Myopia: A Review and Summary

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Overview

It is now widely recognised that Myopia has reached epidemic levels in parts of the world, primarily in the Far East. Myopia is no longer considered just a form of refractive error in need of some form of optical correction. It is fair to say that, increasingly, myopia is now seen as an ocular pathology and a major cause of sight loss globally.[1]

The human costs are considerable in terms of quality of life, but also in economic terms. Uncorrected myopia is the second leading cause of preventable global blindness but also the leading cause of preventable visual impairment in children.[2]

There is an enormous amount of material being released concerning myopia and it's hard to keep up to date with what the current thinking is. I have tried (and hopefully not failed) to bring together the most recent and relevant information so readers can feel they are aware of the myopia trends.

In this series, I will look at the following:

- Epidemiology
- Pathogenesis and pathophysiology – complications of myopia
- Therapies for myopia
- Commercial approaches, communication and the future of myopia

Part 1: Epidemiology and Pathogenesis

Introduction

By definition, **epidemiology** is the study (scientific, systematic, and data-driven) of the distribution (frequency, pattern) and determinants (causes, risk factors) of health-related states and events (not just diseases) in specified populations (neighbourhood, school, city, state, country, global).[3]

This article aims to review the current thinking on the epidemiology of **myopia**.
I have tried to use the latest studies, meta-analyses and systematic reviews published most recently. However, I will add the caveat that the myopia 'landscape' appears to be one which is morphing very rapidly. Between the time I started researching for this article to the point you're reading it now, it's very likely indeed that some data may already be 'obsolete' in as much that newer publications will have been peer reviewed and accepted and perhaps some of the information included herewith has been superseded.

Myopia Definitions

The IMI (International Myopia Institute) was founded through the Brien Holden Institute (BHVI) and the WHO (World Health Organisation). The IMI has released a great deal of valuable material on all areas of myopia and its management. I've used some of this information as well as numerous other papers to compile this series of articles. The IMI has a range of definitions for myopia.

Myopia can be defined or sub-divided in several ways, including:

- Qualitative
- Quantitative
- Descriptive
- Clinical

Qualitative	Quantitative	Descriptive	Clinical
Myopia	Myopia	Pathologic Myopia	Myopic Maculopathy
Axial Myopia	Low Myopia	Myopia Macular Degeneration (MMD)	Presumed Myopic Maculopathy
Refractive Myopia	High Myopia		Myopic Traction Maculopathy (MMT)
Secondary Myopia	Pre-Myopia		Myopia associated glaucoma-like optic neuropathy

From IMI – Defining and Classifying Myopia: A proposed set of standards for clinical and epidemiological studies

Term	Definition
QUALITATIVE	
Myopia	A refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed. This usually results from the eyeball being too long from front to back but can be caused by an overly curved cornea and/or a lens with increased optical power. It is also called near sightedness or short sightedness.
Axial Myopia	A myopic refractive state primarily resulting from a greater than normal axial length
Refractive Myopia	A myopic refractive state that can be attributed to changes in the structure or location of the image forming structures of the eye, i.e., the cornea and lens.
Secondary Myopia	A myopic refractive state for which a single, specific cause (e.g., drug, corneal disease or systemic clinical syndrome) can be identified that is not a recognised population risk factor for myopia development

From IMI – Defining and Classifying Myopia: A proposed set of standards for clinical and epidemiological studies

Term	Definition
QUANTITATIVE	
Myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -0.50D when ocular accommodation is relaxed
Low Myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -0.50D and > -6.00D when ocular accommodation is relaxed.
High Myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -6.00D when ocular accommodation is relaxed.
Pre-Myopia	A refractive state of an eye of ≤ +0.75D and > -0.50D in children where a combination of baseline refraction, age, and other quantifiable risk factors provide a sufficient likelihood of the future development of myopia to merit preventative interventions.

From IMI – Defining and Classifying Myopia: A proposed set of standards for clinical and epidemiological studies

NOTE: The IMI state that we must always use the minus symbol when defining the myopic power and lower than refers to more minus and greater than refers to less minus using standard mathematical approaches.

Term	Definition
DESCRIPTIVE	
Pathologic Myopia	Excessive axial elongation associated with myopia that leads to structural changes in the posterior segment of the eye (including posterior staphyloma, myopic maculopathy, and high myopia-associated optic neuropathy) and that can lead to loss of best-corrected visual acuity.
Myopia Macular Degeneration (MMD)	A vision-threatening condition occurring in people with myopia, usually high myopia that comprises diffuse or patchy macular atrophy with or without lacquer cracks, macular Bruch's membrane defects, CNV and Fuch's spot (Foster-Fuch's spot).

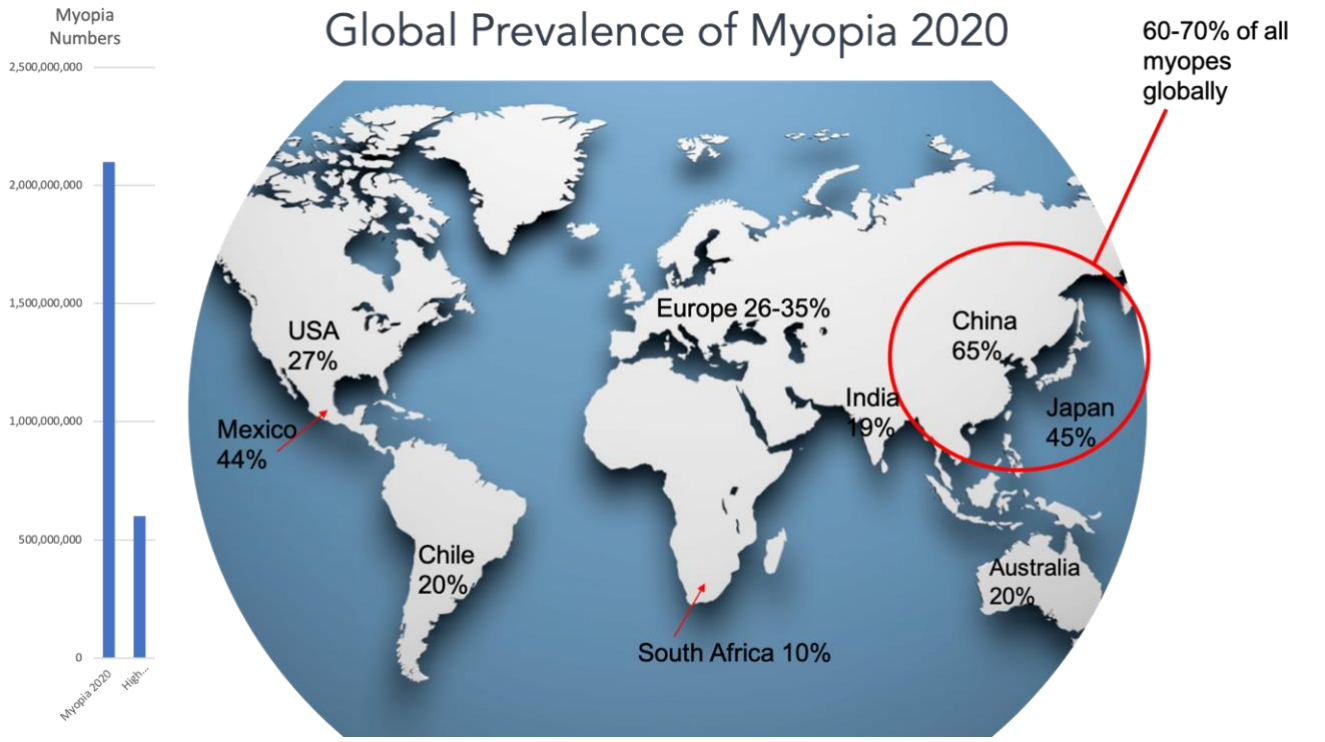
From IMI – Defining and Classifying Myopia: A proposed set of standards for clinical and epidemiological studies

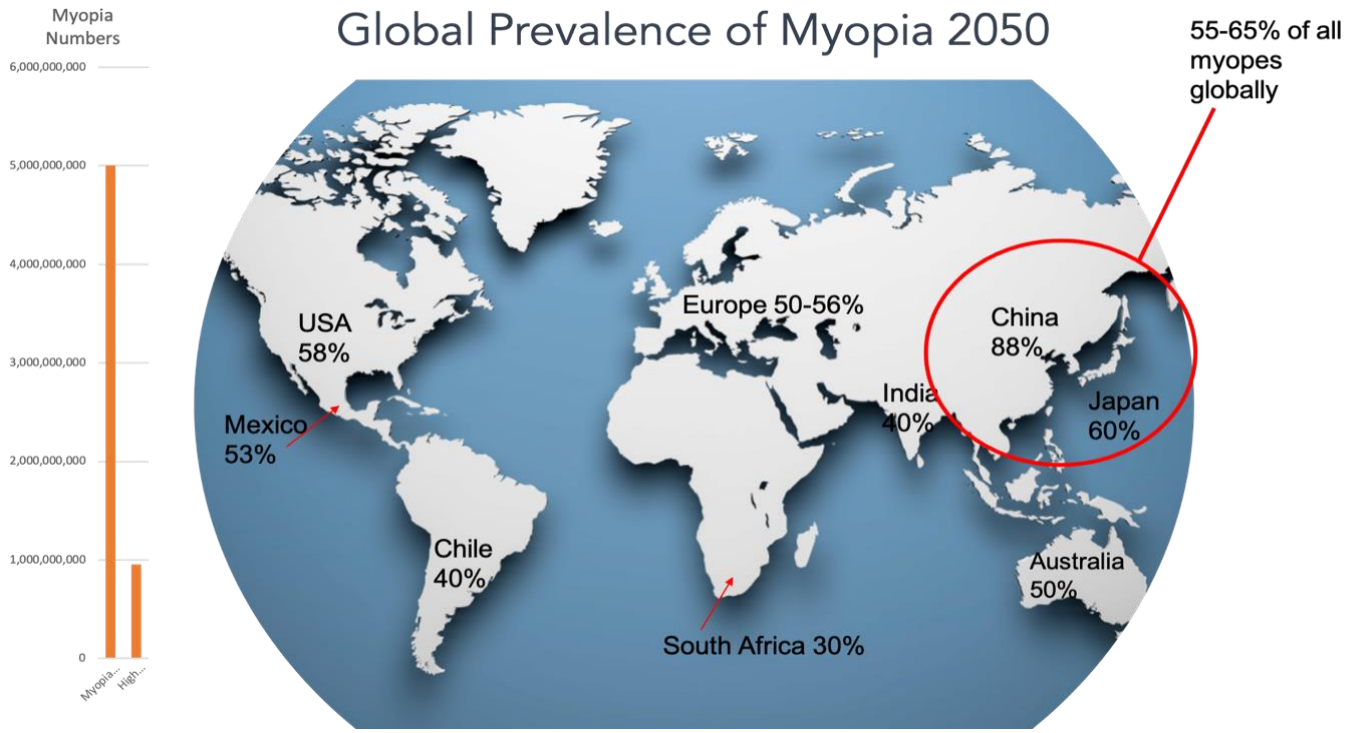
Term	Definition
CLINICAL	
Myopic Maculopathy	Category 0: no myopic retinal degenerative lesion Category 1: tessellated fundus. Category 2: diffuse chorioretinal atrophy Category 3: patchy chorioretinal atrophy Category 4: macular atrophy “Plus” features (can be applied to any category): lacquer cracks, myopic choroidal neovascularisation and Fuch’s spot.
Presumed Myopic Macular Degeneration	A person who has vision impairment and visual acuity that is not improved by pinhole, which cannot be attributed to other causes, and: • The direct ophthalmoscopy records a supplementary lens < -5.00D and shows changes as ‘patchy atrophy’ in the retina or, • The direct ophthalmoscopy records a supplementary lens < -10.00D
Specific clinical conditions characteristic of pathologic myopia	
Myopic Traction Maculopathy (MMT)	A combination of macular retinoschisis, lamellar macula hole and/or foveal retinal detachment (FRD) in eyes with high myopia attributable to traction forces arising from adherent vitreous cortex, epiretinal membrane, internal limiting membrane, retinal vessels and posterior staphyloma.
Myopia-associated glaucoma-like optic neuropathy	Optic neuropathy characterised by a loss of neuroretinal rim and enlargement of the optic cup, occurring in eyes with high myopia with a secondary macrodisc or peripapillary delta zone at a normal IOP.

From IMI – Defining and Classifying Myopia: A proposed set of standards for clinical and epidemiological studies

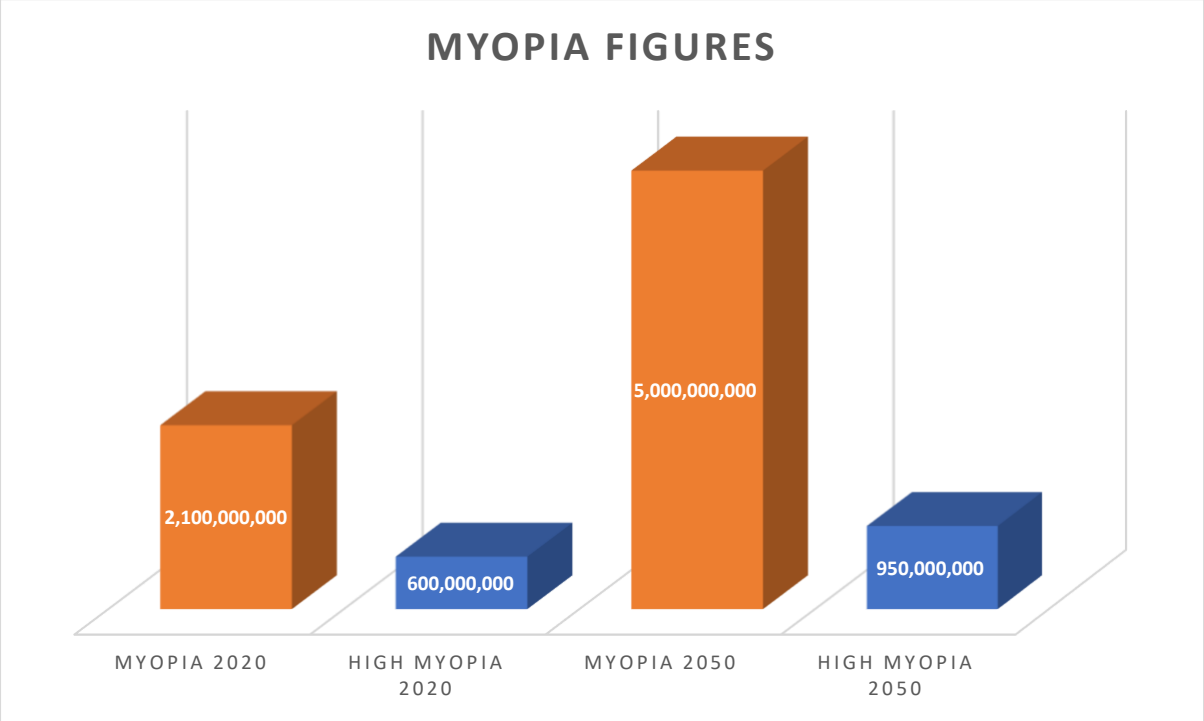
Global Myopia Stats

Most statistics suggest there are around 1.9 to 2.1 billion people with myopia globally at present. The same sources suggest by 2050 between 4.8 and 5.5 billion people will be myopic. Most sources suggest a refraction of ≤-0.50D SER (spherical equivalent refraction) is the point at which someone is myopic.



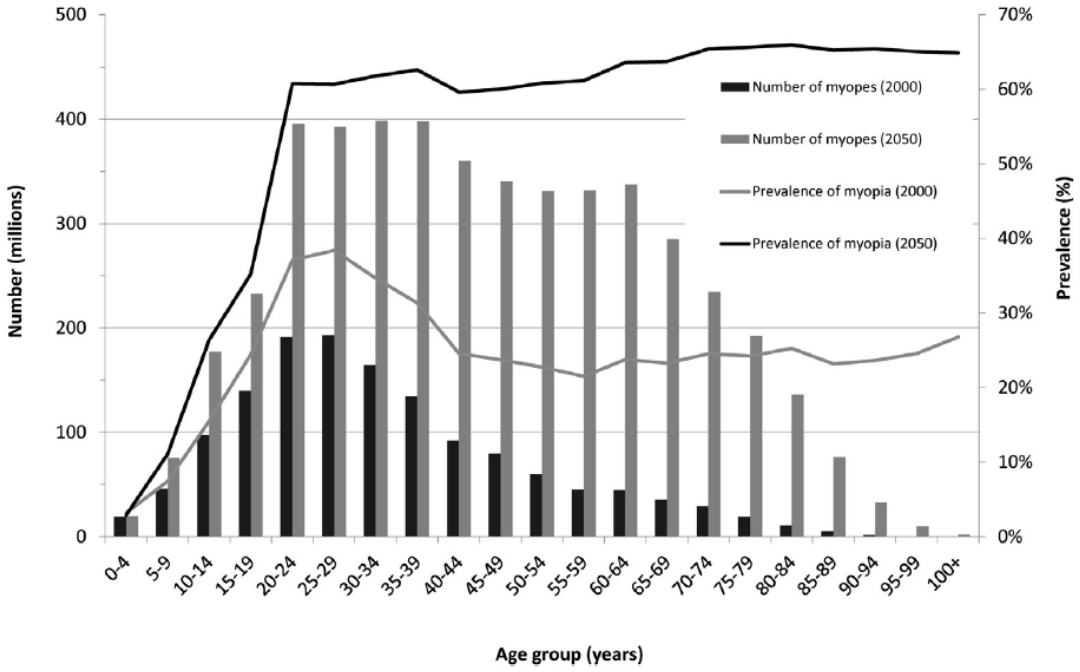


I've used multiple sources and tried to merge the data where possible.

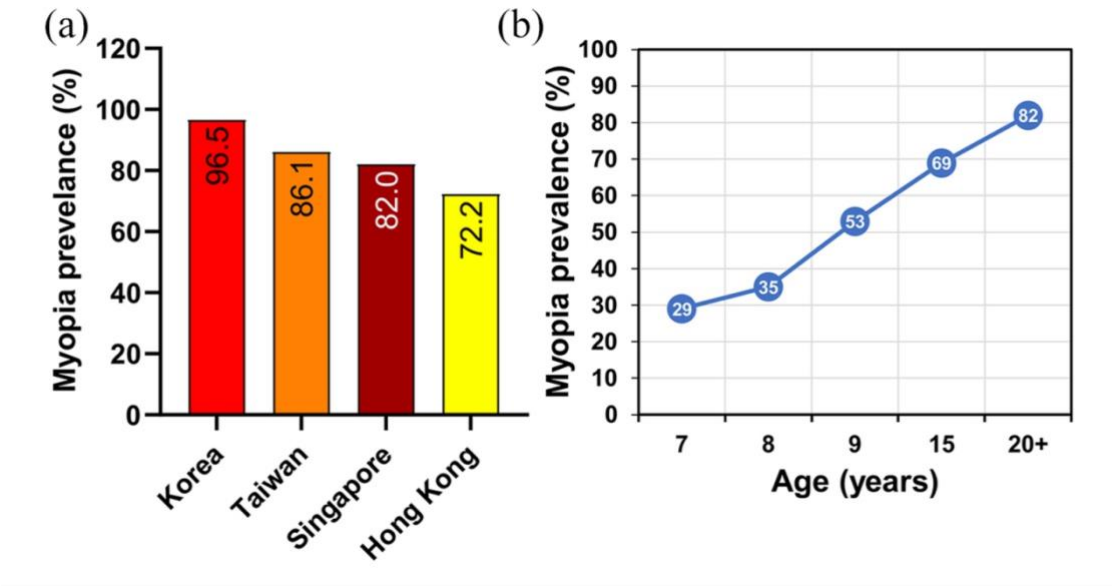


High myopia is generally considered to be ≤-6.00D SER equivalent, though some sources suggest anything below ≤-5.00D SER.

Distribution of Myopia across age groups globally 2000 to 2050[4]



Holden et al - Global Myopia Trends 2000 - 2050



Average myopia prevalence: (a) in young adults of East Asian Countries during 2012–2020 and (b) in Singapore across different age groups during 1999–2001. Muralidharan et al. Light and myopia: from epidemiological studies to neurobiological mechanisms. Ther Adv Ophthalmol 2021, Vol. 13: 1–45

Risk Factors for Myopia and its Progression

It's very evident that there is, of course, some genetic element of myopia. Multiple studies have highlighted numerous genomic variations associated with a much higher risk of developing myopia. This is very evident from the higher prevalence identified in the Far East, but it does not account for all the myopia cases.[5]

The American Academy of Ophthalmology lists the following risk factors for myopia and myopia progression:

- Near work or visual activity with a high accommodative demand
- High level of educational attainment
- Low levels of outdoor activity
- Genetic factors – parental myopia
- Diet
- Television
- Computer games
- Electronic devices
- Pollution
- Female gender
- Season of birth/daylight hours
- Use of a night light
- Younger age at diagnosis
- High IQ score

The major risk factors identified as being the most significant are:

- Genetic / Parental Myopia
- Environmental / Lifestyle
  - Lack of outdoor activity
  - Too much near work
    a) Education
    b) Smart phones, computers, etc

- **Parental income –** this might well become one of the biggest myopia progression risks. If parents can't afford any of the therapies, their children may be at significantly higher risk of sight threatening conditions in later life.

Genetic Factors – it is well established that children with parents who are both myopic have a much higher likelihood of developing myopia themselves. However, this likelihood also increases depending on ethnicity too. Asian children have the highest prevalence of myopia, followed by Hispanics, whilst Caucasians have the lowest childhood prevalence.

The CREAM (Consortium for Refractive Error and Myopia) study has recently shown there are 24 genomic variations which are associated with up to 10X higher risk of myopia.[6]

There have also been suggestions that some therapies for myopia management (MM) are more or less likely to succeed based on certain genetic predispositions, though larger studies are required.

Environmental / Lifestyle – Although genetics increase the pre-disposition to myopia and myopia progression, they simply do not account for the current levels of myopia being witnessed globally, even in the Far East.

Although myopia prevalence is increasing worldwide, genetic predisposition has not significantly changed over the past few decades, this implies that environmental factors, potentially interacting with genetic traits, are the primary cause of the myopia epidemic.[7]

A recent study from Hong Kong and Singapore[8] showed that Covid had caused a significant increase in myopia (SER and axial length) in children. The study concluded that outdoor time had decreased from an average of 1.27 hours per day to an average of 0.41 hours per day whilst at the same time, screen time had increased from an average of 2.45 hours per day to 6.89 hours per day. From this, it was easy to infer that a combination of less time outdoors and increased near work / screen time affected the levels of myopia beyond those perhaps expected due to the genetic pre-disposition. It is likely, however, that the impact of reduced outdoor time and increased near work was high in these children due to their genetic pre-disposition to myopia.

A much older study by Young, F. A. *et al*. *Am. J. Optom. Arch. Am. Acad. Optom.* **46**, 676–685 (1969) showed a large difference between older generations and younger former remote Inuit tribes in Alaska now exposed to modern Western

lifestyle. 2 out of 131 elders in the tribe had myopia, whereas 50% of all the elders' children and grandchildren now living a Western lifestyle had myopia.

A recent review article by Zhao et al[2] listed the following as key risk factors for myopia:

1. Parental myopia – up to 9.47 higher odds ratio (factor vs without factor)
2. Low outdoor activity – up to 1.96 higher odds ratio
3. Time spent on near work/studying/playing – up to 8.33 higher odds ratio
4. High level of education – up to 3.77 higher odds ratio
5. Female gender – up to 2.56 higher odds ratio (Controversial)
6. Urban environment – up to 1.89 higher odds ratio (Controversial)
7. High body mass index – up to 2.7 higher odds ratio (Controversial)
8. Low body mass index – up to 1.4 higher odds ratio (Controversial)

There are fewer studies investigating the effects of gender, urban environment and body mass index, and some studies contradict others. Hence these are considered controversial risk factors. For example, it may be that high body mass index is correlated with less time outdoors and perhaps more time using games consoles or conducting prolonged near tasks. Some studies even postulate that sleep patterns can influence myopisation.

It's very apparent that parental myopia is a strong determinant risk factor which is a genetic risk factor. The amount of near work and/or time spent outdoors are clearly major risk factors and ones that can be changed most easily.

The theories of how increased outdoor activity can have a protective effect against myopia development and progression are many.

These include:

- Higher illuminance levels – animal models found low light levels led to increased axial elongation. However, other studies also found similar effects in human subjects. It has been postulated that high light levels increase the release of dopamine, and this has some form of protective effect not yet fully understood.
- Reduced accommodation / near work due to increased average viewing distance whilst outdoors.
- Reduced pupil size leading to reduced peripheral defocus blur.
- Others such as increased Vitamin D levels and increased spatiotemporal retinal stimulation.

From the protective effect of high illuminance and the animal models of low illuminance, it's clear that time spent indoors could result in increased risk of axial elongation through reduced light exposure. Time spent indoors is also more likely to involve increased near work (such as reading, using a computer / console / smart phone, or doing homework). As we'll see below, there is some syncope likely involved in the pathogenesis and protection mechanisms of myopia development.

A very recent paper by Dhakal, et al conducted an overview of systematic reviews showing that outdoor time is effective at halting the onset of myopia, but likely ineffective at slowing its progress once it has started to develop in children. This has implications for the advice we currently offer. However, as this interesting paper suggests, there are, of course, other health benefits to children if they spend more time outdoors, improving physical and mental health in multiple ways.

Perhaps we should continue with the current advice and just ensure we ask people to do this as a matter of course for all children, especially those who are 'pre-myopic'.

It's also clear that age of onset plays a key role in the levels of myopia progression experienced by subjects. This seems logical, but it may not just be down to more time to 'myopise', it may also be that the emmetropisation drivers are more pronounced in younger subjects.

Theories of Myopisation

Animal studies from the mid 1970's were conducted by Hubel and Wiesel (and also Raviola) in order to understand visual development. Lid suturing of chicks and mice coincidentally led to globe elongation, suggesting lack of visual stimulus, or blurring led to myopic development[9]. Interestingly, where only partial light deprivation occurred on part of the retina, only the affected part of the eye became myopic.

Other studies were conducted where the optic nerves of mice were severed and globe elongation was shown to still take place, suggesting a mechanism within the eye (and not the visual pathway) caused this to occur.

Subsequent studies suggest that defocus in the periphery can cause cessation of globe growth (myopic defocus in the periphery) or continued globe growth (hyperopic defocus blur)[10,11]. The mechanism is not fully understood, but it appears to be related to choroidal thickness variation as a short-term response to blur leading to scleral changes if prolonged. There appears to be some form of muscarinic receptor control also involved.

A very interesting study by Koomson et al ('Relationship between peripheral refraction, axial lengths and parental myopia of young adult myopes' -Journal of Optometry, March 2020) showed that there was significantly more hyperopic defocus in the corrected states of young adult myopes who had myopic parents compared to their counterparts with non-myopic parents.

Many studies have also shown strong links between high AC/A ratios / accommodative lag and myopia development[12,13,14]. Those with higher education levels are more likely to have spent longer doing study and are also likely to continue to do so. Along with this, such individuals are also less likely to spend time outdoors. Even the intensity of reading has been postulated to have an effect on myopia development. Often, socio-economic drivers are at play too.

Several studies suggest that light levels and even light wavelength, including the timing of light exposure, affecting circadian rhythms. Light was first suggested as a

potential cause of ametropia centuries ago and recent studies are starting to suggest these early theories may have been correct[15]. There is evidence of diurnal variation in the anatomy and physiology of the eye through light regulated 'oscillations' in ocular structure. Some of these changes may be regulated in the brain (the suprachiasmatic nucleus) and, it is suggested, some may be retinally driven, via the intrinsically photosensitive retinal ganglion cells (ipRGC) via the pigment melanopsin. Artificial lighting, blue light from smart phones and other devices and poor sleep patterns are therefore all implicated with these potential causes of ametropia.

Ultimately, science does not yet know the actual cause of refractive errors, including myopia.

Imagine a family situation in a prosperous household in Seoul, South Korea.

Both parents are high myopes (<-6.00D SER). They both achieved post graduate qualifications and now have high-powered well-paid jobs that involve long hours. They have two children (brother and sister), both of whom have been driven to be high achievers in education, even attending 'cram schools' and evening lessons. Both have a poor diet and easy access to high sugar and high fat foods.

The influence of their parents also means that both children enjoy reading and they do a lot of their learning on their computers. Neither child spends much time outdoors and lighting levels in their home and classrooms are generally low.

The myopic risk factors affecting the children include genetic pre-disposition due to ethnicity, parental myopia, low time outdoors, increased near work, high AC/A ratio and accommodative lag, low internal light levels, high educational achievement, and perhaps even other factors such as air pollution, female gender, and poor diet.

Clinical Implications

Whatever the causation of myopia, the potential for future ocular complications, particularly with high myopia are considerable.

These potential complications include:

- **Myopic Macular Degeneration (MMD)**
- **Glaucoma**
- **Retinal detachment**
- **Cataract**
- Myopic Neo-vascularisation (MNV)
- Lacquer cracks
- Posterior staphyloma
- Myopic choroidal atrophy
- Myopic traction maculopathy

- Myopic foveoschisis
- Myopic retinoschisis
- Dome shaped macula
- Myopic polypoidal choroidal vasculopathy (PCV)

In terms of the most common conditions, those highlighted in bold are most likely to occur. We will look more closely at these in the second article.

With increasing myopia levels, the risk for all these comorbidities increases significantly.

	Odds Ratio of Visual Impairment by Age 60	**Odds Ratio of Visual Impairment by Age 75**
24-26 mm	1 (reference)	4%
26-28 mm	2 x risk	25%
28-30 mm	11 x risk	27%

	Cataracts	**Retinal Detachment**	**Glaucoma**	**Myopic Maculopathy**
-1.00 to -3.00	2.3	3.1	2.3	2.2
-3.00 to -5.00	3.1	9.0	3.3	9.7
-5.00 to -8.00	5.5	21.5	3.3	40.6
< -8.00	-	44.2	-	126.8

Table showing increasing odds of comorbidities with increasing myopia
Modified from Global Myopia Symposium 2020 and other publications.

Table showing increasing odds of visual impairment with increasing axial length
Modified from Global Myopia Symposium 2020 and other publications.

It's clear that increasing axial length is what leads to the damage in pathologic myopia. Merely measuring the patient's refraction for myopia management (MM) simply will not detect all those at risk of axial elongation and subsequent damage. Therefore, it is imperative that MM should always involve axial length measurement, preferably using optical biometry.

I have seen cases of long axial length where the cornea is also flat, so the amount of myopia SER measured is much lower than if the cornea is 'normal'. Without biometry, the real level of potential damage and the true extent of globe elongation may not be obvious in such patients.

It is not viable for clinicians to try to calculate axial length using refraction and keratometry, many studies have shown that such estimations are not accurate enough and the only sensible approach is to measure axial length[16].

Conclusions

Myopia has numerous causes and there are multiple and varied risk factors which all play a part in affecting the risk of high myopia and the associated comorbidities. Ultimately, the damaging element of myopia is axial elongation. Effective myopia management relies on accurate and repeatable measurement of axial length,

normally through optical biometry as well as cycloplegic refraction in younger children, keratometry and an initial assessment of history and lifestyle.

Optometrists are best placed to help in reducing the rate of progression of this ocular pathology in children and young adults. However, they must ensure that they are confident in understanding the condition and its management. Now is the time to start to help to prevent the long-term risks of sight impairment and severe sight impairment linked to high / pathologic myopia.

In the next part in this small series of articles, we'll look more closely at the pathophysiology of complications arising from myopia.

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