The Risks and Benefits of Myopia Control

Mark A. Bullimore, MCOptom, PhD,[1] Eric R. Ritchey, OD, PhD,[1] Sunil Shah, FRCOphth FRCS (Ed),[2,3] Nicolas Leveziel, MD, PhD,[4,5,6,7,8] Rupert R.A. Bourne, FRCOphth, MD,[8,9] D. Ian Flitcroft, MA DPhil. [10,11]

[1] University of Houston, College of Optometry, Houston, Texas, USA
[2] Birmingham and Midland Eye Centre, Birmingham, UK
[3] Aston University, Birmingham, UK
[4] Centre Hospitalier Universitaire (CHU) Poitiers, Poitiers, France
[5] University of Poitiers, France
[6] Centre d'Investigation Clinique (CIC 1402) , Poitiers, France
[7] Institut National de la Santé et de la Recherche Médicale (INSERM 1084), Poitiers, France
[8] Vision & Eye Research Institute, School of Medicine, Anglia Ruskin University, Cambridge, UK
[9] Department of Ophthalmology, Cambridge University Hospital, Cambridge, UK
[10] Children's University Hospital, Dublin, Ireland
[11] Technological University Dublin, Dublin, Ireland

Corresponding author:

Mark A. Bullimore, bullers2020@gmail.com, 614-202-0299

Conflict of Interest:
Bullimore is a consultant for Alcon Research, Apellis, Arctic Vision, Asclepix, CooperVision, CorneaGen, Essilor, Euclid Systems, Eyenovia, Genentech, Johnson & Johnson Vision, Lentechs, Novartis, Oculus, Paragon Vision Sciences, and Presbia.
Ritchey receives research funding SightGlass Vision and a consultant to Alcon.
Shah, Leveziel and Bourne report no disclosures.
Flitcroft is a consultant to CooperVision, Essilor, Acucela, Nevakar, Alcon, Johnson and Johnson Vision, and Vivior and is conducting trials with Nevakar supplied products.
Acknowledgments:
This work was partially supported by CooperVision, Inc. The authors thank Elizabeth Lumb for suggesting the topic, and Noel Brennan and Paul Chamberlain for suggestions and discussions.

Abstract

Objective: The prevalence of myopia is increasing around the world, stimulating interest in methods to slow its progression. The primary justification for slowing myopia progression is to reduce the risk of vision loss through sight-threatening ocular pathology in later life. The paper analyzes whether the potential benefits of slowing myopia progression by one diopter justify the potential risks associated with treatments.

Methods: First, the known risks associated with various methods of myopia control are summarized, with emphasis on contact lens wear. Based on available data, the risk of visual impairment and predicted years of visual impairment are estimated for a range of incidence levels. Next, the increased risk of potentially sight threatening conditions associated with different levels of myopia are reviewed. Finally, a model of the risk of visual impairment as a function of myopia level is developed, and the years of visual impairment associated with various levels of myopia and the years of visual impairment that could be prevented with achievable levels of myopia control is estimated.

Results: Assuming an incidence of microbial keratitis between 1 and 25 per 10,000 patient years and that 15% of cases result in vision loss, leads to the conclusion that between 38 and 945 patients need to be exposed to five years of wear to produce 5 years of vison loss. Each additional diopter of myopia is associated with a 57%, 20%, 21%, and 30% increase in the risk of myopic maculopathy, open angle glaucoma, posterior subcapsular cataract, and retinal detachment, respectively. The predicted mean years of visual impairment ranges from 4.42 in a –3 D myope to 9.56 in a –8 D myope and a one diopter reduction would lower these by 0.74 and 1.22 respectively.

Conclusions: The potential benefits of myopia control outweigh the risks: the number needed to treat to prevent 5 years of visual impairment is between 4.1 and 6.8 while fewer than 1 in 38 will experience a loss of vision as a result of myopia control.

Introduction

There is compelling evidence that the prevalence of myopia is increasing around the world. The global prevalence is projected to reach 50% by the year 2050 in the absence of effective intervention measures.[1] The rising prevalence of myopia is also accompanied by earlier onset, which in turn leads to an increased risk of high myopia.[2-4] Increased prevalence of myopia, in particular high myopia, in turn is leading to increased visual impairment due to conditions associated with myopia.[5-7] Indeed, myopic maculopathy, also known as myopic macular degeneration, is an increasing cause of visual impairment.[6, 8] The onset of myopic maculopathy is earlier than other major causes of visual impairment, occurring as early as the fifth decade of life,[9] so the years of impairment are commensurately greater than later onset conditions, including age-related macular degeneration (AMD).[10, 11] In both Europe and China, visual impairment from myopic maculopathy is more common than visual loss from diabetic eye disease.[12-14]

These factors have stimulated interest in methods to slow myopia progression, with a number of therapies, including topical atropine, spectacle lenses, dual-focus contact lenses, multifocal soft contact lenses, and overnight orthokeratology showing clinically meaningful slowing of progression.[15-18] The preferred method varies with country and by profession.[19, 20] Regulatory approval can also play a role, although the majority of myopia control in the US is performed off-label as only one device is approved for this indication. The influence of behavioral modifications, such as increased time outdoors and reduced screen time, on progression rate is less clear.[21, 22]

There are, however, varying opinions regarding myopia control. Advocates for myopia control say that “it is unethical not to offer myopia control” and some clinical trials have moved children out of the placebo arm and into the treatment because of the significant treatment benefits.[23, 24] In

contrast, some professional organizations such as the College of Optometrists in the United Kingdom express caution, stating that there is "not enough evidence to support the widespread roll out of myopia control."[25] In addition, some clinicians feel that the increased potential risk of serious ocular infections argue against prescribing contact lenses to children. Other organizations are paying attention to issues related to myopia control. The American Academy of Ophthalmology, for example, has published two Ophthalmic Technology Assessments related to myopia control in recent years,[26, 27] having previously reviewed the safety of one approach,[28] and includes "Prevention of Myopia Progression" in its *Refractive Errors & Refractive Surgery Preferred Practice Pattern*.[29]

In a thoughtful editorial, Modjtahedi and colleagues emphasize the need to increase awareness about the increasing prevalence of myopia.[30] They state that "creating models to accurately stratify patient risk should be a significant focus for future research endeavors" and that "it is essential for ophthalmologists to work with optometrists, who are frontline providers, to determine a collaborative frame work and referral patterns to prevent myopic progression, educate patients on the risks of myopia, and proactively address associated pathology to serve the best interest of our patients."

Methodological Considerations in Risk-Benefit Analysis of Myopia Treatment

These varying perspectives point to the central question that this paper addresses; do the potential benefits of reducing myopia progression with interventions such contact lenses or pharmaceutical options justify the potential risks associated with those treatments? The primary justification for reducing myopia progression is to reduce the risk of vision loss through sight-threatening ocular pathology in later life. Therefore, myopia is being managed because it is a risk factor for visual

impairment. The risk-benefit analysis of any treatment can be considered on a population or an individual basis. Not every patient with a risk factor for a condition will develop the condition, so a number of patients will be treated to avoid one adverse outcome, be it onset of disease or visual impairment. The parameter, number needed to treat (NNT), is widely used in health assessments, and is the reciprocal of the absolute risk reduction (ARR). For example, in the Ocular Hypertension Treatment Study (OHTS),[31] the five-year cumulative probability of developing glaucoma was 9.5% and 4.4% in untreated and treated patients, respectively. Thus, the ARR is 5.1% (= 9.5 – 4.4) and the NNT is 19.6 (= 1 ÷ 0.051). In other words, 20 patients need to be treated for 5 years in order to prevent one case of glaucoma. The ARR and NNT can be balanced by the corresponding parameters; the absolute risk increase (ARI), which is the risk associated with complications of the treatment and the number needed to harm (NNH), which is the number of patients who need to be treated in order to induce a single adverse event. NNH is the reciprocal of ARI.

Slowing myopia progression by one diopter (D) offers the prospect of leaving a myope at –3 D with treatment rather than –4 D, or achieving a final refraction of –7 D with treatment rather than –8 D. On the basis of existing data, both outcomes offer potential benefits but the ARR is much greater in high myopes due to the higher prevalence of myopia-related vision impairment (and the NNT lower) in higher myopes. While the NNT will be greater in lower myopes, they far outnumber higher myopes, even in populations with a high prevalence.[1] The values of NNT and ARR are a function of the effectiveness of a myopia intervention, irrespective of the treatment, and the level of myopia at the start of treatment. In contrast, the values of NNH and ARI relate to the specific method of treatment and are largely independent of the level of myopia. Therefore, the risk-benefit assessment of myopia treatment must consider all these elements, i.e., the effectiveness of an

intervention in slowing down myopia progression, the risk of vision impairment associated with myopia, the level of myopia, and the treatment-modality specific risks. A final consideration is that complications of myopia treatment may occur many decades before any myopia-associated visual loss, so the duration in years of any treatment associated complications affecting vision may greatly exceed the duration of vision loss attributable to myopia later in life.

In order to answer the central question of whether the benefits of active myopia control justify the risks, this review will first summarize the known risks associated with various methods of myopia control, with an emphasis on contact lens wear. Based on available data, the risk of visual impairment and predicted years of visual impairment are estimated for a range of incidence levels. Next, the increased risk of potentially sight threatening conditions associated with different levels of myopia is reviewed. Finally, a model of the risk of visual impairment as a function of myopia level and age is developed, and the years of visual impairment associated with various degrees of myopia and the years of visual impairment that could be prevented with achievable levels of myopia control is estimated.

Risks and Side Effects of Myopia Control

At the time of this review, there are three commonly used myopia control therapies—spectacles, atropine, and contact lenses.

Spectacles

Myopia control with spectacles has a 60-year history, including bifocals,[32-34] progressive addition lenses,[35-37] and, most recently, novel optical designs.[38] In the United States, children are prescribed polycarbonate spectacle lenses and the minimal physical risks associated with these devices are

not increased by the incorporation of a multifocal correction or other designs. Spectacle wear is associated with bicycle crashes in children, although there is no association between myopia or habitual visual acuity and bicycle crashes.[39] The study authors thus attribute the increased risk to a "decrement in the peripheral visual field, thus reducing rider awareness of oncoming vehicles and road obstacles." Of course, correcting myopia and eliminating blurred vision has its own benefits. Some spectacle based myopia treatments, incorporating positive dioptric power will be expected to have modest effects on peripheral vision and it is important that this be quantified.[40] There is also evidence that in the elderly, multifocal and bifocal spectacles, can increase the risk of falls.[41-43] Progressive addition lens and bifocal wearers are twice as likely to fall as non-multifocal wearers,[43] although there is no evidence that the same risks apply in children, perhaps because they rarely wear such lenses.

Atropine

Atropine is an antimuscarinic agent that causes pupil dilation and loss of accommodation, even in concentrations as low as 0.01%.[24, 44] The associated symptoms of photophobia and near vision difficulties vary, as expected, with concentration. This can be mitigated by photochromic lenses, multifocals, or both. In the Atropine for the Treatment of Myopia 2 (ATOM2) study, among children receiving 0.5%, 0.1%, and 0.01% atropine, 70%, 61%, and 6%, requested combined photochromic progressive addition spectacles, respectively while the remainder chose single vision photochromic spectacles.[44] In the Low-Concentration Atropine for Myopia Progression (LAMP) Study, the need for photochromic or progressive addition lenses did not vary with atropine concentration among the over 400 children randomized to 0.01%, 0.025%, 0.05% atropine or placebo.[24] Between 30 and 40% children needed photochromic spectacles in all groups including the placebo. Furthermore, four children needed progressive addition spectacles,

including one in the placebo group. The most common ocular side effect in the aforementioned clinical trials was allergic conjunctivitis which occurred in 3 to 7% of children in each arm, including those receiving placebo in the LAMP Study, suggesting that the preservative or other excipient in the solution may be the causative agent.

With any topically applied drug, there is a risk of systemic absorption. The systemic effects of atropine are well documented and include dryness of skin, mouth and throat due to decreased mucous membrane secretion, restlessness, irritability or delirium due to CNS stimulation, tachycardia, and flushed facial skin due to its non-selective antimuscarinic properties.[45] In spite of atropine's use in a large number of clinical trials for myopia control[24, 44, 46] and for penalization therapy for amblyopia,[47-50] involving hundreds of children there have been no reports of systemic adverse events related to topical atropine.

The Ophthalmic Technology Assessment on Atropine for the Prevention of Myopia Progression in Children by the American Academy of Ophthalmology does not list any safety concerns.[26] The review does not discuss the risks associated with increase retinal light levels and AMD with atropine-induced mydriasis, but this remains a theoretical possibility, although the dilation with low concentrations is modest, along with its impact on any long-term cumulative dose, and may be offset by sunglasses. This theoretical risk is partly mitigated by the fact that myopia is a protective risk factor for AMD,[51-53] possibly by the reduced light flux density that results from a longer eye.[54] There are also potential concerns from premature presbyopia induced by prolonged partial cycloplegia, but we are only aware of anecdotal reports. A seven-year review of atropine in Taiwan, where atropine has been used for several decades, did not include any data on side

effects.[55] This is clearly an area where further data are required. In summary, the risk of vision loss associated with topical atropine, particularly lower concentrations would appear to be very low, but the prescription of photochromic spectacles or soft contact lenses may be required at higher concentrations.

Soft Contact Lenses

The complications associated with soft contact lens wear have been well documented. Non-infectious inflammatory events may involve the cornea, conjunctiva, and periorbital tissues. Those affecting the cornea are collectively termed corneal infiltrative events and include infiltrative keratitis, contact lens associated red eye, contact lens peripheral ulcers and occur at a rates between 300 and 400 per 10,000 patient years in adults.[56-58] These are not considered to be sight-threatening and are managed by temporarily discontinuing contact lens wear, with the possible addition of a topical prophylactic antibiotic. Microbial keratitis is less common, with an incidence of around 20 per 10,000 patient years in adults wearing lenses on an overnight basis but only between 2 and 4 per 10,000 patient years for daily-wear patients. Major studies of the incidence of microbial keratitis associated with soft contact lenses are summarized in Table 1.[59-66] Regardless of the incidence, 15% or fewer of cases of microbial keratitis result in vision loss. [61, 64-66]

With respect to soft contact lenses for myopia control, three important variables influence the risk of corneal infiltrative events and microbial keratitis: storage, material, and patient age. First, many contact lenses designed for myopia control, though not all, are prescribed using a daily disposable replacement schedule.[23] The benefits of eliminating contact lens storage as a risk factor cannot be understated. For example, Stapleton et al. found that the risk of moderate and severe microbial keratitis in daily wear contact lens users was increased 6.4 times by poor storage case hygiene and

5.4 times by infrequent storage case replacement.[67] The authors note the previously-reported associations between solution type and more severe disease for Acanthamoeba and Fusarium keratitis.[68-70] Again, these risks can be substantially reduced with daily disposable lenses. Second, contact lens material can also affect the risk for corneal infiltrative events. Over the past 20 years there has been a shift from traditional hydrogel materials towards silicone hydrogel materials which provide higher oxygen transmission.[71] Silicone hydrogels may increase the risk of corneal infiltrative events, but the broad benefits of these lenses outweigh this risk for many patients.[72]

Third, age is a significant, but non-linear risk factor for contact lens-related adverse events. A retrospective, observational study evaluated the risk factors that interrupt soft contact lens wear among children, teenagers, and young adults.[57] The authors reported 187 corneal infiltrative events in 3,549 patients for 14,305 visits observing 4,663 soft contact lens years including an average of 20 months of soft contact lens wear in 1,054 patients under the age of 18 years. The corneal infiltrative events included 8 cases of microbial keratitis, 110 of infiltrative keratitis, 41 contact lens peripheral ulcers (CLPUs), 14 contact lens-induced acute red eye (CLARE) with infiltrates, and 13 CLARE without infiltrates. The risk of a corneal infiltrative event increased in a nonlinear fashion up to age 21 and then decreased, with the peak years at risk from age 15 to 25 years.

Figure 1 replots the published data on corneal infiltrative events in terms of incidence (cases per 10,000 patient years of wear).[57] The figure demonstrates the marked lower rate of corneal infiltrative events in patients 8 to 12 years old (97 per 10,000 patient years, 95% CI, 31–235) than in patients 13 to 17 years old (335 per 10,000 patient years, 95% CI, 248–443). The incidence of microbial keratitis per 10,000 patient years varied dramatically with age group: 0 (95% CI, 0–70)

in 8- to 12-year olds, 15 (95% CI, 2–48) in the 13- to 17-year olds, 33 (95% CI, 12–73) in the 18- to 25-year olds, and 7 (95% CI, 0.4–37) in the 26- to 33-year olds.

The low rate of corneal infiltrative events in patients 8 to 12 years old from the above retrospective study of soft contact lens wear is supported by prospective studies. Bullimore reviewed data from nine prospective studies representing 1,800 patient years of wear in 7- to 19-year-olds.[73] The majority of the studies were at least one year in duration, fit children as young as 8 years, and represented over 150 patient years.[23, 74-82] Pooling data across the nine studies, 14 corneal infiltrative events were reported representing an incidence of 78 per 10,000 patient years (95% CI, 44–127). None of the studies reported any cases of microbial keratitis, giving a 95% CI of 0 to 21 per 10,000 patient years. A subsequent retrospective review of over 800 patient years of wear in children also found no cases of microbial keratitis,[83] although a recent clinical trial of nearly 900 patient years of wear in children reported one "presumed case."[84]

In summary, the incidence of corneal infiltrative events and microbial keratitis in children 12 years and younger—in whom myopia control is likely to be initiated—is no higher than that observed in adults and may be lower.[85, 86] The peak complication rate at 18-25 years suggests that behavioral and lifestyle factors may have a significant influence.[87] For 8–12-year-olds, parents are more likely to be involved in lens care. It is also possible that young children wearing contact lenses are a pre-selected group, because they are likely to wear them responsibly. If contact lenses were worn by a higher proportion, the low complication rate could conceivably increase.

Overnight Orthokeratology

While the incidence of adverse events associated with soft contact lenses is well established, data for overnight orthokeratology are scarce. Even in large-scale epidemiological studies, where all lens types were considered, no cases of microbial keratitis in orthokeratology wearers are reported.[65] Of course, this reflects the relatively small proportion of patients wearing this particular modality, rather than a low level of risk. Globally, orthokeratology represented 28% of all rigid contact lenses prescribed among minors between 2005 to 2009.[88] In the US, *all* rigid lenses account for around 10% of all contact lenses while patients 15 years and under account for only 11% of lens fits.[71] Recent data suggest a steady, but small, increase in orthokeratology fitting through 2017, but only represents around 1% of all contact lens fits, with large geographical variations.[89] Studies of the incidence of microbial keratitis associated with contact lenses typically accrue cases from hospitals and other tertiary care settings and are unlikely to identify cases associated with overnight orthokeratology due to limited exposure, rather than the underlying risk. Beginning in 2001, case series and case reports of microbial keratitis associated with overnight orthokeratology began to appear in the literature. The first 50 published cases were summarized in a 2005 paper[90] and updated with total of 123 cases two years later.[91]

In 2008, the American Academy of Ophthalmology published an Ophthalmic Technology Assessment for on the *Safety of Overnight Orthokeratology for Myopia*.[28] The main source of adverse events was 38 case reports or noncomparative case series, representing more than 100 cases of infectious keratitis. The report was unable, however, to identify the incidence of complications associated with overnight orthokeratology, nor the risk factors for various complications.

The only comprehensive estimate of the incidence of microbial keratitis associated with overnight orthokeratology comes from a retrospective study, mandated and approved by the US Food and Drug Administration (FDA).[92] Two hundred randomly selected practitioners, stratified by company and number of lens orders were asked to provide details on fitting date, and patient age at fitting, and follow-up duration for up to 50 randomly-selected lens orders. The practitioners were also asked to provide comprehensive information on any of these patients experiencing an episode of painful red eye that required a visit to a practitioner's office. Patients treated by another practitioner or with less than twelve months of documented follow-up were mailed a questionnaire regarding months of lens wear, any adverse events and the name and address of the treating practitioner. Data were submitted by 86 practitioners on 1494 unique patients. Limiting the sample to at least three months of wear from 2005 onwards resulted in 1,317 patients (49% adults 51% children) representing 2,599 patient years of wear. Of the 50 episodes of painful red eye identified, eight presented with a corneal infiltrate of which six were in children. Of these cases, two were judged to be microbial keratitis by a five-person masked, expert review panel and neither resulted in any long-term loss of visual acuity. The overall incidence of microbial keratitis was 7.7 per 10,000 patient years (95% CI, 0.9–27.8). Both cases occurred in children giving an incidence of 14 per 10,000 patient years (95% CI, 1.7–50.4).[92]

In summary, the incidence of microbial keratitis in children wearing overnight orthokeratology is similar to that reported for other overnight modalities in adults, notably extended wear of soft contact lenses (see Table 1).

Modelling Risk of Vision Loss Associated with Myopia Treatment

Given the above evidence, the risk of vision loss with spectacle lenses and atropine are considered negligible, and it is assumed that the majority of risk associated with myopia control will occur with contact lenses. The incidence of microbial keratitis varies with contact lens wear and all available estimates have some uncertainty as indicated by the breadth of the confidence intervals. Overnight orthokeratology in children carries a risk similar to other overnight modalities with the only estimate being 14 per 10,000 patient years (95% CI, 1.7–50).[92] Conversely, daily soft lens wear in children appears to be at least as safe as in adults; daily disposable lenses may further mitigate the risk.[65] Thus, in evaluating vision loss associated with contact lens wear, a range of incidence should be considered.

The above summary of the risks associated with myopia control expresses the data in terms of incidence. These data must be interpreted in terms of years of visual impairment associated with said risk. In order to estimate years of visual impairment, the following assumptions were made:

- 15% of all cases of microbial keratitis result in visual impairment (two lines of visual acuity or more) as this is the most conservative estimate.[65]
- Each myopia control patient is exposed to 5 years of contact lens wear during the period of myopia control and the risk is constant over this time. Five years was chosen so that 1-diopter of control could be reasonably anticipated.[93]
- Any serious adverse event occurs during this five year period of wear, at a mean age of 12 years.
- Mean life expectancy is 82 years (https://www.mortality.org), so each adverse event causing immediate vision impairment results in 70 years lived with this vision impairment.

Table 2 displays the years of vision loss for three levels of risk, expressed as annual incidence per 10,000 patients. The incidence values are intended to span the range reported in the literature from daily wear (1 per 10,000) to overnight wear (25 per 10,000).[65] For example, the incidence of microbial keratitis with daily-disposable soft lenses could be assumed to be 1 per 10,000 patient years of wear.[65] The incidence of vision loss due to microbial keratitis is then estimated to be 0.15 per 10,000 patient years of wear, but five years of exposure would result in a cumulative incidence of vision loss of 0.75 per 10,000 patients (= 5 × 0.15). Finally, this vision loss is experienced for 70 years yielding a value of 53 years of vision loss per 10,000 patients (= 70 × 0.75). The years of vision loss are proportionately higher for incidence values of 5 and 25 per 10,000 patient years, the latter representing the upper limits for overnight orthokeratology. The effect of increasing exposure is easily calculated, e.g., for 10 years of exposure the cumulative incidence of vision loss and the number of years of vision loss would be twice that for five years of exposure. Likewise, using an incidence of 50—the upper 95% limit for overnight orthokeratology in children[92]—the values in the final column would be doubled.

The NNH for one and five years of visual impairment are also shown in Table 2. For example, 38 patients would have to wear contact lenses with a medium risk of microbial keratitis (incidence = 5 per 10,000 patient years) for five years to result in one year of visual impairment. Likewise, 190 patients would have to wear them to result in five years of visual impairment.

The Potential Benefits of Myopia Control

Bullimore and Brennan recently summarized the benefits of lowering levels of myopia.[94] These include better uncorrected and corrected visual acuity, improved vision-related quality of life, and reduced dependence on correction. Likewise, a myope is likely to consider refractive surgery to correct their refractive error once they reach adulthood. In this regard, the lower the level of myopia, the higher the likelihood of minimal residual refractive error, leading to better postoperative uncorrected visual acuity and fewer secondary surgical enhancements. Furthermore, postoperative visual quality is poorer in patients with higher levels of preoperative myopia.[95] Finally, higher myopia, thinner corneas, or both, can make them poor candidates for LASIK due to the increased risk for postoperative corneal ectasia[96] and alternative procedures may be needed. In spite of these visual and refractive benefits of lower levels of myopia, the greatest benefit of lower levels of myopia is a reduced risk of blinding eye disease. The following sections briefly review the association between level of myopia and myopic maculopathy, cataract, retinal detachment and glaucoma. The reader is also referred to the recent comprehensive review by Haarman et al.[7]

Myopia and the Risk of Myopic Maculopathy

There have been a number of large population-based studies of the prevalence of myopic maculopathy in older patients. Bullimore and Brennan[94] summarized data from five that present the prevalence as a function of level of myopia in tabular or graphical form.[97-101] Figure 2A shows the prevalence of myopic maculopathy as a function of degree of myopia for these five studies. Data are taken directly from each publication, digitizing figures to extract values when necessary.[99, 102] Where prevalence was presented with data for ranges of myopia, the midpoint of

each range was used. The highest level of myopia was often defined without an upper limit, so these data are not shown. In all studies, the prevalence of myopic maculopathy increases exponentially at higher levels of myopia. Figure 2B replots the prevalence of myopic maculopathy on a logarithmic scale. This results in an apparent linear relationship, with all studies showing a similar trajectory.

Since publication of the above data, four more reports of the relation between myopia level and the prevalence of myopic maculopathy have been published,[102-105] plus a fifth that does not contain sufficient categories.[106] All available studies are summarized in Table 3 and represent data from over 10,000 myopes. The definition of myopia varies among studies, with two limited to high myopia. Likewise, the definition of myopic maculopathy varies slightly among studies with data for "macular complications" used from one.[105] Linear regression was performed on each dataset and the results displayed in Table 3. The slope of log(prevalence) per diopter ranges from 0.095 to 0.271. Taking the antilog of these slopes gives the ratio of prevalence to diopter—a range of 1.24x to 1.87x with a crude average of 1.58x. Expressed as a percentage, each diopter of myopia increases the prevalence of myopic maculopathy by 58%. Restated, controlling myopia progression such that a patient's refractive error is lower by 1 D should reduce the likelihood of them developing myopic maculopathy by 37% (= 1 – 1/1.58). Furthermore, given the apparent constant slope of the data in Figure 2B, this treatment benefit is constant across a range of myopia severities. Thus, while the overall risk of myopic maculopathy is higher in a –6 D myope than in a –3 D myope, slowing progression by 1 D during childhood should lower the risk by 37% in both.

Myopia and the Risk of Other Ophthalmic Diseases

Cataract

Myopia is associated with other eye diseases. With respect to cataract, the association between myopia and posterior subcapsular (PSC) cataract is the most robust.[107] A few studies have reported the prevalence of PSC at different degrees of myopia (Table 4).[108-111] The same methodology as described in the previous section was used to determine the relation. The slope of log(prevalence) per diopter ranges from 0.017 to 0.103. Converting to a ratio of prevalence to diopters of myopia shows a range of 1.02x to 1.40x with a crude average of 1.21x. Thus, each diopter of myopia increases the prevalence of PSC cataract by 21%. While not directly comparable, Pan et al. reported that each diopter of myopia increases the odds of PSC cataract by 1.14x in a sample of 5,474 Singaporean Malays.[108] For cortical cataract, three of the studies in Table 4 show ratios of prevalence to diopter between 0.96x and 1.01x while one shows a ratio of 1.16x.[111] These same four studies show no relation between degree of myopia and nuclear cataract. The ratio of prevalence to diopters of myopia ranges from 0.95x to 0.99x with a crude average of 0.97x. It is important to note that many studies do show a relation between any myopia and nuclear cataract.[107] Unfortunately, this relation is confounded by the myopic shift associated with nuclear cataract. Studies that have measured the ocular components find that nuclear cataract is associated with myopia, but not with axial length or its surrogates.[107, 108, 112]

Retinal Detachment

The association between retinal detachment and myopia is well established. While the global incidence of retinal detachment has been estimated at 0.01% per year,[113] three case-control studies allow quantification of the relation between myopia level and incidence of retinal detachment

(Table 5).[114-116] Other studies are listed that have based estimates of the relation on their cases of retinal detachment and published estimates of the distribution of refractive error.[10, 117, 118] The data from the most recent study[119] were combined with recent estimates of myopia prevalence in the United Kingdom[120] to derive the relation. The slope of log(incidence) per diopter ranges from 0.096 to 0.173. Converting to a ratio of incidence to diopters of myopia shows a range of 1.15x to 1.49x with a crude average of 1.30x. Thus, each diopter of myopia increases the incidence of retinal detachment by 30%.

Glaucoma

Individuals with myopia have around twice the risk of developing open angle glaucoma compared with those without myopia. A meta-analysis of eight large studies estimated odds ratios of 2.46 (95% CI, 1.93–3.15) and 1.77 (95% CI, 1.41–2.23) for myopia above and below –3 D, respectively.[121] Table 6 summarizes data from five studies that present data on prevalence of open angle glaucoma for three or more levels of myopia.[122-127] The slope of log(prevalence) per diopter ranges from 0.045 to 0.096. Converting to a ratio of prevalence to diopters of myopia shows a range of 1.09x to 1.39x with a crude average of 1.20x. Thus, each diopter of myopia increases the prevalence of open angle glaucoma by 20%. Longer axial length is independently associated with an increased prevalence of open angle glaucoma.[128, 129] Kuzin et al. estimated that each millimeter longer axial length was associated with a 26% higher prevalence.[129] While the association between degree of myopia and prevalence of open angle glaucoma appears robust, there appears to be little or no relationship between myopia and rate of progression of glaucoma,[130, 131] although higher myopes may have more severe disease and present diagnostic challenges.

Myopia and the Risk of Visual Impairment

Myopic maculopathy is associated with poorer visual acuity.[97, 102] Vongphanit et al. reported that 39% of 67 eyes with myopic maculopathy had visual impairment, based on a definition of 20/40 or worse.[97] Wong et al. reported that among 119 study participants identified as having myopic maculopathy, 26 (21.8%) had visual impairment in at least one eye, based on the same criterion.[102] Finally, Gao et al. report that visual impairment was present in 10 participants (17.5%) based on the better eye, and using the criterion of worse than 20/60.[99] While most of these studies, and the others in Table 3, precede the international photographic classification and grading system for myopic maculopathy,[132] the criteria used to define myopic maculopathy are broadly similar: Category 2 (diffuse chorioretinal atrophy), Category 3 (patchy chorioretinal atrophy), Category 4: (macular atrophy) or one of the ‘‘plus’’ features: lacquer cracks, myopic choroidal neovascularization, and Fuchs spot. Category 1 (tessellated fundus) is not usually considered to represent myopic maculopathy as it is not associated with vision loss. The risk of vision loss is also dependent on age, refractive error and myopic maculopathy category.

Of course, any increase in the risk of visual impairment associated with myopia will be due to a range of diseases including myopic maculopathy. Given that multiple myopia-associated diseases can lead to visual impairment, the relevant parameter is the cumulative risk of all myopia associated pathologies. A few studies report visual impairment from all causes as a function of level of myopia.[98, 105, 133, 134] Among these, Tideman et al. published the most comprehensive data on visual impairment and myopia, analyzing data from 15,404 adults (mean age 61±11 years) in whom refractive error and visual acuity had been measured.[134] In their Figure 2, they plot the cumulative risk of visual impairment as a function of age for five levels of myopia for a criterion of 20/67 (0.3 decimal acuity). Their graph was digitized, and the cumulative risk of visual

impairment is replotted as a function of myopia level for five ages in Figure 3. The midpoint of each refractive error range was used and a value of –16 D chosen for the highest range. The data show a clear exponential trend at all ages, a feature that is emphasized by plotting them on a logarithmic scale. On the logarithmic scale, all ages follow a similar, near parallel trajectory. The best-fit slopes of these lines (not shown) range from 1.24 to 1.31x indicating that the cumulative risk of visual impairment increases by between 24 and 31% per diopter of myopia across a broad age range.

From the values in Figure 3, the odds of visual impairment were calculated using a reference prevalence of 1.26%. This reference was calculated from the distribution of visual acuity among the four population-based cohorts used by Tideman et al., excluding the case-control study (their Table 1).[134] Figure 4 shows the $\log_{10}$odds ratio of visual impairment as a function of age for five levels of myopia. Multiple linear regression was used to estimate $\log_{10}$odds ratio as a function of age and refractive error. The equation for best-fit regression line shown in Figure 4 is:

$$\text{Log}_{10}\text{Odds Ratio for Visual Impairment} = 0.057\text{Age} - 0.122\text{Rx} - 4.03$$

Thus:

$$\text{Cumulative Odds of Visual Impairment} = 10^{(0.057\text{Age} - 0.122\text{Rx} - 4.03)}$$

Note that the coefficients show that the impact of one diopter of myopia is around twice that of one year of aging.

Using this equation, the age-related cumulative risk of visual impairment can be modeled for different myopia levels. Figure 5 shows the cumulative risk of visual impairment as a function of age for seven levels of myopia and two different definitions of visual impairment. On the left is the model for the criterion for visual impairment used in the original data[134] (worse than 20/67 or

6/20) which is similar to the WHO's ICD-11 definition of moderate visual impairment (worse than 20/60 or 6/18). The model on the right is for the US definition of visual impairment (worse than 20/40) which is also the WHO's ICD-11 definition of mild visual impairment. These were calculated using the above equations for the odds of visual impairment but using an overall prevalence of 3.63%. This value was again calculated from the visual acuity distribution among the four population-based cohorts used by Tideman et al., excluding the case-control study (their Table 1).[134] As would be expected both sets of curves follow a sigmoidal pattern.

In order to further assess the impact of age and myopia on the visual impairment for individuals and the population, the above functions were combined with life expectancy data for the US population (https://www.mortality.org) to estimate the number of visually impaired persons per 10,000 births as a function of age and myopia. A simple combination of the functions results is a series of asymmetric bell curves shown in Figure 6. The peak of the distribution shifts from 86 years for –2 D of myopia to 81 years for –8 D, and thereafter decreases by approximately one year for each additional diopter of myopia up to –15 D (not shown). The presence of an earlier peak in higher myopes than in lower myopes reflects the earlier onset of myopia-related retinal complications[105] than conditions where myopia is not a risk factor and may be protective, i.e., AMD and diabetic retinopathy.[125] Beyond the peak, the influence of mortality outweighs the increased risk of visual impairment, resulting in a steadily decreasing probability of living with visual impairment.

The mean number of years of visual impairment experienced by a patient over their lifetime may be estimated by simply integrating the area under each curve. For example, a –3 D myope will experience an average of 4.42 years of visual impairment (US definition and WHO definition of

moderate visual impairment), whereas a –8 D myope will experience 9.56 years of visual impairment. These data are summarized in Table 7. Furthermore, the benefit of slowing myopia progression by one diopter of myopia can be calculated as the difference in years of visual impairment (Table 7). Controlling myopia such that a patient destined to be a –3 D myope instead ends up as a –2 D myope should prevent an average of 0.84 years of visual impairment (= 5.25 – 4.42). Likewise, one diopter of myopia control such that, ultimately, a –8 D myope is instead a –7 D myope would save 1.22 years of visual impairment (= 9.56 – 8.35).

Table 7 also shows the number of patients needed to treat (NNT)—the number slowed by one diopter—to prevent five years of visual impairment. For –3 D of myopia the NNT is 6.75, while for –8 D of myopia the NNT is 4.11. Finally, the reduction in myopia needed to prevent one year of visual impairment in a given patient can be estimated. For –3 D of myopia a 1.38-D reduction is needed, but for –8 D of myopia, only a 0.82-D reduction is required. To put these figures in context, the NNT for preventing one nonfatal heart attack in asymptomatic adults 40 years or older with statin medications is 217, and the NNT to prevent one nonfatal stroke, 313.[135]

The corresponding data for the WHO definition of moderate visual impairment are shown in Table 8. Both the mean years of visual impairment and the years of visual impairment prevented by a 1 diopter reduction in myopia are smaller than for the US definition. Likewise, the NNT to prevent one year of visual impairment and the reduction in myopia needed to prevent one year of visual impairment are higher.

Comparing the Risks and Benefits of Myopia Control

The above model shows the potential benefit of slowing myopia progression such that a patient ends up with one diopter less than their original refractive trajectory. Recent randomized clinical trials suggest that one diopter of myopia control is achievable given that a 0.73 D reduction in progression was achieved with three years of treatment with a daily-disposable soft contact lens incorporating a dual-focus optical design,[23] a 0.71 D reduction with three years of executive bifocal spectacle wear,[33] and a 0.82 D reduction with two years of 1% atropine therapy.[46] While few studies have reported myopia control on patients beyond 3 years,[136, 137] the above results suggest that one diopter is feasible, but would take up to five years of treatment.[93]

The above model predicts that one diopter of myopia control can prevent between 0.74 and 1.22 years (9 to 15 months) of visual impairment for myopia levels between –3 and –8 D. Referring back to the years of visual impairment that might be associated with five years of contact lens wear (Table 2), the range corresponding to the published range of incidence levels of microbial keratitis is between 53 and 1,312 years of visual impairment per 10,000 patients. This represents a range of 0.0053 to 0.1312 years per patient. This leads to the reasonable conclusion that the benefits of myopia control far outweigh the risks of the five years of contact lens wear required to achieve this one diopter of control. Another way to compare risk and benefit is using NNH and NNT. For the range of values in Table 2 the NNH for five years of visual impairment is between 38 and 945. In other words, even for the highest incidence of microbial keratitis (25 per 10,000 years), 38 patients would need to be exposed to induce five years of visual impairment. In contrast, only 4.11 to 6.75 patients would need to have their ultimate myopia level reduced by one diopter to prevent five years of visual impairment. For the level of risk that might be expected for myopia control using daily disposable contact lenses, (1 per 10,000 years) the NNH outweighs the NNT by a

ratio of 140 for a –3 D myope (=945/6.75) and 230 for a –8 D myope (=945/4.11). Thus, for therapies that carry low risk, the benefits are compelling, but for smaller amounts of myopia control, or higher levels of risk, the benefits are still meaningful. For example, slowing myopia by 0.50 D—equivalent to slowing axial elongation by 0.18 mm[138]—would still lower the risk of myopic maculopathy by 20% and, on average, prevent six months of visual impairment.

This comparison reflects conservative estimates of the total treatment benefit from myopia control derived from current methods of management.[93] The benefits would scale up if a greater level of myopia control could be achieved, especially for higher myopes. For example, the data in Table 7 can be used to calculate the benefit of 2-diopters of control in a patient destined to be a –7 D myope (8.35 – 6.19 = 2.16 years of visual impairment) or 3-diopters of slowing in a patient who would otherwise end up at –6 D myope (7.22 – 4.42 = 2.8 years of visual impairment).

An important consideration is that values for visual impairment associated with myopia are for bilateral impairment (tables 7 and 8), whereas the estimates of vision loss associated with contact lens wear in Table 2 are monocular and correspond to rates based on two lines loss of visual acuity.[65] Bilateral cases of contact lens-related microbial keratitis are rare. For example, among the 367 cases reported by Dart et al., only one was bilateral.[66] Even in large case series of acanthamoeba keratitis bilateral infection occurs in only 5 of 183[139] and 3 of 154 cases.[140] Furthermore, while some cases of vision loss due to contact lens-associated infections require corneal transplants, less severe cases might be ameliorated with rigid contact lenses or phototherapeutic keratectomy.[141, 142] In summary, the binocular visual impairment associated with contact lenses is far lower than the binocular visual impairment associated with each additional diopter of myopia. Of course, a patient who has reduced vision in one eye is then at greater risk of

bilateral visual impairment throughout the rest of their life as a result of other causes[143] and the loss of binocularity could impact future career choices and quality of life.

Limitations of Model

A number of assumptions are required to produce a model of risk/benefit from myopia control and the accuracy of such a model is dependent on the validity of these assumptions. Our model of visual impairment and myopia uses some interpolation regarding age as only data through 75 years were available. It is possible that relation between myopia and visual impairment is different at older ages, for example, the prevalence of age-related macular degeneration is lower in myopes.[125] The rising worldwide prevalence of myopia is leading to secular trends. A large population-based Japanese study reported that the age-adjusted prevalence of myopic maculopathy doubled in a decade.[8] Likewise, there has been a 44% increase in the incidence of retinal detachment in the Netherlands over a 7-year period that the authors attribute to myopia, although this is a small contributor to visual impairment.[144] A similar increase was previously reported in Scotland.[145] The inclusion of both age and myopia level in the model of visual impairment should make it relatively robust moving forward.

The assessment of vision loss associated with contact lens wear assumes that the risk is constant over time and independent of refractive error. As demonstrated in Figure 1, the incidence of contact lens-related adverse events increases as children become teenagers,[57] presumably due to engaging in behavior likely to increase the risk of adverse events.[87] Likewise, higher myopes are more likely to engage in risky behavior related to their contact lenses.[146, 147] A value of 15% for the proportion of cases of microbial keratitis was chosen, based on the two lines loss of visual acuity.[64, 65] Other studies have reported rates of 4% for a criterion of 20/40 or worse[66] and 5% based on 20/70 or

worse.[61] The calculations in Table 2 are all linear, so the effect of replacing 0.15 with a different value is easily calculated. Our model of visual impairment associated with contact lens assumes that the design of the lens does not play a role and that the increased risk is due to increased exposure. Intuitively, those additional years of wear would occur when the child is younger and their myopia relatively low.

The current model assumes a fixed treatment effect with myopia control. While the efficacy of these technologies show a reduction in subsequent years of treatment,[93] a more sophisticated model or simulation could explore variations in treatment duration, treatment effect, or both. The model also uses data from only one paper reporting predominantly white Europeans, although a recent clinic-based French study of nearly 200,000 myopic adults show a similar relationship between myopia level and visual impairment.[105] Both studies include all causes of visual impairment and thus account for age-related increases in AMD and the potentially protective effect of myopia. It will be important to extend these results to other populations as data become available, particularly Asians where the prevalence of myopia is higher. It should be noted that the prevalence of visual impairment in this Dutch population[148] is lower than other comparable populations.[149, 150]

Recent comprehensive reviews of the efficacy of myopia control are available,[17, 93, 151] but long-term data on myopia control and whether the benefits are sustained are scarce. Few published studies are longer than three years in duration. Of the 26 studies considered by Brennan et al., only four exceed two years and the majority of reports in the literature are one year in duration.[93] Likewise few studies demonstrate more than 1 D of treatment effect,[136, 137, 152] and caution must be exercised when extrapolating the findings of shorter duration trials, as slowing of progression in

the first year of treatment is greater than in subsequent years.[93] Nonetheless, a recent report of the only FDA-approved myopia control device demonstrates a six-year 0.53 mm slowing of axial elongation, which in dioptric terms approaches 1.50 D.[152]

The extent to which benefits are sustained once treatment is withdrawn is not settled. Dramatic post-treatment acceleration, or rebound, has been reported with 1% atropine, but does not seem to occur with spectacle[35] or soft contact lens therapies.[75, 153] Nonetheless, some level of rebound should be assumed until proven otherwise.[93] The choice of treatment will be ultimately be determined by a discussion among practitioner, parent, and patient, but influenced by regional practice patterns and scope of practice.

The use of NNT and their comparison with NNH is not beyond reproach.[154-156] NNTs vary with baseline or event rate and a NNT without the treatment period and follow-up period is difficult to interpret. For these reasons, a range of rates of visual impairment was explored**,** with care to specify the duration of treatment and calculate years living with any impairment. Comparisons between different outcomes, for example, risks of microbial keratitis in contact lens wear with risk of vision impairment due to increasing myopia could also be criticized.[157] In contrast, the analyses express both NNH and NNT in a single metric—years of visual impairment. A further valid criticism of the presentation of NNH and NNT is the absence of confidence intervals. The naive approach to calculating a confidence interval for NNT is by inverting the limits for ARR, but this does not yield a valid interval. Our approach has been to explore a range of underlying assumptions and present data for a range of risks and benefits. Finally, the analysis assumes that all years of visual impairment are created equal, which may or not be valid. For example, visual impairment earlier

in life may impact earning potential and comparing this with later-onset visual impairment where comorbidities may exist is a complex problem.[158]

Finally, this is not a cost-benefit analysis and future work should consider the cost associated with myopia control, including those associated with adverse events, along the potential savings associated with any reduction in ocular morbidity. Nonetheless, some brief comment is warranted. First, there have been few attempts to estimate the costs of visual impairment. Frick et al.[159] used Medical Expenditure Panel Survey data to estimate the effect of visual impairment with total medical expenditures, components of expenditures, days of informal care received (direct costs), and health utility (indirect costs) among patients 40 years and older in the United States. The direct costs of visual impairment (individual excess medical expenditures) were estimated to be $1,037 (for 2004). Adjusted for 2021, this is $1,446. For indirect costs, Frick et al. assumed visual impairment corresponds to a loss of 0.05 quality-adjusted life years (QALYs) and use a "common but arbitrary value for a QALY in the US of $50,000" resulting in $2,500[160] Adjusted for 2020 gives $3,779. Frick et al. acknowledge that their estimate of the economic impact is limited, because it does not include productivity loss.[159] Furthermore, all estimates can vary dramatically with the underlying assumptions. For example, other authors apply an upper limit of $100,000 per QALY and consider the difference between 20/20 and 20/40 to represent 0.12 QALYs.[158]

The costs associated with myopia control are also challenging to estimate. At the time of writing only one device or drug is FDA-approved for myopia control in the US and was only launched in the past year, although it has been available in other countries for some years. Analyses would need to include costs of drugs or lenses, but these are incremental as the child will already be

wearing spectacles or contact lenses. The cost of additional office visits and measurements, including axial length will also need to be incorporated. All these costs will vary across countries.

The cost to families of myopia control when that treatment is not generally covered by vision or medical insurance may mean that the prevention or slowing of myopia to reduce the risk of visual impairment later in life may be at the expense of other medical conditions, such as oral care.[161] This can potentially exacerbate health disparities in underserved communities as highlighted in a recent Prevent Blindness report, particularly minority communities.[162] The supplemental material in the recently published report of the American Academy of Ophthalmology Task Force on Myopia,[163] includes a number of goals, including "Encouraging government and commercial insurers to cover myopia control as part of their medical and vision benefits would further expand the interventions available to clinicians and might allay future vision loss and costs associated with higher degrees of myopia. Health disparities in myopic minority children in the United States are likely to be amplified unless insurance coverage for myopia treatments is expanded." We feel that all stakeholders should consider this issue.

Finally, those at the greatest risk of developing maculopathy and visual impairment are those with higher levels of myopia.[134] Likewise, our model shows that the greatest individual reductions in visual impairment from myopia control are accrued in higher myopes. Given the strong relation between age of onset and ultimate severity of myopia,[2, 4] it is most important to direct efforts at those children who develop myopia relatively early. As Brennan et al.[93] recently stated, "Because of the risks of complications later in life and our current inability to predict with great accuracy

those who go on to higher degrees of myopia, this leads us to recommend that all young myopes (say 12 years of age and below) deserve to be treated."

One question that is currently unresolvable, is whether the observed associations of refractive error and ocular disease are directly causal and whether a reduction in myopia with treatment will reduce the associated risks. Due to the 40 or more-year delay between myopia treatment and the increased risk of vision loss, this is a challenging question to address. One suggestion that there is a causal relationship is the increasing prevalence of myopic maculopathy associated vision loss in countries that have experienced the most rapid increases in myopia prevalence and severity such as China where myopic maculopathy has risen to become the leading cause of vision impairment.[14, 164] Myopic maculopathy is also the leading cause of uncorrectable visual impairment among Chinese Americans.[165]

Conclusion

In summary, we have reviewed the risks associated with various myopia control therapies, particularly contact lenses, and the predicted visual loss from five years for therapy. We have examined the increased risk of ocular disease associated with increasing levels of myopia and, more importantly, the relation between visual impairment and myopia level. Finally, we compare the potential benefits of reducing a patient's ultimate level of myopia by one diopter. Our model suggests the potential benefits of myopia control outweigh the risks: the number needed to treat to prevent 5 years of visual impairment is between 4.1 and 6.8 while fewer than 1 in 38 will experience the same loss of vision as a result of myopia control.

References

1. Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology 2016;123:1036-42.
2. Chua SY, Sabanayagam C, Cheung YB, et al. Age of Onset of Myopia Predicts Risk of High Myopia in Later Childhood in Myopic Singapore Children. Ophthalmic Physiol Opt 2016;36:388-94.
3. Parssinen O, Kauppinen M. Risk Factors for High Myopia: A 22-Year Follow-up Study from Childhood to Adulthood. Acta Ophthalmol 2019;97:510-8.
4. Hu Y, Ding X, Guo X, et al. Association of Age at Myopia Onset with Risk of High Myopia in Adulthood in a 12-Year Follow-up of a Chinese Cohort. JAMA ophthalmology 2020.
5. Fricke TR, Jong M, Naidoo KS, et al. Global Prevalence of Visual Impairment Associated with Myopic Macular Degeneration and Temporal Trends from 2000 through 2050: Systematic Review, Meta-Analysis and Modelling. Br J Ophthalmol 2018;102:855-62.
6. Wong TY, Ferreira A, Hughes R, et al. Epidemiology and Disease Burden of Pathologic Myopia and Myopic Choroidal Neovascularization: An Evidence-Based Systematic Review. Am J Ophthalmol 2014;157:9-25 e12.
7. Haarman AEG, Enthoven CA, Tideman JWL, et al. The Complications of Myopia: A Review and Meta-Analysis. Invest Ophthalmol Vis Sci 2020;61:49.
8. Ueda E, Yasuda M, Fujiwara K, et al. Trends in the Prevalence of Myopia and Myopic Maculopathy in a Japanese Population: The Hisayama Study. Invest Ophthalmol Vis Sci 2019;60:2781-6.
9. Cohen SY, Laroche A, Leguen Y, et al. Etiology of Choroidal Neovascularization in Young Patients. Ophthalmology 1996;103:1241-4.
10. Perkins ES. Morbidity from Myopia. Sight Sav Rev 1979;49:11-9.
11. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. Lancet 2012;379:1739-48.
12. Evans JR, Fletcher AE, Wormald RP, et al. Causes of Visual Impairment in People Aged 75 Years and Older in Britain: An Add-on Study to the MRC Trial of Assessment and Management of Older People in the Community. Br J Ophthalmol 2004;88:365-70.
13. Kelliher C, Kenny D, O'Brien C. Trends in Blind Registration in the Adult Population of the Republic of Ireland 1996-2003. Br J Ophthalmol 2006;90:367-71.
14. Zhao J, Xu X, Ellwein LB, et al. Causes of Visual Impairment and Blindness in the 2006 and 2014 Nine-Province Surveys in Rural China. Am J Ophthalmol 2019;197:80-7.
15. Huang J, Wen D, Wang Q, et al. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-Analysis. Ophthalmology 2016;123:697-708.
16. Walline JJ, Lindsley K, Vedula SS, et al. Interventions to Slow Progression of Myopia in Children. The Cochrane database of systematic reviews 2011:CD004916.

17. Wildsoet CF, Chia A, Cho P, et al. IMI - Interventions Myopia Institute: Interventions for Controlling Myopia Onset and Progression Report. Invest Ophthalmol Vis Sci 2019;60:M106-M31.

18. Walline JJ, Lindsley KB, Vedula SS, et al. Interventions to Slow Progression of Myopia in Children. The Cochrane database of systematic reviews 2020;1:CD004916.

19. Leshno A, Farzavandi SK, Gomez-de-Liano R, et al. Practice Patterns to Decrease Myopia Progression Differ among Paediatric Ophthalmologists around the World. Br J Ophthalmol 2019.

20. Wolffsohn JS, Calossi A, Cho P, et al. Global Trends in Myopia Management Attitudes and Strategies in Clinical Practice. Cont Lens Anterior Eye 2016;39:106-16.

21. Deng L, Pang Y. Effect of Outdoor Activities in Myopia Control: Meta-Analysis of Clinical Studies. Optom Vis Sci 2019;96:276-82.

22. Lanca C, Saw SM. The Association between Digital Screen Time and Myopia: A Systematic Review. Ophthalmic Physiol Opt 2020;40:216-29.

23. Chamberlain P, Peixoto-de-Matos SC, Logan NS, et al. A 3-Year Randomized Clinical Trial of MiSight Lenses for Myopia Control. Optom Vis Sci 2019;96:556-67.

24. Yam JC, Jiang Y, Tang SM, et al. Low-Concentration Atropine for Myopia Progression (LAMP) Study: A Randomized, Double-Blinded, Placebo-Controlled Trial of 0.05%, 0.025%, and 0.01% Atropine Eye Drops in Myopia Control. Ophthalmology 2019;126:113-24.

25. Myopia Management. College of Optometrists https://www.college-optometrists.org/the-college/policy/myopia-management.html. Accessed: July 3, 2019.

26. Pineles SL, Kraker RT, VanderVeen DK, et al. Atropine for the Prevention of Myopia Progression in Children: A Report by the American Academy of Ophthalmology. Ophthalmology 2017;124:1857-66.

27. VanderVeen DK, Kraker RT, Pineles SL, et al. Use of Orthokeratology for the Prevention of Myopic Progression in Children: A Report by the American Academy of Ophthalmology. Ophthalmology 2019;126:623-36.

28. Van Meter WS, Musch DC, Jacobs DS, et al. Safety of Overnight Orthokeratology for Myopia: A Report by the American Academy of Ophthalmology. Ophthalmology 2008;115:2301-13 e1.

29. Chuck RS, Jacobs DS, Lee JK, et al. Refractive Errors & Refractive Surgery Preferred Practice Pattern(R). Ophthalmology 2018;125:P1-P104.

30. Modjtahedi BS, Ferris FL, 3rd, Hunter DG, Fong DS. Public Health Burden and Potential Interventions for Myopia. Ophthalmology 2018;125:628-30.

31. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: A Randomized Trial Determines That Topical Ocular Hypotensive Medication Delays or Prevents the Onset of Primary Open-Angle Glaucoma. Arch Ophthalmol 2002;120:701-13; discussion 829-30.

32. Mandell RB. Myopia Control with Bifocal Correction. Am J Optom Arch Am Acad Optom 1959;36:652-8.

33. Cheng D, Woo GC, Drobe B, Schmid KL. Effect of Bifocal and Prismatic Bifocal Spectacles on Myopia Progression in Children: Three-Year Results of a Randomized Clinical Trial. JAMA ophthalmology 2014;132:258-64.

34. Grosvenor T, Perrigin DM, Perrigin J, Maslovitz B. Houston Myopia Control Study: A Randomized Clinical Trial. Part Ii. Final Report by the Patient Care Team. Am J Optom Physiol Opt 1987;64:482-98.

35. Berntsen DA, Sinnott LT, Mutti DO, Zadnik K. A Randomized Trial Using Progressive Addition Lenses to Evaluate Theories of Myopia Progression in Children with a High Lag of Accommodation. Invest Ophthalmol Vis Sci 2012;53:640-9.

36. Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group. Progressive-Addition Lenses Versus Single-Vision Lenses for Slowing Progression of Myopia in Children with High Accommodative Lag and near Esophoria. Invest Ophthalmol Vis Sci 2011;52:2749-57.

37. Gwiazda J, Hyman L, Hussein M, et al. A Randomized Clinical Trial of Progressive Addition Lenses Versus Single Vision Lenses on the Progression of Myopia in Children. Invest Ophthalmol Vis Sci 2003;44:1492-500.

38. Lam CSY, Tang WC, Tse DY, et al. Defocus Incorporated Multiple Segments (Dims) Spectacle Lenses Slow Myopia Progression: A 2-Year Randomised Clinical Trial. Br J Ophthalmol 2020;104:363-8.

39. Zhang M, Congdon N, Li L, et al. Myopia, Spectacle Wear, and Risk of Bicycle Accidents among Rural Chinese Secondary School Students: The Xichang Pediatric Refractive Error Study Report No. 7. Arch Ophthalmol 2009;127:776-83.

40. Lu Y, Lin Z, Wen L, et al. The Adaptation and Acceptance of Defocus Incorporated Multiple Segment Lens for Chinese Children. Am J Ophthalmol 2020;211:207-16.

41. Lord SR, Dayhew J, Howland A. Multifocal Glasses Impair Edge-Contrast Sensitivity and Depth Perception and Increase the Risk of Falls in Older People. J Am Geriatr Soc 2002;50:1760-6.

42. Johnson L, Buckley JG, Scally AJ, Elliott DB. Multifocal Spectacles Increase Variability in Toe Clearance and Risk of Tripping in the Elderly. Invest Ophthalmol Vis Sci 2007;48:1466-71.

43. Elliott DB. The Glenn A. Fry Award Lecture 2013: Blurred Vision, Spectacle Correction, and Falls in Older Adults. Optom Vis Sci 2014;91:593-601.

44. Chia A, Chua WH, Cheung YB, et al. Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1%, and 0.01% Doses (Atropine for the Treatment of Myopia 2). Ophthalmology 2012;119:347-54.

45. North RV, Kelly ME. A Review of the Uses and Adverse Effects of Topical Administration of Atropine. Ophthalmic Physiol Opt 1987;7:109-14.

46. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the Treatment of Childhood Myopia. Ophthalmology 2006;113:2285-91.

47. Repka MX, Cotter SA, Beck RW, et al. A Randomized Trial of Atropine Regimens for Treatment of Moderate Amblyopia in Children. Ophthalmology 2004;111:2076-85.

48. Pediatric Eye Disease Investigator Group, Repka MX, Kraker RT, et al. A Randomized Trial of Atropine Vs Patching for Treatment of Moderate Amblyopia: Follow-up at Age 10 Years. Arch Ophthalmol 2008;126:1039-44.

49. Repka MX, Kraker RT, Beck RW, et al. Treatment of Severe Amblyopia with Atropine: Results from 2 Randomized Clinical Trials. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus 2009;13:529.

50. Pediatric Eye Disease Investigator Group Writing C, Wallace DK, Kraker RT, et al. Randomized Trial to Evaluate Combined Patching and Atropine for Residual Amblyopia. Arch Ophthalmol 2011;129:960-2.

51. Wang JJ, Mitchell P, Smith W. Refractive Error and Age-Related Maculopathy: The Blue Mountains Eye Study. Invest Ophthalmol Vis Sci 1998;39:2167-71.

52. Ikram MK, van Leeuwen R, Vingerling JR, et al. Relationship between Refraction and Prevalent as Well as Incident Age-Related Maculopathy: The Rotterdam Study. Invest Ophthalmol Vis Sci 2003;44:3778-82.

53. Cheung CM, Tai ES, Kawasaki R, et al. Prevalence of and Risk Factors for Age-Related Macular Degeneration in a Multiethnic Asian Cohort. Arch Ophthalmol 2012;130:480-6.

54. Quigley MG, Powell I, Wittich W. Increased Axial Length Corresponds to Decreased Retinal Light Dose: A Parsimonious Explanation for Decreasing Amd Risk in Myopia. Invest Ophthalmol Vis Sci 2018;59:3852-7.

55. Fang YT, Chou YJ, Pu C, et al. Prescription of Atropine Eye Drops among Children Diagnosed with Myopia in Taiwan from 2000 to 2007: A Nationwide Study. Eye (Lond) 2013;27:418-24.

56. Szczotka-Flynn L, Diaz M. Risk of Corneal Inflammatory Events with Silicone Hydrogel and Low Dk Hydrogel Extended Contact Lens Wear: A Meta-Analysis. Optom Vis Sci 2007;84:247-56.

57. Chalmers RL, Wagner H, Mitchell GL, et al. Age and Other Risk Factors for Corneal Infiltrative and Inflammatory Events in Young Soft Contact Lens Wearers from the Contact Lens Assessment in Youth (CLAY) Study. Invest Ophthalmol Vis Sci 2011;52:6690-6.

58. Szczotka-Flynn L, Jiang Y, Raghupathy S, et al. Corneal Inflammatory Events with Daily Silicone Hydrogel Lens Wear. Optom Vis Sci 2014;91:3-12.

59. Poggio EC, Glynn RJ, Schein OD, et al. The Incidence of Ulcerative Keratitis among Users of Daily-Wear and Extended-Wear Soft Contact Lenses. N Engl J Med 1989;321:779-83.

60. Seal DV, Kirkness CM, Bennett HG, et al. Population-Based Cohort Study of Microbial Keratitis in Scotland: Incidence and Features. Cont Lens Anterior Eye 1999;22:49-57.

61. Cheng KH, Leung SL, Hoekman HW, et al. Incidence of Contact-Lens-Associated Microbial Keratitis and Its Related Morbidity. Lancet 1999;354:181-5.

62. Lam DS, Houang E, Fan DS, et al. Incidence and Risk Factors for Microbial Keratitis in Hong Kong: Comparison with Europe and North America. Eye (Lond) 2002;16:608-18.

63. Morgan PB, Efron N, Hill EA, et al. Incidence of Keratitis of Varying Severity among Contact Lens Wearers. Br J Ophthalmol 2005;89:430-6.

64. Efron N, Morgan PB, Hill EA, et al. Incidence and Morbidity of Hospital-Presenting Corneal Infiltrative Events Associated with Contact Lens Wear. Clin Exp Optom 2005;88:232-9.

65. Stapleton F, Keay L, Edwards K, et al. The Incidence of Contact Lens-Related Microbial Keratitis in Australia. Ophthalmology 2008;115:1655-62.

66. Dart JK, Radford CF, Minassian D, et al. Risk Factors for Microbial Keratitis with Contemporary Contact Lenses: A Case-Control Study. Ophthalmology 2008;115:1647-54, 54 e1-3.

67. Stapleton F, Edwards K, Keay L, et al. Risk Factors for Moderate and Severe Microbial Keratitis in Daily Wear Contact Lens Users. Ophthalmology 2012;119:1516-21.

68. Joslin CE, Tu EY, Shoff ME, et al. The Association of Contact Lens Solution Use and Acanthamoeba Keratitis. Am J Ophthalmol 2007;144:169-80.

69. Chang DC, Grant GB, O'Donnell K, et al. Multistate Outbreak of Fusarium Keratitis Associated with Use of a Contact Lens Solution. JAMA 2006;296:953-63.

70. Khor WB, Aung T, Saw SM, et al. An Outbreak of Fusarium Keratitis Associated with Contact Lens Wear in Singapore. JAMA 2006;295:2867-73.

71. Efron N, Nichols JJ, Woods CA, Morgan PB. Trends in Us Contact Lens Prescribing 2002 to 2014. Optom Vis Sci 2015;92:758-67.

72. Szczotka-Flynn L, Chalmers R. Incidence and Epidemiologic Associations of Corneal Infiltrates with Silicone Hydrogel Contact Lenses. Eye Contact Lens 2013;39:49-52.

73. Bullimore MA. The Safety of Soft Contact Lenses in Children. Optom Vis Sci 2017;94:638-46.

74. Chalmers RL, Hickson-Curran SB, Keay L, et al. Rates of Adverse Events with Hydrogel and Silicone Hydrogel Daily Disposable Lenses in a Large Postmarket Surveillance Registry: The Tempo Registry. Invest Ophthalmol Vis Sci 2015;56:654-63.

75. Cheng X, Xu J, Chehab K, et al. Soft Contact Lenses with Positive Spherical Aberration for Myopia Control. Optom Vis Sci 2016;93:353-66.

76. Li L, Moody K, Tan DT, et al. Contact Lenses in Pediatrics Study in Singapore. Eye Contact Lens 2009;35:188-95.

77. Paquette L, Jones DA, Sears M, et al. Contact Lens Fitting and Training in a Child and Youth Population. Cont Lens Anterior Eye 2015;38:419-23.

78. Plowright AJ, Maldonado-Codina C, Howarth GF, et al. Daily Disposable Contact Lenses Versus Spectacles in Teenagers. Optom Vis Sci 2015;92:44-52.

79. Sankaridurg P, Chen X, Naduvilath T, et al. Adverse Events During 2 Years of Daily Wear of Silicone Hydrogels in Children. Optom Vis Sci 2013;90:961-9.

80. Walline JJ, Jones LA, Mutti DO, Zadnik K. A Randomized Trial of the Effects of Rigid Contact Lenses on Myopia Progression. Arch Ophthalmol 2004;122:1760-6.

81. Walline JJ, Jones LA, Rah MJ, et al. Contact Lenses in Pediatrics (Clip) Study: Chair Time and Ocular Health. Optom Vis Sci 2007;84:896-902.

82. Walline JJ, Jones LA, Sinnott L, et al. A Randomized Trial of the Effect of Soft Contact Lenses on Myopia Progression in Children. Invest Ophthalmol Vis Sci 2008;49:4702-6.

83. Cheng X, Brennan NA, Toubouti Y, Greenaway NL. Safety of Soft Contact Lenses in Children: Retrospective Review of Six Randomized Controlled Trials of Myopia Control. Acta Ophthalmol 2020;98:e346-e51.

84. Walline JJ, Walker MK, Mutti DO, et al. Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial. JAMA 2020;324:571-80.

85. Chalmers RL, McNally JJ, Chamberlain P, Keay L. Adverse Event Rates in the Retrospective Cohort Study of Safety of Paediatric Soft Contact Lens Wear: The Recss Study. Ophthalmic Physiol Opt 2021;41:84-92.

86. Woods J, Jones D, Jones L, et al. Ocular Health of Children Wearing Daily Disposable Contact Lenses over a 6-Year Period. Cont Lens Anterior Eye 2021.

87. Wagner H, Richdale K, Mitchell GL, et al. Age, Behavior, Environment, and Health Factors in the Soft Contact Lens Risk Survey. Optom Vis Sci 2014;91:252-61.

88. Efron N, Morgan PB, Woods CA, International Contact Lens Prescribing Survey C. Survey of Contact Lens Prescribing to Infants, Children, and Teenagers. Optom Vis Sci 2011;88:461-8.

89. Morgan PB, Efron N, Woods CA, et al. International Survey of Orthokeratology Contact Lens Fitting. Cont Lens Anterior Eye 2019;42:450-4.

90. Watt K, Swarbrick HA. Microbial Keratitis in Overnight Orthokeratology: Review of the First 50 Cases. Eye Contact Lens 2005;31:201-8.

91. Watt KG, Swarbrick HA. Trends in Microbial Keratitis Associated with Orthokeratology. Eye Contact Lens 2007;33:373-7; discussion 82.

92. Bullimore MA, Sinnott LT, Jones-Jordan LA. The Risk of Microbial Keratitis with Overnight Corneal Reshaping Lenses. Optom Vis Sci 2013;90:937-44.

93. Brennan NA, Toubouti YM, Cheng X, Bullimore MA. Efficacy in Myopia Control. Prog Retin Eye Res 2020 https://doi.org/10.1016/j.preteyeres.2020.100923.

94. Bullimore MA, Brennan NA. Myopia Control: Why Each Diopter Matters. Optom Vis Sci 2019;96:463-5.

95. Bailey MD, Olson MD, Bullimore MA, et al. The Effect of LASIK on Best-Corrected High- and Low-Contrast Visual Acuity. Optom Vis Sci 2004;81:362-8.

96. Twa MD, Nichols JJ, Joslin CE, et al. Characteristics of Corneal Ectasia after Lasik for Myopia. Cornea 2004;23:447-57.

97. Vongphanit J, Mitchell P, Wang JJ. Prevalence and Progression of Myopic Retinopathy in an Older Population. Ophthalmology 2002;109:704-11.

98. Liu HH, Xu L, Wang YX, et al. Prevalence and Progression of Myopic Retinopathy in Chinese Adults: The Beijing Eye Study. Ophthalmology 2010;117:1763-8.

99. Gao LQ, Liu W, Liang YB, et al. Prevalence and Characteristics of Myopic Retinopathy in a Rural Chinese Adult Population: The Handan Eye Study. Arch Ophthalmol 2011;129:1199-204.

100. Asakuma T, Yasuda M, Ninomiya T, et al. Prevalence and Risk Factors for Myopic Retinopathy in a Japanese Population: The Hisayama Study. Ophthalmology 2012;119:1760-5.

101. Choudhury F, Meuer SM, Klein R, et al. Prevalence and Characteristics of Myopic Degeneration in an Adult Chinese American Population: The Chinese American Eye Study. Am J Ophthalmol 2018;187:34-42.

102. Wong YL, Sabanayagam C, Ding Y, et al. Prevalence, Risk Factors, and Impact of Myopic Macular Degeneration on Visual Impairment and Functioning among Adults in Singapore. Invest Ophthalmol Vis Sci 2018;59:4603-13.

103. Xiao O, Guo X, Wang D, et al. Distribution and Severity of Myopic Maculopathy among Highly Myopic Eyes. Invest Ophthalmol Vis Sci 2018;59:4880-5.

104. Hopf S, Korb C, Nickels S, et al. Prevalence of Myopic Maculopathy in the German Population: Results from the Gutenberg Health Study. Br J Ophthalmol 2020;104:1254-9.

105. Leveziel N, Marillet S, Dufour Q, et al. Prevalence of Macular Complications Related to Myopia - Results of a Multicenter Evaluation of Myopic Patients in Eye Clinics in France. Acta Ophthalmol 2020;98:e245-e51.

106. Bikbov MM, Gilmanshin TR, Kazakbaeva GM, et al. Prevalence of Myopic Maculopathy among Adults in a Russian Population. JAMA Netw Open 2020;3:e200567.

107. Pan CW, Cheng CY, Saw SM, et al. Myopia and Age-Related Cataract: A Systematic Review and Meta-Analysis. Am J Ophthalmol 2013;156:1021-33 e1.

108. Pan CW, Boey PY, Cheng CY, et al. Myopia, Axial Length, and Age-Related Cataract: The Singapore Malay Eye Study. Invest Ophthalmol Vis Sci 2013;54:4498-502.

109. Chang MA, Congdon NG, Bykhovskaya I, et al. The Association between Myopia and Various Subtypes of Lens Opacity: SEE (Salisbury Eye Evaluation) Project. Ophthalmology 2005;112:1395-401.

110. Wong TY, Foster PJ, Johnson GJ, Seah SK. Refractive Errors, Axial Ocular Dimensions, and Age-Related Cataracts: The Tanjong Pagar Survey. Invest Ophthalmol Vis Sci 2003;44:1479-85.

111. Wong TY, Klein BE, Klein R, et al. Refractive Errors and Incident Cataracts: The Beaver Dam Eye Study. Invest Ophthalmol Vis Sci 2001;42:1449-54.

112. Lim R, Mitchell P, Cumming RG. Refractive Associations with Cataract: The Blue Mountains Eye Study. Invest Ophthalmol Vis Sci 1999;40:3021-6.

113. Mitry D, Charteris DG, Fleck BW, et al. The Epidemiology of Rhegmatogenous Retinal Detachment: Geographical Variation and Clinical Associations. Br J Ophthalmol 2010;94:678-84.

114. Ogawa A, Tanaka M. The Relationship between Refractive Errors and Retinal Detachment--Analysis of 1,166 Retinal Detachment Cases. Jpn J Ophthalmol 1988;32:310-5.

115. Risk Factors for Idiopathic Rhegmatogenous Retinal Detachment. The Eye Disease Case-Control Study Group. Am J Epidemiol 1993;137:749-57.

116. Zou H, Zhang X, Xu X, et al. Epidemiology Survey of Rhegmatogenous Retinal Detachment in Beixinjing District, Shanghai, China. Retina 2002;22:294-9.

117. Burton TC. The Influence of Refractive Error and Lattice Degeneration on the Incidence of Retinal Detachment. Trans Am Ophthalmol Soc 1989;87:143-55; discussion 55-7.

118. Bohringer HR. Statistics on the Frequency and Risks on Retinal Detachment. Ophthalmologica 1956;131:331-4.

119. Mitry D, Charteris DG, Yorston D, et al. The Epidemiology and Socioeconomic Associations of Retinal Detachment in Scotland: A Two-Year Prospective Population-Based Study. Invest Ophthalmol Vis Sci 2010;51:4963-8.

120. Cumberland PM, Bao Y, Hysi PG, et al. Frequency and Distribution of Refractive Error in Adult Life: Methodology and Findings of the Uk Biobank Study. PLoS One 2015;10:e0139780.

121. Marcus MW, de Vries MM, Junoy Montolio FG, Jansonius NM. Myopia as a Risk Factor for Open-Angle Glaucoma: A Systematic Review and Meta-Analysis. Ophthalmology 2011;118:1989-94 e2.

122. Ramakrishnan R, Nirmalan PK, Krishnadas R, et al. Glaucoma in a Rural Population of Southern India: The Aravind Comprehensive Eye Survey. Ophthalmology 2003;110:1484-90.

123. Xu L, Wang Y, Wang S, et al. High Myopia and Glaucoma Susceptibility the Beijing Eye Study. Ophthalmology 2007;114:216-20.

124. Qiu M, Wang SY, Singh K, Lin SC. Association between Myopia and Glaucoma in the United States Population. Invest Ophthalmol Vis Sci 2013;54:830-5.

125. Pan CW, Cheung CY, Aung T, et al. Differential Associations of Myopia with Major Age-Related Eye Diseases: The Singapore Indian Eye Study. Ophthalmology 2013;120:284-91.

126. Chon B, Qiu M, Lin SC. Myopia and Glaucoma in the South Korean Population. Invest Ophthalmol Vis Sci 2013;54:6570-7.

127. Shen L, Melles RB, Metlapally R, et al. The Association of Refractive Error with Glaucoma in a Multiethnic Population. Ophthalmology 2016;123:92-101.

128. Perera SA, Wong TY, Tay WT, et al. Refractive Error, Axial Dimensions, and Primary Open-Angle Glaucoma: The Singapore Malay Eye Study. Arch Ophthalmol 2010;128:900-5.

129. Kuzin AA, Varma R, Reddy HS, et al. Ocular Biometry and Open-Angle Glaucoma: The Los Angeles Latino Eye Study. Ophthalmology 2010;117:1713-9.

130. Springelkamp H, Wolfs RC, Ramdas WD, et al. Incidence of Glaucomatous Visual Field Loss after Two Decades of Follow-Up: The Rotterdam Study. European journal of epidemiology 2017;32:691-9.

131. Lee JY, Sung KR, Han S, Na JH. Effect of Myopia on the Progression of Primary Open-Angle Glaucoma. Invest Ophthalmol Vis Sci 2015;56:1775-81.

132. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International Photographic Classification and Grading System for Myopic Maculopathy. Am J Ophthalmol 2015;159:877-83 e7.

133. Verhoeven VJ, Wong KT, Buitendijk GH, et al. Visual Consequences of Refractive Errors in the General Population. Ophthalmology 2015;122:101-9.

134. Tideman JW, Snabel MC, Tedja MS, et al. Association of Axial Length with Risk of Uncorrectable Visual Impairment for Europeans with Myopia. JAMA ophthalmology 2016;134:1355-63.

135. Chou R, Dana T, Blazina I, et al. Statins for Prevention of Cardiovascular Disease in Adults: Evidence Report and Systematic Review for the Us Preventive Services Task Force. JAMA 2016;316:2008-24.

136. Hiraoka T, Kakita T, Okamoto F, et al. Long-Term Effect of Overnight Orthokeratology on Axial Length Elongation in Childhood Myopia: A 5-Year Follow-up Study. Invest Ophthalmol Vis Sci 2012;53:3913-9.

137. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, et al. Long-Term Efficacy of Orthokeratology Contact Lens Wear in Controlling the Progression of Childhood Myopia. Curr Eye Res 2017;42:713-20.

138. Walline JJ, Robboy MW, Hilmantel G, et al. Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Association for Pediatric Ophthalmology and Strabismus, American Optometric Association, American Society of Cataract and Refractive Surgery, and Contact Lens Association of Ophthalmologists Co-Sponsored Workshop: Controlling the Progression of Myopia: Contact Lenses and Future Medical Devices. Eye Contact Lens 2018;44:205-11.

139. Carvalho FR, Foronda AS, Mannis MJ, et al. Twenty Years of Acanthamoeba Keratitis. Cornea 2009;28:516-9.

140. Walochnik J, Scheikl U, Haller-Schober EM. Twenty Years of Acanthamoeba Diagnostics in Austria. J Eukaryot Microbiol 2015;62:3-11.

141. Sher NA, Bowers RA, Zabel RW, et al. Clinical Use of the 193-Nm Excimer Laser in the Treatment of Corneal Scars. Arch Ophthalmol 1991;109:491-8.

142. Fagerholm P. Phototherapeutic Keratectomy: 12 Years of Experience. Acta Ophthalmol Scand 2003;81:19-32.

143. Rahi J, Logan S, Timms C, et al. Risk, Causes, and Outcomes of Visual Impairment after Loss of Vision in the Non-Amblyopic Eye: A Population-Based Study. Lancet 2002;360:597-602.

144. van Leeuwen R, Haarman AEG, van de Put MAJ, et al. Association of Rhegmatogenous Retinal Detachment Incidence with Myopia Prevalence in the Netherlands. JAMA ophthalmology 2021;139:85-92.

145. Mitry D, Chalmers J, Anderson K, et al. Temporal Trends in Retinal Detachment Incidence in Scotland between 1987 and 2006. Br J Ophthalmol 2011;95:365-9.

146. Zadnik K, Mutti DO, Cutter GR, Chalmers RL. The Effect of Degree of Refractive Error on Hydrogel Contact Lens-Induced Complications and Patient Self-Management Behaviors. Optom Vis Sci 2001;78:652-6.

147. Chalmers RL, Keay L, Long B, et al. Risk Factors for Contact Lens Complications in Us Clinical Practices. Optom Vis Sci 2010;87:725-35.

148. Klaver CC, Wolfs RC, Vingerling JR, et al. Age-Specific Prevalence and Causes of Blindness and Visual Impairment in an Older Population: The Rotterdam Study. Arch Ophthalmol 1998;116:653-8.

149. Klein R, Klein BE, Linton KL, De Mets DL. The Beaver Dam Eye Study: Visual Acuity. Ophthalmology 1991;98:1310-5.

150. Attebo K, Mitchell P, Smith W. Visual Acuity and the Causes of Visual Loss in Australia. The Blue Mountains Eye Study. Ophthalmology 1996;103:357-64.

151. Bullimore MA, Richdale K. Myopia Control 2020: Where Are We and Where Are We Heading? Ophthalmic Physiol Opt 2020;40:254-70.

152. Chamberlain P, Hammond D, Arumugam B, Bullimore MA. Measured and Predicted Axial Elongation in the MiSight 1 Day Clinical Trial – 6 Year Results. Invest Ophthalmol Vis Sci 2021;98:4151.

153. Ruiz-Pomeda A, Prieto-Garrido FL, Hernandez Verdejo JL, Villa-Collar C. Rebound Effect in the Misight Assessment Study Spain (Mass). Curr Eye Res 2021.

154. Smeeth L, Haines A, Ebrahim S. Numbers Needed to Treat Derived from Meta-Analyses--Sometimes Informative, Usually Misleading. BMJ 1999;318:1548-51.

155. Hutton JL. Number Needed to Treat and Number Needed to Harm Are Not the Best Way to Report and Assess the Results of Randomised Clinical Trials. Br J Haematol 2009;146:27-30.

156. Stang A, Poole C, Bender R. Common Problems Related to the Use of Number Needed to Treat. J Clin Epidemiol 2010;63:820-5.

157. Gifford KL. Childhood and Lifetime Risk Comparison of Myopia Control with Contact Lenses. Cont Lens Anterior Eye 2020;43:26-32.

158. Brown GC, Brown MM, Chaudhry I, Stein JD. Opportunities to Reduce Potential Bias in Ophthalmic Cost-Utility Analysis. JAMA ophthalmology 2021.

159. Frick KD, Gower EW, Kempen JH, Wolff JL. Economic Impact of Visual Impairment and Blindness in the United States. Arch Ophthalmol 2007;125:544-50.

160. Hirth RA, Chernew ME, Miller E, et al. Willingness to Pay for a Quality-Adjusted Life Year: In Search of a Standard. Med Decis Making 2000;20:332-42.

161. Patrick DL, Lee RS, Nucci M, et al. Reducing Oral Health Disparities: A Focus on Social and Cultural Determinants. BMC Oral Health 2006;6 Suppl 1:S4.

162. Children's Vision and Eye Health: A Snapshot of Current National Issues (2nd Edition). https://preventblindness.org/wp-content/uploads/2020/07/Snapshot-Report-2020condensedF.pdf: Prevent Blindness; 2020.

163. Modjtahedi BS, Abbott RL, Fong DS, et al. Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children: The Academy's Task Force on Myopia. Ophthalmology 2020.

164. Tang Y, Wang X, Wang J, et al. Prevalence and Causes of Visual Impairment in a Chinese Adult Population: The Taizhou Eye Study. Ophthalmology 2015;122:1480-8.

165. Varma R, Kim JS, Burkemper BS, et al. Prevalence and Causes of Visual Impairment and Blindness in Chinese American Adults: The Chinese American Eye Study. JAMA ophthalmology 2016;134:785-93.

Figure Legends

Figure 1.

The incidence of different inflammatory events involving the cornea and iris as a function of patient age. Data are replotted from Chalmers et al.[57] CLARE = contact lens-induced acute red eye, CLPU = contact lens peripheral ulcer.

Figure 2.

The prevalence of myopic maculopathy plotted with both linear (left) and logarithmic (right) scales, replotted from Bullimore and Brennan[94]. The logarithmic scale emphasizes the similar trajectory of each data set, the additional risk associated with each diopter.

Figure 3.

The cumulative risk of visual impairment as a function of level of myopia for five ages. The left panel uses a linear scale, while the right panel uses a logarithmic scale. Data are from Figure 2 of Tideman et al.[134]

Figure 4.

The $\log_{10}$ odds of visual impairment as a function of level of myopia for five ages plotted a logarithmic scale. Based on data from Tideman et al.[134]

Figure 5.

Model of visual impairment as a function of age (years) for different levels of myopia and two different definitions of visual impairment. The left panel is [134] (worse than 20/67 or 6/20) which is similar to the WHO's ICD-11 definition of moderate visual impairment (worse than 20/60 or 6/18), while the right panel is for the US definition (worse than 20/40) which is also the WHO's ICD-11 definition of mild visual impairment.

Figure 6.

By combining the risk of visual impairment as a function of age for different levels of myopia with mortality data, the probability of a patient living with visual impairment (VI) can be determined.

The mean number of years of visual impairment experienced by a patient over their lifetime may be estimated by integrating the area under each curve.

Figure 1

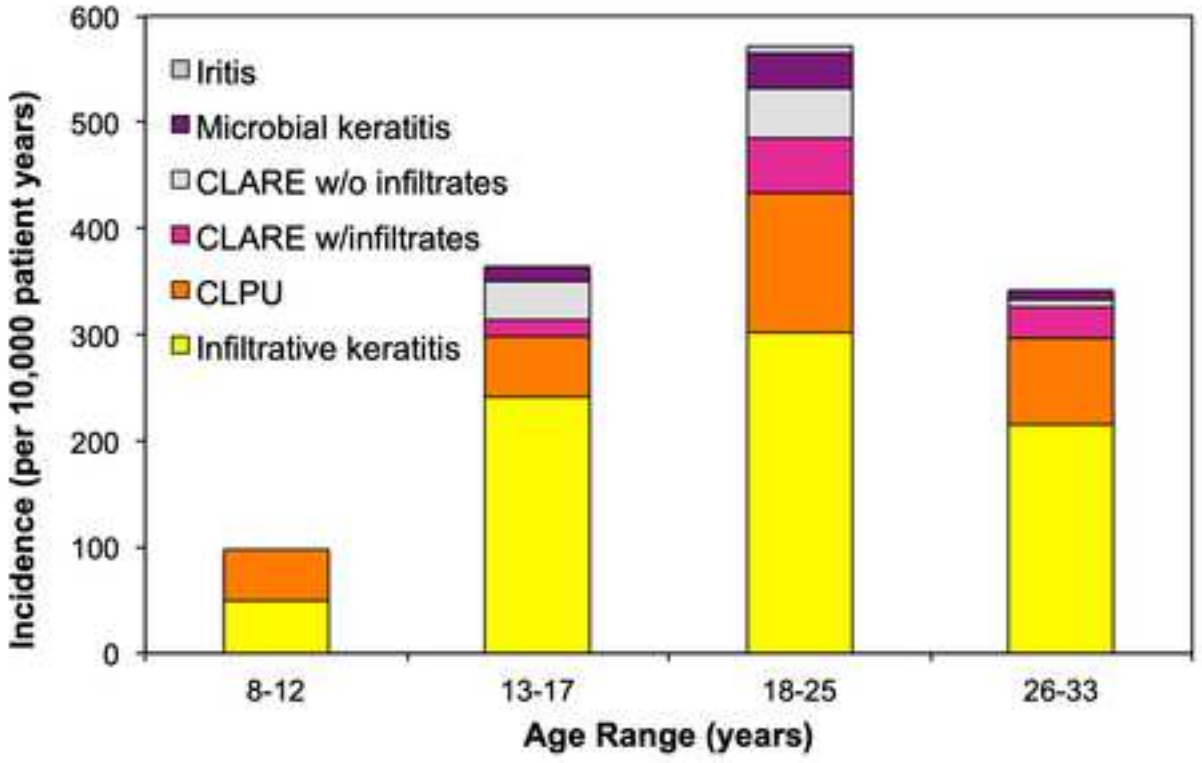
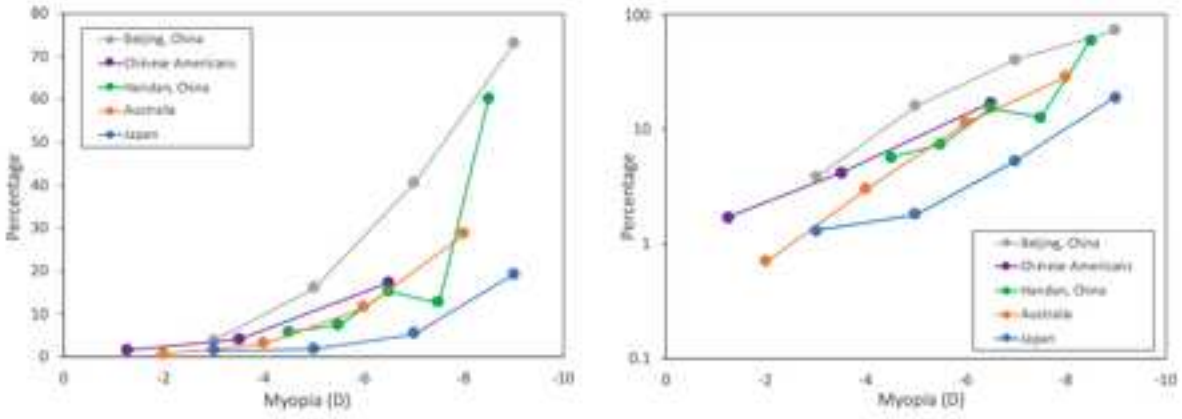


Figure 2



Figure

Click here to access/download;Figure;Figure 3.tiff

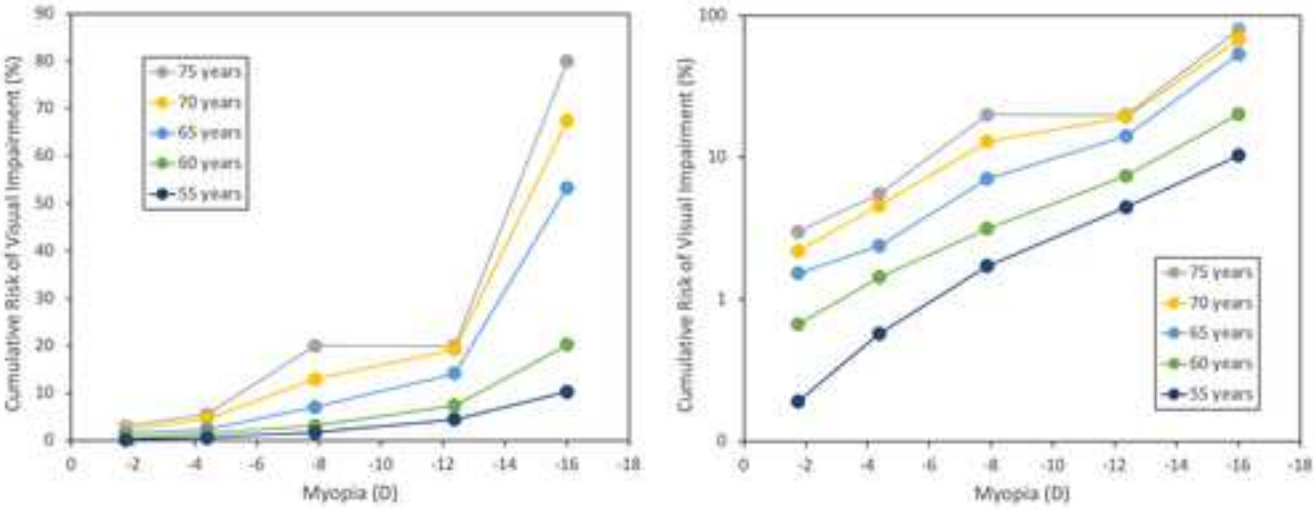


Figure 4

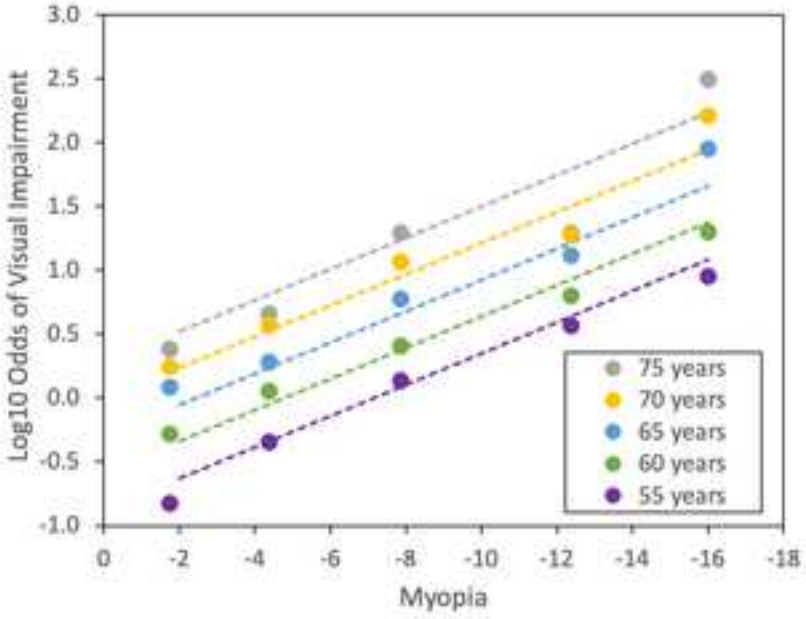


Figure 5

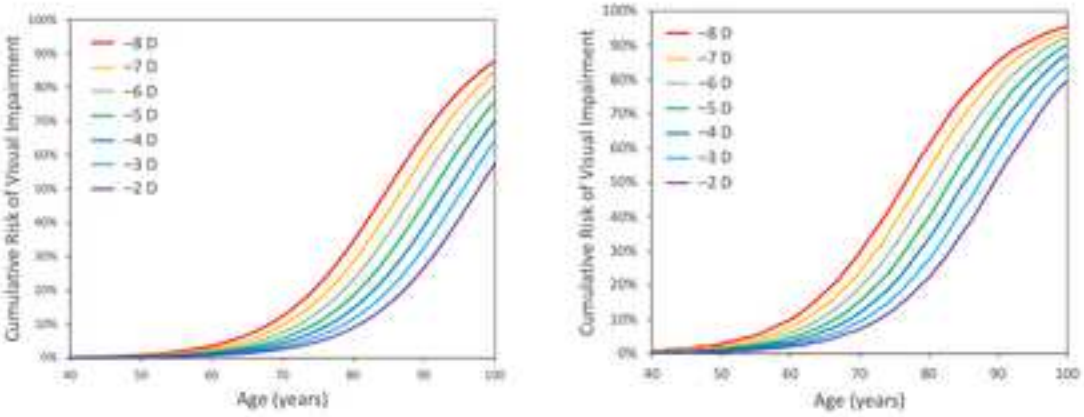


Figure 6

Click here to access/download;Figure;Figure 6.tiff

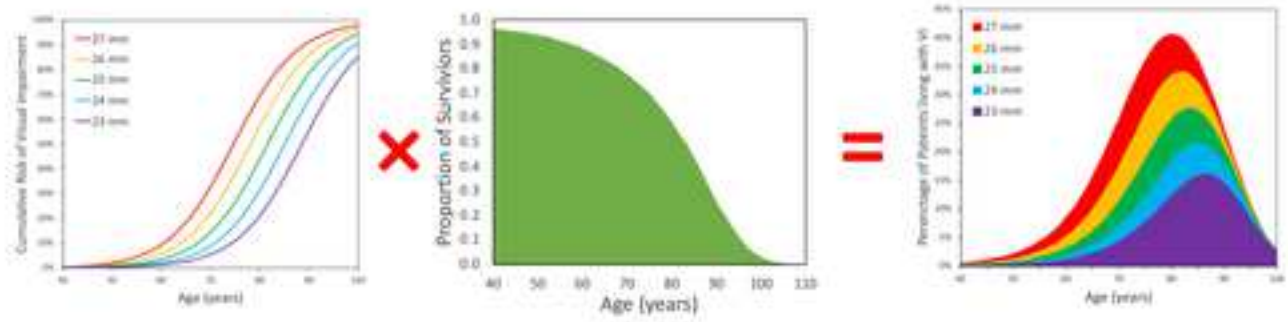


Table 1. Incidence of microbial keratitis in adults associated with daily and regular overnight wear of soft contact lenses. Two studies distinguish between hydrogel and silicone hydrogel soft contact lenses, so both values are shown.[63, 65] When available, the percentage of cases leading to vision loss is shown. Vision loss is defined as two lines loss of visual acuity[64, 65], 20/40 or worse[66], or 20/70 or worse.[61]

Country of Study	Year	Number of Cases	Incidence of microbial keratitis (per 10,000 years of wear)		Percentage of Cases Leading to Vision Loss
			Daily Wear	Overnight Wear	
United States[59]	1989	137	4.1	20.9	—
Scotland[60]	1999	20	2.4	—	—
Netherlands[61]	1999	92	3.5	20.0	5%
Hong Kong[62]	2002	59	3.1	9.3	
England[63, 64]	2005	38	6.4/0.0	96.4/19.8	0%
Australia[65]	2008	244	1.9/11.9	19.5/25.4	15%
England[66]	2008	349	—	—	4%

Table 2. Vision loss associated with three levels of risk of microbial keratitis (MK). It is assumed that 15% of cases of microbial keratitis result in vision loss, that exposure is five years, and that any vision loss is experienced for 70 years after the event. All values are per 10,000 patients.

Variable	Multiplier	Low Risk	Medium Risk	High Risk
Annual incidence of MK		1	5	25
Annual incidence of vision loss	× 15%	0.15	0.75	3.75
Accumulated incidence of vision loss	× 5 years	0.75	3.75	18.75
Years of vision loss accrued	× 70 years	53	263	1,312
NNH for one year of vision loss	10,000/ years vision loss	189	38	7.5
NNH for five years of vision loss	5 × 10,000/ years vision loss	945	190	38

MK: microbial keratitis; NNH: number needed to harm.

Table 3. Summary of studies of the relation between degree of myopia and the prevalence of myopic maculopathy.

Population	Age Range (Mean)	N	Myopes (definition)	Slope (logPrevalence per Diopter)	Ratio of Prevalence to Diopter	Increase per Diopter	Decrease per Diopter
Australia[97]	≥49 (66)	3,583	603 (< –1 D)	0.271	1.87x	+87%	–46%
Beijing, China[98]	≥40 (56±10)	4,319	1,191 (< –0.5 D)	0.213	1.63x	+63%	–39%
Chinese Americans[101]	≥50	4,144	1,523 (≤ –0.5 D)	0.192	1.56x	+56%	–36%
Handan, China[99]	≥30 (52±12)	6,409	1,705 (< –0.5 D)	0.228	1.69x	+69%	–41%
Hisayama, Japan[100]	≥40 (63±11)	1,892	1,619 eyes (≤ 0 D)	0.199	1.58x	+58%	–37%
Singapore[102]	40 to 80 (57±10)	8,716	3,108 (≤ –0.5 D)	0.095	1.24x	+24%	–20%
Zhongshan, China[103]	40 to 70 (22±12)	96	96 (≤ –6 D)	0.230	1.70x	+70%	–41%
France[105]	60+		(≤ –0.5 D)	0.143	1.39x	+39%	–28%
Germany[104]	35 to 74 (51±10)	519	519 (≤ –6 D)	0.182	1.52x	+52%	–34%

Table 4. Summary of studies of the relation between degree of myopia and the prevalence of posterior subcapsular cataract.

Population	Age Range (Mean)	N	Myopes	Slope (logPrevalence per Diopter)	Ratio of Prevalence to Diopter	Increase per Diopter	Decrease per Diopter
Beaver Dam, US[111]	43 to 84 (61±11)	4,470	1,149	0.145	1.40x	+40%	–28%
Singapore Chinese[110]	40 to 79	1,029	340	0.009	1.02x	+2%	–2%
Salisbury, US[109]	65 to 84 (73±5)	5,040 eyes	736 eyes	0.103	1.27x	+27%	–21%
Singapore Indian[108]	40 to 84 (59±10)	5,768	1,498	0.060	1.15x	+15%	–13%

Table 5. Summary of studies of the relation between degree of myopia and the incidence of retinal detachment.

Population	**Cases**	**Controls**	**Slope (logIncidence per Diopter)**	**Ratio of Incidence to Diopter**	**Increase per Diopter**	**Decrease per Diopter**
Japan[114]	1,166	11,671	0.113	1.30x	+30%	–23%
EDCCS, US[115]	253	1,138	0.110	1.29x	+29%	–22%
China[116]	61	61	0.059	1.15	+15%	–13%
Switzerland[118]	195	—	0.096	1.25x	+25%	–20%
England[10]	452	—	0.173	1.49x	+49%	–33%
Iowa, US[117]	172	—	0.156	1.43x	+43%	–30%
Scotland[119]	1,202	—	0.096	1.25x	+25%	–20%

Table 6. Summary of studies of the relation between degree of myopia and the prevalence of primary open angle glaucoma.

Population	Age Range (Mean)	N	Myopes	Slope (logPrevalence per Diopter)	Ratio of Prevalence to Diopter	Increase per Diopter	Decrease per Diopter
India[122]	40 to 90 (51)	5150	—	0.032	1.08x	+8%	–7%
Beijing[123]	40 to 101 (56±10)	4,319	978	0.066	1.16x	+16%	–14%
NHANES, US[124]	40 and older	5,277	1,241	0.053	1.13x	+13%	–12%
Singapore Indian[125]	40 to 84 (59±10)	5,768	1,498	0.144	1.39x	+39%	–28%
South Korea[126]	40 and older	13,433	2,986	0.082	1.21x	+21%	–17%
Kaiser, US[127]	35 and older (58±12)	437,438	—	0.037	1.09x	+9%	–8%

Table 7. Mean lifetime years of visual impairment (VI) as a function of level of myopia using the US definition of 20/40, which is WHO definition of mild visual impairment. Also shown are mean years of visual impairment prevented by a 1 D reduction in a patient's ultimate level of myopia, the number of patients needed to treat (NNT) in order to prevent 5 years of visual impairment, and the reduction in myopia needed to prevent one year of visual impairment.

Myopia Level (D)	Mean Years of VI per Patient	Years of VI Prevented by 1 Diopter Reduction	Number Needed to Treat to Prevent 5 years of VI	Reduction Needed to Prevent One Year of VI (D)
–3	4.42	0.74	6.75	1.38
–4	5.25	0.84	5.97	1.22
–5	6.19	0.93	5.35	1.07
–6	7.22	1.03	4.85	0.97
–7	8.35	1.13	4.44	0.88
–8	9.56	1.22	4.11	0.82

Table 8. Mean lifetime years of visual impairment (VI) as a function of level of myopia using the WHO definition of moderate visual impairment: 20/60. Also shown are mean years of visual impairment prevented by a 1 D reduction in a patient's ultimate level of myopia, the number of patients needed to treat (NNT) in order to prevent 5 years of visual impairment, and the reduction in myopia needed to prevent one year of visual impairment.

Myopia Level (D)	Mean Years of VI per Patient	Years of VI Prevented by 1 Diopter Reduction	Number Needed to Treat to Prevent 5 years of VI	Reduction Needed to Prevent One Year of VI (D)
–3	2.06	0.41	12.24	—
–4	2.55	0.49	10.29	2.33
–5	3.12	0.57	8.77	1.88
–6	3.78	0.66	7.58	1.58
–7	4.53	0.75	6.63	1.36
–8	5.39	0.85	5.87	1.18