012; Kim et al., 2013) This suggests that the processes underlying the epidemics are quite similar, and that an explanation of the epidemic in Orthodox Jewish boys in terms of educational pressures and perhaps limited time outdoors is likely to apply. The evidence certainly suggests that educational exposures in the affected group are particularly high, but differences in time spent outdoors have not been examined. In contrast, it would be difficult to explain the high prevalence of myopia in Orthodox Jewish boys as compared to their sister siblings in terms of familial factors, including diet.

The situation of the boys attending Orthodox Jewish schools is as close to a socially imposed controlled trial as is likely to occur, although it is clearly not randomized. The results suggest strongly that educational pressure is a causal factor. Zylbermann et al (1993) emphasised both educational pressure and aspects of the learning style adopted for religious studies (such as variations in print size, and a rocking posture used during religions studies which imposes regular changes in focus) in their analysis, but the latter are clearly not shared with children in East and Southeast Asia. However, education for the two affected groups is very similar in terms of early onset and increase in study pressures. Comparing the two epidemics provides a strong argument that education is a major causal factor.

5.3 Does education explain everything?

While accepting a role for education, some have argued that education cannot provide the whole explanation. In Singapore, adjustment for education reduced, but did not completely eliminate ethnic differences in myopia, suggesting that other factors were involved (Wu et al., 2001). This issue will be discussed in more detail in Section 9.4. Similarly, the E3 meta-analysis of European data suggested that there were independent additive birth cohort and education effects (Williams et al., 2015a). The problem with the E3 meta-analysis is the assumption that an educational category will have the same educational content for different birth cohorts. For example, the category "primary" is applied to all subjects with 16 or less years of education, but in the earlier cohorts, many will have had much less than 16 years education, whereas in the later birth cohorts, most will have achieved this level. Over the time period covered by these cohorts, there has also been a marked change in overall educational achievements, and it seems likely that when primary school education in the strict sense of the term (generally six years of school,), provided only sufficient preparation for children to work as unskilled workers, it would have been much less intensive than primary school education as preparation for a further six years of school, followed in many cases by higher level studies. While we do not regard these papers as conclusive, we do not want to argue that education is the only factor, because another independent factor, the time that children spend outdoors, has already been established.

6. Time outdoors as a protective factor

There is now consistent evidence that children who spend more time outdoors are less likely to be or become myopic (Dirani et al., 2009; French et al., 2013a,b; Guggenheim et al., 2012; Guo et al., 2013; He et al., 2015; Ip et al., 2008; Jones et al., 2007; Jones-Jordan et al., 2011,2012; Khader et al., 2006; Lin et al., 2014; Mutti et al., 2002; Onal et al., 2007; Parssinen and Lyyra, 1993; Rose et al., 2008a,2008b; Sherwin et al., 2012; Wu et al., 2010; Wu et al., 2013; Wu et al., 2015a,b; Xiong et al., 2017; You et al., 2012, 2014). Only a few studies have failed to confirm the association (Low et al., 2010; Lu et al., 2009). About 2 hours a day outdoors, out of school hours, in western countries, eliminates the additional risk associated with more near work (Rose et al., 2008a), as well the risk associated with having myopic parents (Jones et al., 2007). The evidence from randomized clinical trials which have shown that increased time outdoors reduces incident myopia (He et al., 2015;Wu et al., 2013), provides evidence of a causal association. There is no systematic evidence of changes in outdoor exposures over the time in which the prevalence of myopia has changed, because data of this kind have not been collected. However, the anecdotal case is strong that over time, in many parts of the world, over recent decades, children have adopted lifestyles based on more time indoors.

Collection of data on time outdoors has so far largely been carried out using questionnaires, of limited validity, but they appear to be sufficiently robust to establish the consistent associations. Children from developed counties in East and Southeast Asia consistently report much less time outdoors than children in Australia or the US (French et al., 2013a,b,c,d; He et al., 2015; Jones et al., 2007; Jones-Jordan et al., 2011; Jones-Jordan et al., 2012; Rose et al., 2008a,b). More data will no doubt become available rapidly, with the development of objective methods of measurement such as the use of HOBO light meters (Alvarez and Wildsoet, 2013; Dharani et al., 2013; Schmid et al., 2013) and a wrist-borne device known as the Actiwatch (Read et al., 2014, 2015), and most recently, the availability of spectacle-mounted devices capable of measuring light exposures and nearwork exposures simultaneously (www.clouclip.com). Developing a comprehensive picture of exposures to risk factors for children in different locations, which takes account of both school time, and out-of-school time, is an important priority.

7. Linking risk factors to biology

7.1 Time outdoors

Studies on animal models have shown that, at least in the form-deprivation model, bright light exposures can completely abolish the development of experimental myopia (Ashby et al., 2009; Ashby and Schaeffel, 2010; Karouta and Ashby, 2015; Lan et al., 2013, 2014, 2016; Norton, 2016; Smith et al., 2012, 2013). It now also generally accepted that the mechanism initially proposed (Rose et al., 2008a), involving light-induced release of dopamine (Boelen et al., 1998; McCarthy et al., 2007; Megaw et al., 2001, 2006), which is known to inhibit axial elongation (Iuvone et al. 1991; McCarthy et al., 2007; Stone et al., 1989) has been confirmed. The evidence is against an active role for UV exposures (French et al., 2013a; Guggenheim et al., 2014), or physical activity per se (Rose et al., 2008a; Guggenheim et al., 2012), although both are higher when children are outdoors. Thus, there is a clear biological pathway for an effect.

7.2 Education

In contrast, the biological link is not so clear for education. Near work seems to be a significant factor, and while some have written it off (Mutti and Zadnik, 2009), a recent meta-analysis has concluded that it plays a significant role (Huang et al., 2015).

Originally, it was thought that the additional accommodation involved in nearwork would be the key factor, but this view has been undermined by evidence that accommodation is not important in animal studies of experimental myopia (Schmid and Wildsoet, 1996; Wildsoet et al., 1993), and that the site of action of anti-muscarinic drugs such as atropine, which block myopic progression in animals as well as humans, is not on accommodation (McBrien et al., 1993a,b). With the demonstration in animal studies of powerful effects of defocus on the rate of axial elongation (Schaeffel and Feldkaemper, 2015; Wallman and Winawer, 2004), thinking on this issue is now dominated by the possibility that interacting defocus signals, perhaps associated with accommodative lag, play an important role. These pathways to prevention are currently being explored with optical devices, including multifocal soft contact lenses, but the molecular and cellular pathways involved are still obscure.

8. The paradox of progression

8.1 Time outdoors does not appear to regulate progression.

While the biological pathways that lead to delay in the onset of myopia seem to be reasonably clear, there is general agreement that there is little evidence for regulation of progression, defined as myopic shifts in refraction in those who are already myopic (French et al., 2013a,b; He et al., 2015; Jones et al., 2007; Jones-Jordan et al., 2012; Rose et al., 2008a; Wu et al., 2013; Xiong et al., 2017). However, Parssinen et al. (2014) have reported that increased time outdoors was associated with slower progression in a study with 23 years of follow-up.

A difference in association with time outdoors between onset and progression is surprising, given that axial elongation is the basis of both processes. If progression is not regulated by the same factors as onset of myopia, then this needs to be explained, but there is no obvious explanation so far. An alternative explanation is that the failure to find associations of progression with the known risk factors is due to the restricted range of exposures seen in myopic children, many of whom are myopic because of the high educational pressures and limited time outdoors to which they have been exposed. This will make it harder to get significant associations, particularly when the data on exposures is obtained from imprecise questionnaires.

8.2 Seasonal differences in myopia progression

Consistent with this idea, there is considerable evidence that myopic progression can be actively regulated, since there are marked seasonal effects on myopic progression in populations of both European and East Asian ancestry (Cui et al., 2013; Donovan et al., 2012b; Gwiazda et al., 2014). Myopic progression is faster in winter than in summer, with up to two-fold variations reported. These make seasonal effects as powerful as the best pharmacological and optical interventions to slow myopic progression. The effects are consistent with an impact of educational pressures and time outdoors, and indeed, a doubling of time outdoors in the summer break compared to school terms (21.8 vs 10.3 hours per week), with an almost four-fold reduction in study time (1.7 vs 9.4 hours per week) has been reported (Deng et al., 2010). It is important to resolve this question, because, if time outdoors does prove to regulate progression as well as onset, then increased time outdoors will be more effective in preventing high myopia.

9. Why is the myopia epidemic concentrated in East and Southeast Asia?

9.1 Are genetic differences important?

The tight geographical localization of the myopia epidemic has led to the plausible hypothesis that the populations of these regions might be genetically more susceptible to environmental risk factors than other populations. However, when dealing with ethnic differences, it is vital to consider cultural factors as explanations, because human ethic/racial groups are rather similar in overall genetic terms, while differentiation in terms of cultural factors, while difficult to quantify, is often extreme (Risch, 2006).

It is clear that children in East and Southeast Asia do not develop myopia without relevant environmental exposures, since the prevalence of myopia in older cohorts, and in those with low educational levels, is consistently low. Differential genetic susceptibility to environmental risk factors has therefore often been assumed, but there is, as yet, little evidence of significant differences in “myopia susceptibility” genes in GWAS analyses between populations of European and East Asian ancestry (Verhoeven et al., 2013).

9.2 Educational pressure is high in the developed countries of East and Southeast Asia

In contrast, the evidence for educational differences in the countries with a high prevalence of myopia is strong. This can be seen in international educational surveys, where the dominance of the high prevalence of myopia countries is clear (Morgan and Rose, 2013). There are two common international surveys, the Program in Student Assessment (PISA) and the Trends in Maths and Science Survey (TIMSS). These surveys are well-funded, and have statistical power that is rarely possible in ophthalmic epidemiology. PISA 2015(available at https://www.oecd.org/pisa/pisa-2015-results-in-focus.pdf) reported on performance of students aged 15 in three areas, scientific, reading, and mathematical literacy. Singapore, Japan, South Korea, Taiwan or Chinese Taipei, and Beijing, Shanghai, Jiangsu and Guangdong representing mainland China, and Hong Kong and Macao took part. These countries dominated the top rankings in all testing domains, with stronger performance in mathematical literacy than in scientific literacy and reading literacy. Some countries, such as Finland, Canada and Australia, which have lower prevalences of myopia, also occupy significant rankings, suggesting that high educational outcomes in PISA are not necessarily associated with an epidemic of myopia. In the TIMSS surveys (available at *timss2015.org/*), Singapore, Japan, South Korea, Taiwan and Hong Kong took part, and their dominance of the ranking was even clearer. These locations took the top 6 places in all domains, with only the Russian Federation and Slovenia taking top 6 position in one domain each. This comparison provides an objective demonstration of the high educational outcomes achieved in the developed countries of East and Southeast Asia, which parallel the high prevalence of myopia.

We (Morgan and Rose, 2013) have previously suggested that systems in which educational pressure starts early, often because access to selective or accelerated learning streams is competitive, may be an important difference between the countries which have strong education systems and which develop an epidemic of myopia, and those which have not. These systems also impose high homework loads and parents make extensive use of out-of-school classes to promote their children's learning.

9.3 And less time is spent outdoors

The limited questionnaire data available suggests that the time that children spend outdoors is lower in the developed countries of East and Southeast Asia. In the Sydney Myopia Study, children of European origin spent over 21 hours a week outdoors outside of school hours, compared to nearly 14 in children of East Asian origin at the age of 6-7, who have a higher prevalence of myopia (French et al., 2013b; Rose et al., 2008a). This compared to only 3 hours per week in Chinese children of similar age growing up in Singapore (Rose et al., 2008b). Similarly, Chinese-Canadian children reported only 6 hours per week outdoors, compared to 10.5 for Canadian children of European origin (Cheng et al., 2007). Similar low levels have been reported for Chinese children in Guangzhou (5 hours per week) (He et al., 2015) and Shantou (6 hours per week) (Lu et al., 2009) of similar age. In Sydney, levels of time outdoors remain high, but drop slightly with age (French et al., 2013c), whereas in Singapore, time outdoors for 12 year-olds appears to rise to around 21 hours per week (Dirani et al., 2009), comparable to that reported from Australia. The low level of time outdoors in young children in East and Southeast Asia may therefore be particularly critical for the development of myopia, but more accurate data from objective measurements is required.

9. 4 Explaining ethnic differences in the prevalence of myopia in Singapore

Singapore provides a multi-ethnic laboratory in which the role of environmental factors in generating racial/ethnic differences can be assessed. The prevalence of myopia is different between the three major ethnic groups, with Chinese more myopic than Indians and Malays (Au Eong et al., 1993; Koh et al. 2012; Wu et al., 2001), but all groups are more myopic than in other parts of the world. It is important to note that the prevalence of myopia in children of Indian (or South Asian) origin is much higher in Singapore than in India (Dandona et al., 1999, 2002a,b; Murthy et al., 2002; Saw et al., 2002; Saxena et al., 2015), as is that of children of Malay origin than in Malaysia (Saw et al., 2006). This suggests that it is the environmental exposures that children receive in Singapore which are important in setting the prevalence of myopia, rather than genetic background. It is also important to note that the gaps between the ethnic groups have been closing over time.

Singapore produces detailed educational statistics which show that educational outcomes are higher for Chinese compared to Indians and Malays (available at *https://www.moe.gov.sg/about/publications/education-statistics*). Wu et al. (2001), in the 1996-7 sample of conscripts, therefore adjusted for educational differences, and the prevalence risk ratio for myopia for Chinese was reduced from 1.3 to 1.1, and from 1.1 to 1.0 for Indians, with Malays as the reference group. Similarly, the prevalence risk ratio for high myopia was reduced from 3.0 to 1.5 for Chinese and from 1.3 to 1.2 for Indians, relative to the Malay population. The authors concluded that myopia was strongly associated with education, but that the remaining ethnic differences could be explained by genetic background or other environmental factors.

This sort of adjustment is widely used in ophthalmic epidemiology, where it is generally used to establish the existence of "independent risk factors." However, there are limits to the effectiveness of this procedure (Brotman et al., 2005). Important issues are that complete abolition of associations can only be expected with high quality definition and measurement of variables, and that independence can only be reasonably established when all of the major variables have been adjusted for. Conversely, if covariates are included in the analysis, then associations may be improperly eliminated. When the paper by Wu et al. was published, the importance of time outdoors as a variable was not recognized, but it is now known that children from the three ethnic groups differ in the amount of time that they spend outdoors, with Malays reporting more time outdoors than Indians and then Chinese (Dirani et al, 2012). Adjustment for this variable would probably reduce the differences between ethnic groups even further, suggesting that most, if not all, of the differences between ethnic groups can be explained in terms of differences in educational and outdoor exposures.

These results suggest that the epidemics of myopia and high myopia have resulted from a perfect storm of factors. The developed countries of East and Southeast Asia adopted mass comprehensive education to support their economic development. Perhaps because of a long cultural emphasis on education as the pathway to success, competitive aspects of the educational process have been emphasized, with a high parental commitment to the educational success of their children. And this has been combined with cultural patterns that tend to avoid time outdoors, reflected in the low amounts of time outdoors reported.

Important questions for the future are whether this epidemic is likely to spread to other countries in the region, which may follow the lead of their economically successful neighbours, and whether it will spread to other countries around the world as they seek to compete with the "winners" in PISA and TIMSS. In at least one country in Southeast Asia, Vietnam, performance in the PISA and TIMSS surveys is increasing, and it will be an important test case to follow.

10. A framework for myopia prevention

Seet et al. (2001) developed a framework for understanding the emergence of an epidemic of myopia in Singapore, and for prevention of myopia. They distinguished between distal factors which covered broad social factors such as urbanization and meritocracy, intermediate factors such as indoor environment and near work activity and proximal factors such as genetics and biology. With the advantage of over 15 additional years of research, we propose a more developed hierarchy of causal factors, based on broad social changes, increasingly focusing on factors more specifically related to education and myopia, and linking them to specific changes in processes that directly influence the rate of axial elongation, which is the primary biological pathway which dictates the development of myopia (Figure 6).

There have been many social changes during the process of urbanization and industrialization, with increased population density, pollution, changes in diet, but only the development of modern schooling systems can be convincingly associated with the increasing prevalence of myopia, and only the particularly intensive forms of education system common in the developed countries of East and Southeast Asia, combined with lifestyles that deprive children of protective time outdoors can be convincingly associated with the epidemics of myopia. It is unlikely that the more general social changes can be reversed, or even if reversal is really desirable.

10.1 Reform of myopigenic education systems

Some characteristics of the school systems in the developed countries of East and Southeast Asia can be called into question. These systems share high participation and completion rates with those of western countries, but are characterized by early competition for selective learning streams and schools. Similarly, there is a strong focus on directed rather than exploratory learning, large amounts or homework and/or extensive use of out-of-school classes and tutorials, which may deprive children of time outdoors.

Many of these aspects can, over time, be modified by administrative actions. For example, China has defined the prevention of myopia as a task for schools, and has moved to limit the importance of key schools, thus reducing competition, and to limit homework loads. These steps have often been opposed by parents, teachers and educational administrators because of concerns about educational outcomes, but the results of international testing suggest that good outcomes can be obtained with less structured practices. There is, in fact, considerable debate over whether the education provided in many systems in East and Southeast Asia may end up stifling creative thinking (Zhao, 2014). Action on these issues may be driven by concern about issues other than myopia, such as concern about student mental health, fitness and obesity, as well as a desire to produce more flexible thinkers. But, if fully implemented, they could have a major impact on the prevalence of myopia, provided that private educational services do not provide alternative routes to high educational pressure. Until action is taken at this level, schools will continue to place students under pressure to become myopic, ensuring a continuing challenge.

10.2 The immediate priority is increased time outdoors

The most immediate path to myopia prevention in schools is to increase the amount of time that children spend outdoors within school hours (He et al., 2015; Wu et al., 2013). These two school-based clinical trials (one in Guangzhou, China and the other in Kaohsiung, Taiwan) have shown that this approach can produce reductions of 25-50% in cases of incident myopia over one to three years. If these reductions can be sustained for at least the duration of primary school, this would make a major impact on the prevalence of myopia and high myopia and the risk of myopic pathology. This policy is now being implemented in Taiwan with the aim of getting children outdoors for 2 hours a day, and initial signs are promising. A major focus has been to ensure that children get out of their classrooms during school recesses, but some schools are experimenting with outdoor education in many areas of the curriculum, to add to the amount of time that children get outdoors. Getting children outdoors as a myopia prevention poicy has also been adopted in Singapore, but it is not yet seen as a task for schools, but rather as an option for parents. So far, there is no published evidence on effectiveness.

These matters are not directly under the control of clinicians, but clinicians and professional associations could play an advocacy role. There may also be a role for reducing study pressures and increasing time outdoors in clinical practice, particularly as advice to parents of children who appear to be at high risk of developing myopia, high myopia and pathological myopia.

10.3 Pharmacological and optic interventions

There are also interventions to slow the progression of myopia, which are best described as myopia control. Currently there are several interventions available, of which the use of low dose-atropine (Chia et al., 2016) and orthokeratology (Swarbrick et al., 2015) are the best validated (Huang et al., 2016). Both are subject to uncertainties about long-term safety, which need further work. But there are certainly things that clinicians can now do for progressing myopes. Recently, the baseline data for a large randomized clinical trial of multifocal soft contact lenses has been published (Walline et al. 2017), which will provide some definitive data in this area. Depending on the outcome of further research, increasing time outdoors may also provide an effective intervention in this area.

10.4 A systematic school-based approach

Adopting the realistic aim of limiting the development of high myopia and pathological myopia, a school-based approach could consist of implementation of increased time outdoors, and monitoring the development of refractive errors to ensure prompt referral to clinicians for further interventions (Morgan, 2016). There is nothing novel about using schools in this way, but in many places school-based vision monitoring has virtually disappeared. At least in the countries currently faced with high prevalence of myopia and high myopia, this approach could have profound effects. Taiwan has already taken this route.

11. Future directions

At one level, future directions in this area are dominated by the need to take action. At the public health level, school-based interventions to increase the amount of time that children spend outdoors provide an immediate approach to reducing the onset of myopia, which should flow through to reductions in the prevalence of high myopia. There is a further need to explore changes to curriculum and school systems to reduce educational pressures, so that more time outdoors is available. Further research into the activity patterns of children using objective measurement techniques is needed, so that protective exposures can be more precisely defined.

Research over the past 20 years means that paediatric practice can no longer simply follow the progression of a young myope, correcting their refractive error as it worsens, particularly when they are at risk of high and pathological myopia. Interventions to slow progression based on low-dose atropine and orthokeratology can now be implemented for children at high risk of high myopia. However, both these strategies are invasive, and further research into myopic control using customized spectacles and contact lenses, such as multifocal soft contact lenses, and other pharmacological agents, is desirable.

An area about which little is known is how high myopia turns into pathological myopia. What are the risk factors and processes involved is an important area for research to guide clinical practice. But we should recognise that much has already been achieved, and something can now be done at both the public health and clinical levels to slow down the development of myopia and high myopia.

12. Conclusions

Overall, we conclude that the increasing prevalences of myopia and high myopia can be largely explained by two causal factors, increased educational pressures and reductions in the amount of time that children spend outdoors, both of which promote the development of myopia. Increases in the prevalence of myopia can be traced back to the emergence of modern western education systems over 100 years ago. A perfect storm of high educational pressures and limited time outdoors has converged to produce an epidemic of myopia.

It is unlikely that the broad social changes of industrialization and urbanization provide routes to prevention for the foreseeable future. But the specific forms that school organization has taken in East and Southeast Asia may be modifiable in ways which will reduce the amounts of near work and deprivation of time outdoors imposed on children, particularly in the early years of schooling. Coupled with increases in the amount of time that children spend outdoors at school, again particularly in the early years, this approach already shows promise as a preventive strategy. It is inevitable that some children will fall through the cracks, but they may be helped by clinical interventions designed to slow the progression of myopia to high, and then pathological myopia.

These two factors alone provide a good explanation for the epidemic of myopia in the developed countries of East and Southeast Asia and in Jewish boys attending Orthodox schools. Many other risk factors have been proposed, but the evidence for these two factors is strong, and other reported risk factors need systematic analysis to determine if they are simply aspects of education, or mediated by differences in time outdoors.

There is another epidemic of myopia which has been described, in Inuit communities in Canada and the United States. Much less is known about this epidemic, but it appears to have different characteristics to the other two epidemics, since the level of educational pressure in those communities was not nearly as high as that in Orthodox Jewish schools for boys or the school systems in developed countries East and Southeast Asia. We suggest that this epidemic may be more influenced by deprivation of light exposures outdoors than educational pressures per se, and it is worth noting that one of the early papers noted the protective effect of absenteeism from school to go hunting for seals outdoors (Morgan et al., 1975). Had this insight been followed up, instead of being denounced because it did not fit with the dominant idea that myopia was under almost complete genetic control (Sorsby et al, 1970), effective public health prevention of myopia might have been on the agenda well before now.

ACKNOWLEDGEMENTS

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. The authors have no conflicts of interest to declare.

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LEGENDS TO FIGURES

FIGURE 1

Geographical localization of the epidemic of myopia.

Most of the countries in East Asia are known to have a high prevalence of myopia, but in Southeast Asia, only Singapore is known to have a high prevalence of myopia. At present, the epidemic of myopia is confined to the developed countries of East and Southeast Asia.

FIGURE 2A

Estimated prevalence of myopia in different cohorts of young adults aged around 20

Data taken from:

Hong Kong: Goh and Lam, 1994; Lam et al., 1994

Taiwan: Ding et al., 2017; Lin et al., 2004; Shih et al., 2009

Singapore: Au Eong et al., 1993a,b: Chew et al., 1988; Koh et al., 2014; Tay et al., 1992; Wong et al, 2000; Wu et al., 2001

South Korea: Jung et al., 2012; Kim et al., 2013; Lee et al., 2013

FIGURE 2B

Estimated prevalence of myopia in different cohorts of young adults aged around 20

Data taken from:

He et al., 2004,2009; Xiang et al., 2013, unpublished data from the Guangzhou RESC, and Guangzhou Twin Eye Study

FIGURE 3

Reported prevalence of myopia and high myopia in various sites in East and Southeast Asia

Data taken from the following sources:

Lin et al., 2004;,Jung et al., 2012; Lee et al., 2013; Wu et al., 2013a; Koh et al., 2014; Guo et al., 2015, and unpublished data from the Guangzhou Twin Eye Study.

FIGURE 4
Relationship between prevalence of myopia in adults and state of development of the education system
Data taken from:
Czepita et al., 2007; Dandona et al., 2002b: Ding et al., 2017; French et al, 2013a; Guo et al., 2015; Holm, 1937; Jung et al. 2013; Koh et al., 2014; Lin et al., 2004; Maul et al., 2000: McCullough et al. 2016; Murthy et al., 2002; Naidoo et al., 2003; Pokharel et al, 2000; Shih et al., 2009; Skeller, 1954; Wu et al., 2013a; Zhao et al., 2000; and unpublished data from the Guangzhou Twin Eye Study

FIGURE 5
Comparison of the distribution of spherical equivalent refraction error in young adults in Guangzhou with that of Jewish boys in Israel attending Orthodox Jewish schools
Data taken from:
Zylbermann et al., 1993, and unpublished data from the Guangzhou Twin Eye Study

FIGURE 6
Distal and proximal environmental factors leading to the epidemics of myopia.
Broad social factors develop specific forms which impose excessive pressures on the biological pathways that control eye growth. Educational pressure promotes the development of myopia, as does reduced time outdoors in schools in the developed countries of East and Southeast Asia. Modifying these environmental factors may be able to reduce the myopia epidemics to levels produced by western education systems, without compromising educational outcomes.
These environmental factors converge on pathways that control axial elongation, which is the major regulated pathway leading to the development of myopia. Pharmacological and optical interventions can attempt to reverse directly the changes induced by these environmental factors (for example increase the release of dopamine by light or pharmacologically), or inhibit processes down-stream of these regulatory events that are part of increased axial elongation.

FIGURE 1

Geographical localization of the epidemic of myopia. Most of the countries in East Asia are known to have a high prevalence of myopia, but in Southeast Asia, only Singapore is known to have a high prevalence of myopia. Thus, at present, the epidemic of myopia is confined to the developed countries of East and Southeast Asia.

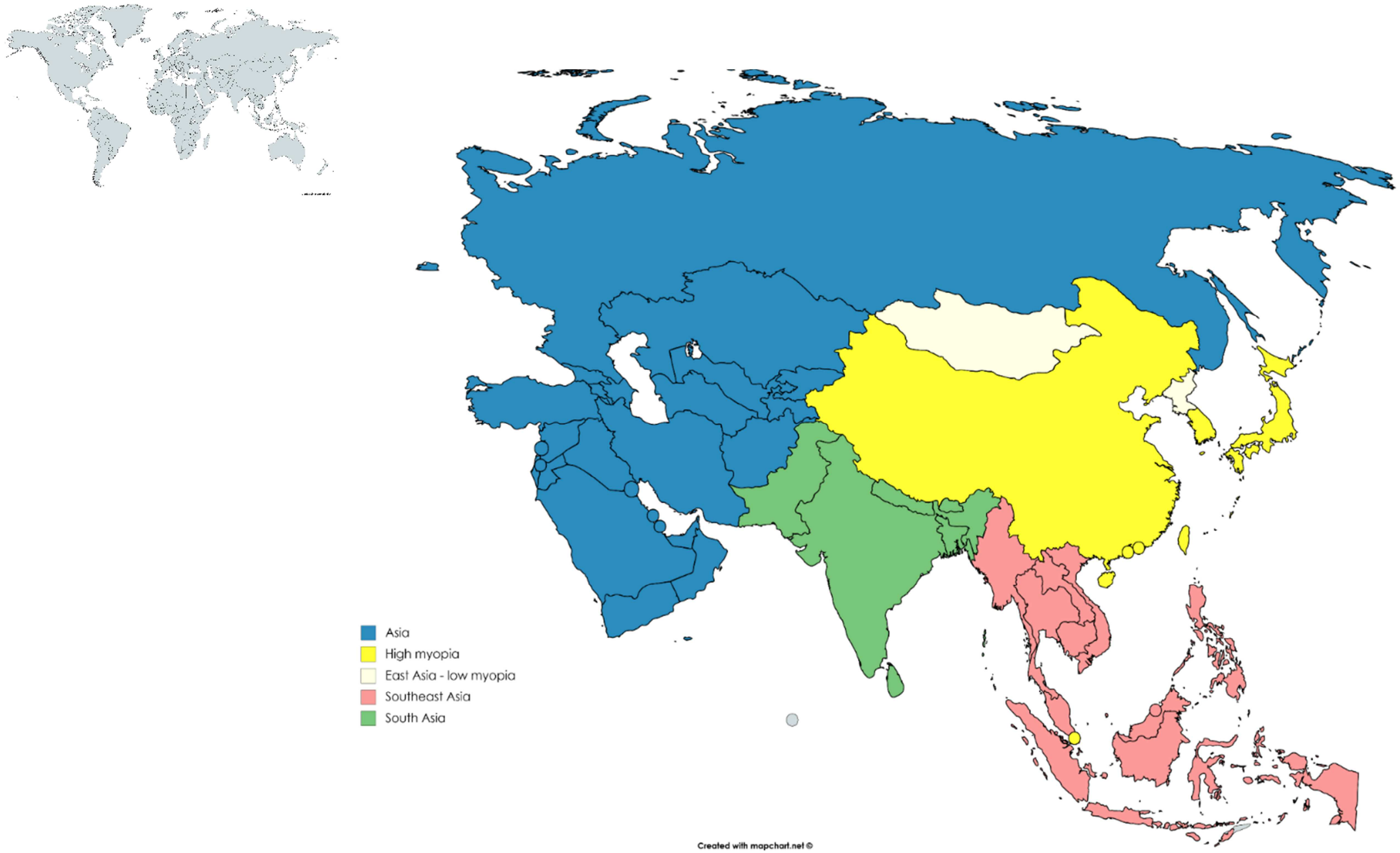


FIGURE 2A Estimated prevalence of myopia in Hong Kong, Singapore, South Korea and Taiwan at the age of 20

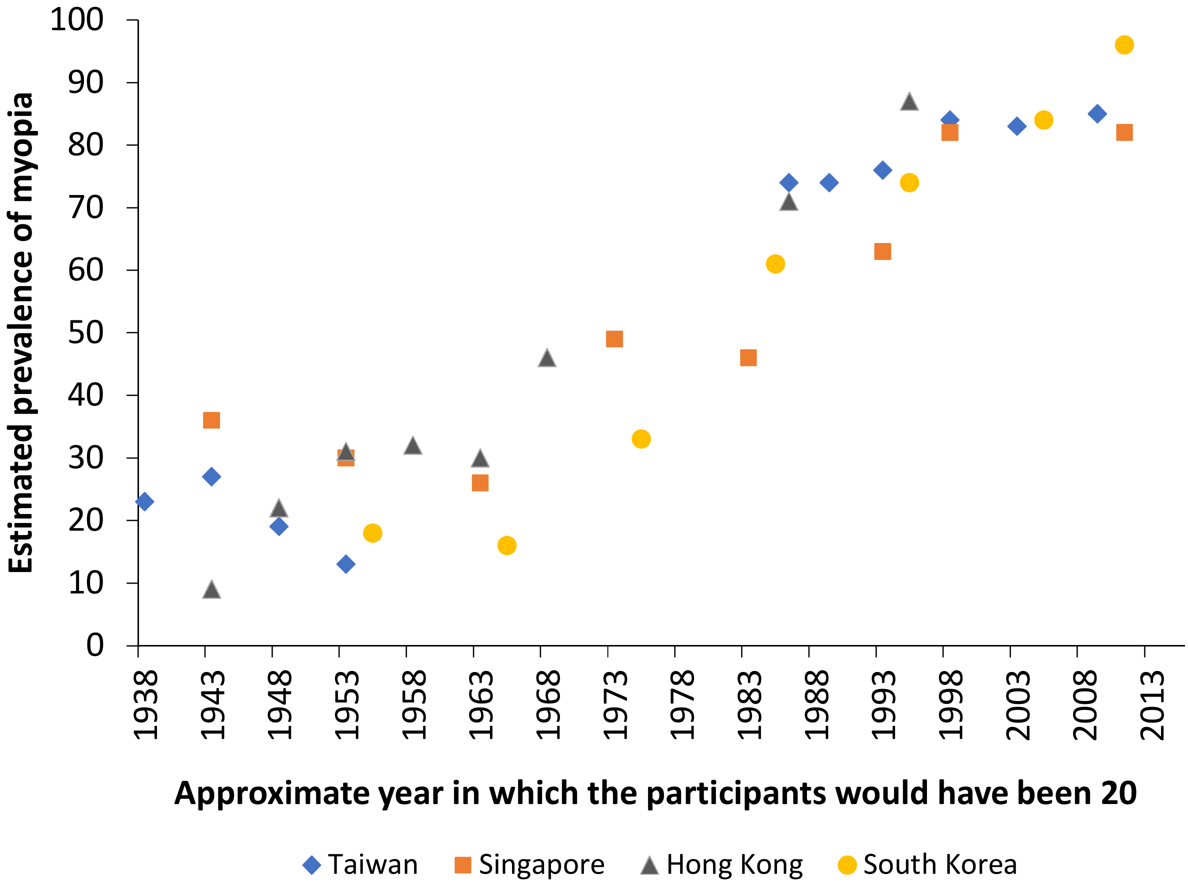
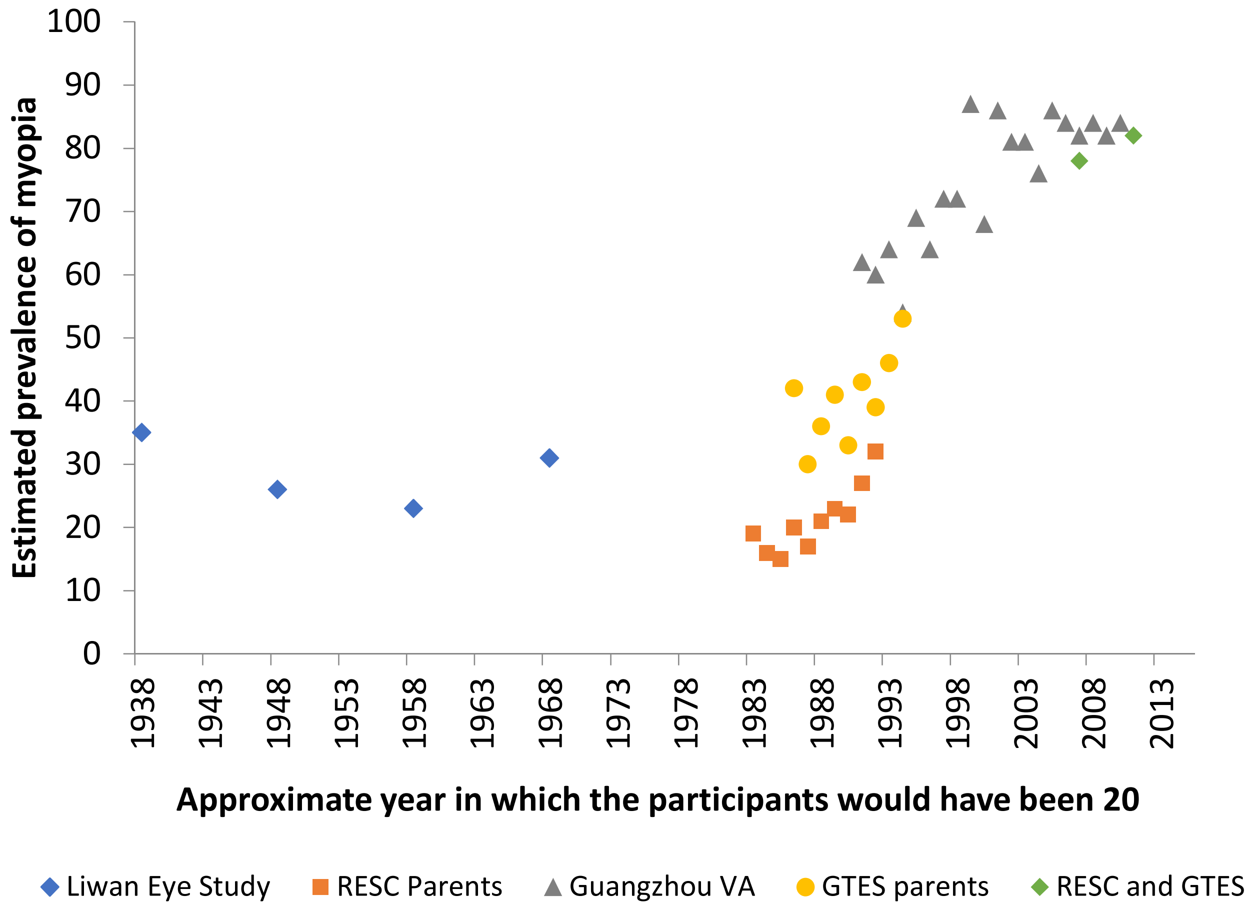


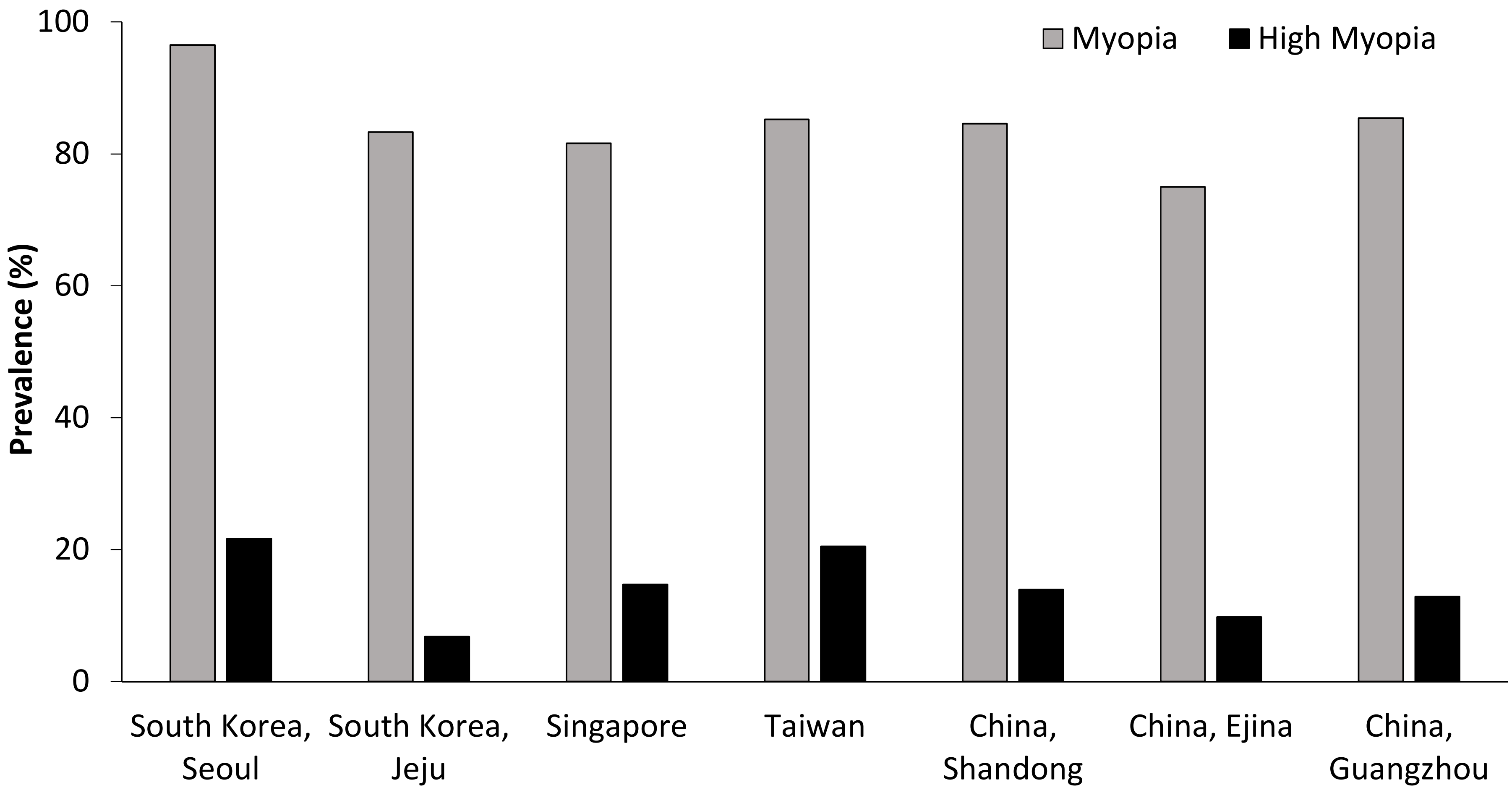
FIGURE 2B Estimated prevalence of myopia in Guangzhou, China at the age of 20 years



Data taken from the following sources:

(He, Zeng et al. 2004, He, Huang et al. 2009) and unpublished data from the Guangzhou Refractive Error in Study in Children (RESC) and Guangzhou Twin Eye Study (GTES)

FIGURE 3 Prevalence of myopia and high myopia in school-leavers in selected areas of East Asia



Data taken from the following sources:

(Lin, Shih et al. 2004, Jung, Lee et al. 2012, Lee, Jee et al. 2013, Wu, Bi et al. 2013, Koh, Yang et al. 2014, Guo, Yang da et al. 2015) and unpublished data from the Guangzhou Twin Eye Study

FIGURE 4 Relationship between the prevalence of myopia and state of the education system

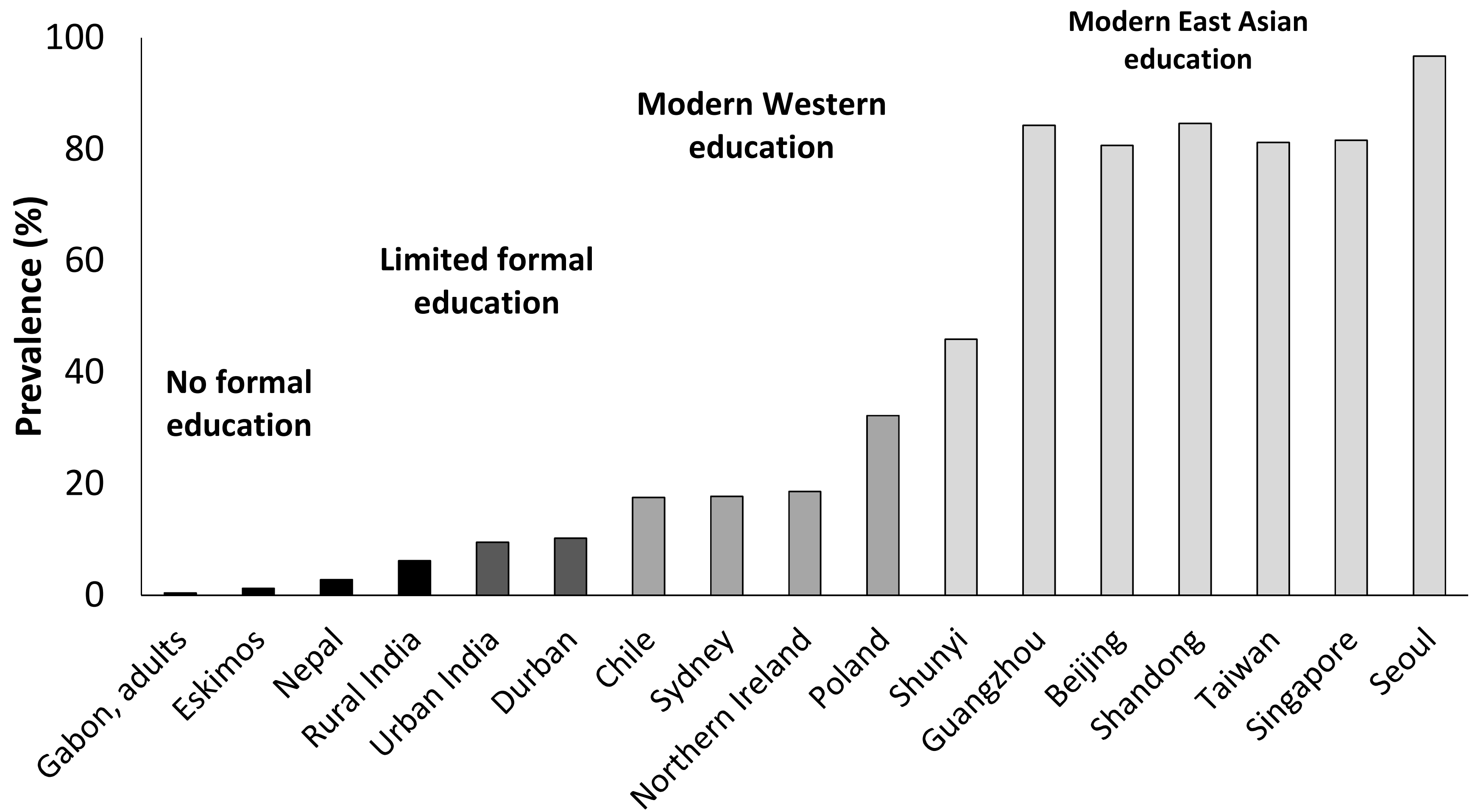


FIGURE 5 Distribution of refraction in Chinese students and orthodox Jewish boys

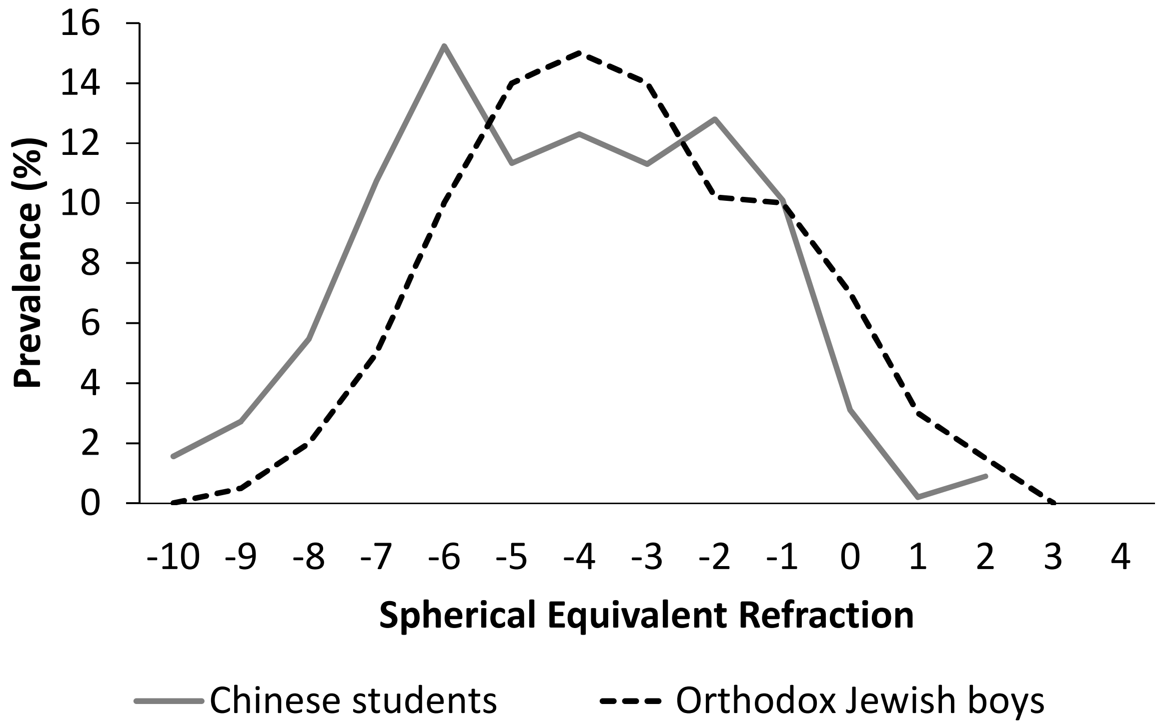
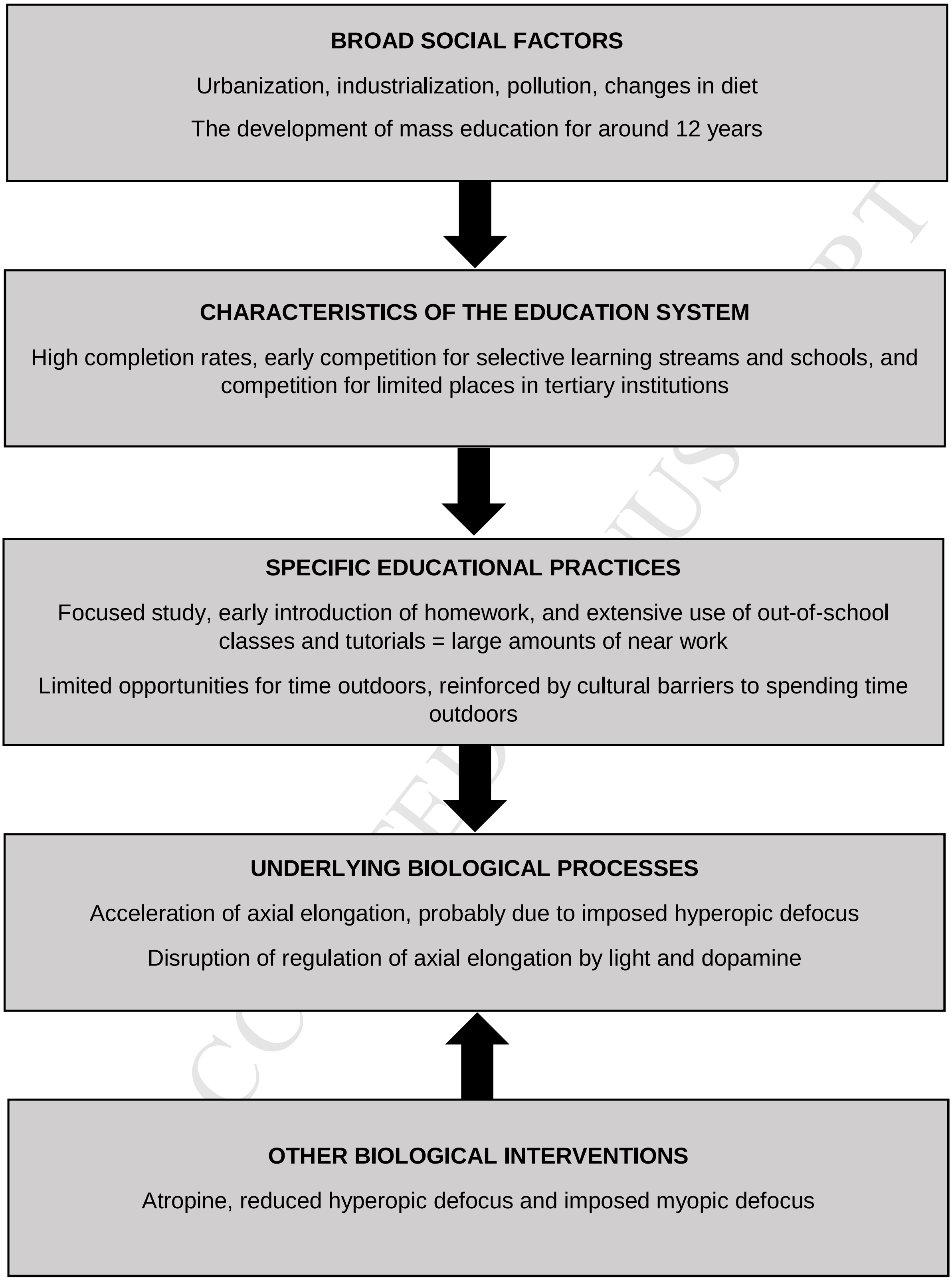


FIGURE 7


BROAD SOCIAL FACTORS
Urbanization, industrialization, pollution, changes in diet
The development of mass education for around 12 years
CHARACTERISTICS OF THE EDUCATION SYSTEM
High completion rates, early competition for selective learning streams and schools, and competition for limited places in tertiary institutions
SPECIFIC EDUCATIONAL PRACTICES
Focused study, early introduction of homework, and extensive use of out-of-school classes and tutorials = large amounts of near work
Limited opportunities for time outdoors, reinforced by cultural barriers to spending time outdoors
UNDERLYING BIOLOGICAL PROCESSES
Acceleration of axial elongation, probably due to imposed hyperopic defocus
Disruption of regulation of axial elongation by light and dopamine
OTHER BIOLOGICAL INTERVENTIONS
Atropine, reduced hyperopic defocus and imposed myopic defocus

Highlights

- There is an epidemic of myopia in the developed countries of East and Southeast Asia
- A related epidemic of high myopia is due to early onset myopia and rapid myopic progression
- There is a new and highly prevalent form of high myopia, which is acquired rather than genetic
- Intense education and limited time outdoors play major causal roles in both epidemics
- These modifiable risk factors are already being used in schools to contain the epidemics