Special Issue

IMI – Clinical Management Guidelines Report

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Best practice clinical guidelines for myopia control involve an understanding of the epidemiology of myopia, risk factors, visual environment interventions, and optical and pharmacologic treatments, as well as skills to translate the risks and benefits of a given myopia control treatment into lay language for both the patient and their parent or caregiver. This report details evidence-based best practice management of the pre-, stable, and the progressing myope, including risk factor identification, examination, selection of treatment strategies, and guidelines for ongoing management. Practitioner considerations such as informed consent, prescribing off-label treatment, and guides for patient and parent communication are detailed. The future research directions of myopia interventions and treatments are discussed, along with the provision of clinical references, resources, and recommendations for continuing professional education in this growing area of clinical practice.

Keywords: myopia control, myopia progression, clinical considerations, patient communication, practitioner education

1. Identifying the Myopia Management Patient

1.1 Risk Factors

Myopia has been traditionally viewed as a consequence of interplay between genetic, ethnic, and environmental risk factors,[1,2] and the important associations are detailed below.

1.1.1 Refractive Error and Eye Growth. In a normal eye, the process of eye growth is regulated to proceed from hypermetropia to emmetropia, rapidly within the first year of life and then more slowly until emmetropia is achieved in mid childhood.[3] The process of emmetropization is designed to match the increasing axial length of the eye with the focal lengths (reducing power) of the cornea and crystalline lens.[4] Although axial elongation during emmetropization occurs more rapidly in younger (6–10 years) than older (12–16 years) children,[5] in myopia, this process is accelerated and overshoots emmetropization.[6] In a myopic eye, the fastest growth in axial length appears to be the year before onset, with children who become myopic showing significantly more axial elongation up to 3 years before onset and through to 5 years after onset.[7]

With refractive error being the key clinical measurement, lower hyperopia than age-normal can indicate risk of myopia development; future myopes show less hyperopic refractions for up to 4 years before onset of myopia compared with age-matched counterparts who stayed emmetropic.[7] In an ethnically diverse, U.S.-based study that included more than 4500 children, first grade (age 6) children measuring +0.75 diopters (D) or less by cycloplegic refraction had increased risk of becoming myopic between second and eighth grades (ages 8–14 years) compared with those with +0.75 D or greater refraction, with the risk of myopia increasing with number of myopic parents.[8,9] Additional cutoff points for age-normal hyperopia, below which myopia risk is significant, are suggested to be +0.50 D or less for ages 7 to 8 years, +0.25 D or less for ages 9 to 10 years, and emmetropia for age 11 years.[10]

1.1.2 Age. Myopia can be classified by age as childhood or "school" myopia[6] and late onset (after 15 years of age).[11,12] The major factor contributing to faster childhood myopia progression is younger age at myopia onset, with this factor being

independent of sex, ethnicity, school, time spent reading, and parental myopia.[13–15]

1.1.3 Family History and Ethnicity. Myopia is heritable, with the risk of developing myopia increased threefold or more among children with two myopic parents compared with children with no myopic parents.[1,2,16,17] Additionally, ethnic background also plays a role in myopia susceptibility. In Australia, East Asian children aged 11 to 15 years are eight times more likely to be myopic than their Caucasian counterparts.[18] In British children of a similar age, exposed to the same schooling environment, those of South Asian ethnicity had a 25% prevalence of myopia, followed by black African Caribbeans at 10% and white Europeans at 4%.[19]

There is debate on whether childhood myopia is inherited as a genetic susceptibility, influenced by the myopigenic environment created by myopic parents, or both. Children of myopic parents have been shown to spend less time outdoors and more time reading than children of emmetropic parents,[20] both of which are associated with myopia onset and progression.

1.1.4 Visual Environment. Although there is a genetic component in myopia development, the visual environment appears to be a major contributor to school-aged myopia.[6] Children who become myopic appear to spend less time outdoors compared with their nonmyopic counterparts.[21] Additionally, the risk of myopia development and progression is significantly associated with reading at very close distances (<20 cm) and for continuous periods of time (>45 minutes) rather than being associated with total time spent on all near activities.[22,23] These factors may be related to short-term changes in central axial length that have been shown to occur in progressing and higher (early-onset) young adult myopes after both short-term, high (6 D) demand[24] and prolonged, standard working distance (3 D) near work demand.[25] The balance between less time spent outdoors and more time spent on near work has yet to be comprehensively defined.

It is not clear whether the beneficial effect of time spent outdoors is due to the brightness of light exposure,[26,27] increased short-wavelength (360–400 nm) and UV light exposure,[28,29] the more uniform dioptric field of view across the retina when outdoors compared with indoor environments,[30] or other mechanisms. Although increased time spent outdoors is effective in attenuating the onset of myopia, there is little evidence that outdoor time regulates progression of existing myopes, as measured by refraction.[21] More detail on visual environment interventions can be found in the IMI – Interventions for Controlling Myopia Onset and Progression Report.

1.1.5 Educational Activities. A much higher prevalence of myopia has been reported among many Asian and South East Asian countries; a commonality between these countries is the focus on academic achievement and an intense education system.[31,32] Examples include test driven, highly competitive education systems in Asia and Asian communities[33–35] and the high prevalence of myopia in Orthodox Jewish boys compared with girls in Jerusalem, where the boys spend much more time reading religious texts at close working distances.[36]

A number of reports have indicated that a school curriculum consisting of greater near work demands is associated with a higher rate of myopia[36,37] and a faster rate of myopia progression.[38] There have also been suggestions that extensive engagement in afterschool tutorials may impose additional workload to the school children and is associated with a high prevalence rate of myopia.[39] Mendelian randomization analyses have shown that every additional year of education is associated with a more myopic refractive error of –0.27 D.[40]

Individuals with a high genetic risk and university-level education had a higher risk of myopia than those with a high genetic risk and only primary-level schooling. The combined effect of genetic predisposition and education on the risk of myopia appears to be substantially higher than the sum of these two effects.[40,41]

1.1.6 Binocular Vision. There is a reported association between higher levels of esophoria and accommodative lag at near in myopic children and young adults compared with emmetropes.[42–45] Myopic children and young adults also show reduced accommodative facility[45,46] and enhanced accommodative convergence (elevated accommodative convergence to accommodation [AC/A] ratios) compared with age-matched emmetropes.[47–49] Conjecture exists, however, as to whether accommodative errors are a feature rather than a cause of myopia: some studies show a higher accommodative lag associated with myopia progression in children and adults,[45,50] whereas others do not.[51–53]

1.2 Identifying and Managing the Premyope

The child at risk of developing myopia can be identified by comparing their refractive error to the age-normal as detailed in Section 1.1. Having one or two myopic parents increases risk, along with less time spent outdoors and more time spent reading.[27,54,55] The premyope may also show specific binocular vision disorders (see Section 4.3 for more detail), including reduced accommodative responses, increased accommodative lag, and higher AC/A ratios.[56] The effect of managing these disorders on myopia development has not yet been defined. Recommending an increase in time spent outdoors is the key evidence-based strategy that appears effective in reducing the incidence of myopia across numerous studies.[21]

2. Discussing Myopia and Associated Risks With Parent and Patient

2.1 Lay Terminology Discussion of Causes

Patients and parents must be informed on the probable causes and risk factors for myopia to enable them to understand their child's risk profile and reduce their exposure to avoidable risk (see Section 1). Written lay education is important to consolidate in-office verbal education and serves as a reference between visits.

As children with parental myopia are more likely to develop myopia than those without, and those with parents with high myopia are at risk of developing myopia earlier than their peers and becoming more myopic than children of nonmyopic parents, it is important to discuss a child's risk for myopia development and/or progression with the parents and/or caregivers.

Despite the undeniable and unavoidable influence of heritability and ethnicity, it has been established that eye growth is significantly influenced by the visual environment. Therefore, it is important that these risk factors are discussed to encourage healthy visual habits, such as spending more time outdoors and reducing near work demand, to delay myopia onset or reduce myopia progression.

2.2 Lay Terminology Discussion of Eye Health Risk

Discussions of the risks and consequences of myopia should take place with parents of children at risk of developing myopia (see Section 1.2), as well as children who are already myopic, with emphasis on the latter. Myopic eyes typically demonstrate excessive axial elongation and structural changes,

making them more at risk of developing retinal holes, tears or detachments, myopic maculopathy, glaucoma, and cataract.[30] The higher the myopia and the longer axial length becomes, the higher the lifetime risk of developing these comorbities.[30,57] It is therefore vital that patients and parents are made aware of the potential risks associated with being myopic.

Written lay education and online risk calculators have an important role in complementing in-office verbal education to encourage behaviours that could reduce myopia onset and progression (see Sections 3, 5, and 6). Patient and parent education regarding all evidence-based treatment options is important in aiding decision making, when taken in view of practitioner prescribing based on examination findings. For more detail on the evidence of specific treatment types, see the IMI – Interventions for Controlling Myopia Onset and Progression Report.

3. Myopia Control Treatments: Risks, Benefits, and Expectations

3.1 Lay Terminology Discussion of Options

It is important to educate patients and parents on the evidence-based treatment options available (see Sections 4 and 5 for identifying treatments based on examination findings). Written material is beneficial to support in-office verbal education. Examples of evidence-based education by treatment modality are provided below and can be adapted based on availability of these treatments to the practitioner and the individual. Detail on the scientific evidence supporting various myopia control treatment options can be found in the IMI – Interventions for Controlling Myopia Onset and Progression Report.

Examples of parent- and patient-appropriate explanations of myopia control options are as follows. Orthokeratology (OK) lenses are rigid gas permeable contact lenses worn overnight to reduce nearsightedness by temporarily and reversibly reshaping the cornea (front surface of the eye).[58] Multifocal soft contact lenses (MFSCLs) have two or more powers in them and were originally designed to correct both far vision and near/intermediate vision in adults. Both contact lens treatments are thought to slow the progression of nearsightedness in children by focusing light at the periphery of the eye in alignment or in front of the retina.[59] Atropine is a prescription eye drop used to temporarily dilate (open) the pupil and limit the ability to accommodate (focus). It is thought to slow the progression of nearsightedness through interaction with some of the receptors in the eye that control eye growth.[60]

3.2 Lay Terminology Discussion of Efficacy and Additional Correction Benefits

Parents should be provided information on expected efficacy and other potential benefits of myopia control treatments. Detail on efficacy of the myopia control treatment options can be found in the IMI – Interventions for Controlling Myopia Onset and Progression Report. Furthermore, discussion of the responsibility of presenting this information to the public to avoid bias is provided in the IMI – Industry Guidelines and Ethical Considerations for Myopia Control Report. Examples of evidence-based education in lay language are provided below. Note that references compare myopia control treatment to traditional single vision spectacle or contact lens correction.

No current myopia control treatment can permanently stop or reverse the progression of nearsightedness, although cessation of progression is sometimes observed in clinical practice. Generally, nearsighted children wearing traditional single vision glasses or contact lenses will continue to increase in nearsightedness by approximately 0.50 to 1.00 D (units of measurement) per year, as accelerated eye growth occurs.[61] The myopia control treatments discussed below are expected to slow the rate of progression; which means the average child would still have some progression in nearsightedness. Measurements of the child's prescription and the length of the eye can provide more information about the effectiveness of various treatments. The myopia control treatment effect for an individual child may be higher or lower than the average and is based on numerous factors, and the long-term effectiveness is not fully understood as the available data only extend to 1 to 5 years of treatment.

OK lenses are expected to slow myopia progression by approximately 30% to 60%.[62–65] Additional benefits include not having to wear a vision correction during the day. Some parents also like that they can oversee contact lens wear since lenses are only worn at night.

MFSCL are expected to slow myopia progression by about 30% to 50%, although studies have investigated several different lens designs, some of which have shown higher results.[66–70] This correction also allows part-time wear, but this may reduce the myopia control effect.[67]

Children wearing soft contact lenses have been shown to have improvements in self-perception and self-esteem compared with children wearing glasses.[71] Although not studied, it is expected that similar improvements would be found with OK contact lenses because these children do not need to wear glasses during waking hours, where full myopia correction has been achieved.

Atropine eye drops can be expected to slow myopia progression by approximately 30% to 80%, although significant adverse effects (light sensitivity and reduced near vision) can occur with stronger dosages.[72–74] Lower strength doses (i.e., 0.01%) may have less side effects but may not be as effective as higher strengths (i.e., 0.5% and 1.0%),[73] although rebound effects—accelerated myopia progression—after cessation of higher strength atropine treatment have been found.[74] It is also important to note that despite effects on slowing the level of myopia, the effect of low dose (0.01%) atropine on slowing eye growth has not been convincingly established.[75]

Specific spectacle lens options can also provide treatment effects for some children of approximately 20% to 50%, in specific populations.[76,77]

3.3 Lay Terminology Discussion of Safety and Other Risks and Challenges

Finally, parents should be informed of potential risks and side effects associated with myopia control treatments. Examples of lay education on general risks are provided below, and education on how to minimize risks is provided in Section 6.

To date, no studies have examined children using myopia control treatments for more than 5 years, and not all the studies reported safety information, but data from clinical trials and record reviews do provide information on the major risks associated with myopia control treatments.

The most significant risk associated with contact lenses is microbial keratitis (a bacterial infection of the clear front of the eye called the cornea), which in a small percentage of cases can result in vision impairment. The rate of new cases of microbial keratitis in children wearing overnight OK lenses is 13 in 10,000 per year.[78] For soft contact lenses, the rate of corneal infiltrative events is about 15 per 10,000 per year for children age 13 to 17 years.[79] The rate of microbial keratitis for children 8 to 12 years of age wearing soft contact lenses appears to be less than that of adults or teenagers, but cannot be accurately estimated with the data available.[79,80]

Other risks associated with the use of contact lenses include other types of infections or inflammation (swelling) or abrasions (scratches) of the eye. Most of these complications do not result in any long-term damage to the eye.

Compared with glasses, children may notice mildly blurred vision or changes in their focusing with either OK or MFSCLs.[81,82]

The most common side effects associated with the use of atropine eye drops are a temporary stinging or burning, blurred vision, and sensitivity to lights.[83] Lower strength doses may cause less of these side effects.[73,84]

Although generally showing lower efficacy than other options,[85] the risks of side effects with spectacle lens corrections is minimal.

3.4 Informed Consent and Prescribing Off-Label Treatments

Despite being widely accepted as evidence based, currently available treatment options for myopia control are yet to be approved by the US Food and Drug Administration (FDA) so their use must be considered "off-label." At the time of writing, two daily disposable MFSCLs (Coopervision Misight and Visioneering Technologies NaturalVue) had received approval from EU regulatory authories CE marking (certification standard) for myopia control, which is recognized in Europe, Australia, New Zealand, Canada, and parts of Asia and is independent of FDA approval. Further information on the relevance of off-label treatments, lack of FDA approval, or presence of CE marking in particular countries is provided below—the practitioner should also seek specific advice from their representative organizations in their country where required.

Due to this complex regulatory environment and the involvement of children as patients, providing proper informed consent is an important part of myopia management. Full disclosure to parents/carers and patients on myopia control treatment efficacy, risks and benefits, and off-label use (where relevant) should be included. The informed consent form used by the University of California Berkeley Myopia Control Clinic is provided in the Supplementary Material as an example—note that spectacle lens options are not included in this instance. For more detail on the ethical considerations of practitioners in prescribing for myopia control—including regulatory advice on off-label prescribing, consent forms, and avoiding bias in information provided to parents and patients—refer to the IMI – Industry Guidelines and Ethical Considerations for Myopia Control Report.

The practitioner should be aware of regulatory and professional requirements regarding use of off-label treatments in their country of practice. The definition and legality of use of off-label treatment varies significantly across the world, and the practitioner should ensure they understand the legislative, regulatory, and professional aspects of off-label prescribing in their country. For example, in the United States, off-label treatment is defined as "FDA-approved drugs/medical devices used for nonapproved indications," which is considered legal as long as there is sufficient evidence supporting the efficacy and safety in such application.[86]

In the United Kingdom, optometrists with "additional supply" or independent prescribing qualifications are able to use and supply 0.5% and 1.0% doses of atropine for indications involving temporary cycloplegia or mydriasis. The use of lower doses (i.e., 0.01%) for myopia control is not currently listed on the Optometrists' Formulary[87]; therefore, further advice from professional organizations may be prudent.

The European Union legislation "does not regulate the way medicinal products are ultimately used in medical practice. The prescribing of a medicinal product, on-label or off-label, is a decision taken within the relationship between a patient and his or her treating healthcare professional (HCP). The way Member States organize their healthcare system and the way HCPs conduct their practice is not a topic that falls within the remit of the EU."[88]

In Australia, according to the National Prescribing Service (NPS), off-label prescribing is "unavoidable and very common, especially if your practice includes children." Off-label prescribing means that the Therapeutic Goods Administration (TGA) has not approved the indication, route of administration, or patient group. It does not mean that the TGA has rejected the indication. Commonly the TGA has not been asked to evaluate the indication. There is no legal impediment to prescribing off-label; however, the onus is on the prescriber to defend their prescription for an indication that is not listed in the product information. If, in the opinion of the prescriber, the off-label prescription can be supported by reasonable quality evidence, for example, the indication is identified in the Australian Medicines Handbook, the prescriber should proceed if this is in the patient's best interests. It is best if your patient knows that their prescription is off-label and why you are recommending the drug. Making a note of this "conversation" in the patient's records and possibly even recording that the patient "consented" would be good practice.[89] Similar advice is provided for New Zealand practitioners,[90] with comparable legislation or advice existing for optometrists in Hong Kong and Canada—with the exception of Coopervision's Misight lens, which has received a myopia control indication from Health Canada.[91] In China, only certain products can be prescribed by practitioners with specific licenses—more detail can be found in the IMI – Industry Guidelines and Ethical Considerations for Myopia Control Report.

4. Key Elements of the Baseline Exam for Myopia Control

4.1 Standard Procedure for Examination

The following summarizes the standard procedures for examination of myopes:

1. History taking: age, sex, history of ocular and general health, ocular surgery, ocular and general health parental history of myopia, age of onset of myopia, history of myopia progression (if available), previous myopia control treatments if any.
2. Refraction: noncycloplegic and/or cycloplegic refraction as indicated. The IMI – Defining and Classifying Myopia Report defines myopia by refraction "when ocular accommodation is relaxed. These definitions avoid the requirement for objective refraction so as to be independent of technique, but by making reference to relaxation of accommodation are compatible with both cycloplegic and standard clinical subjective techniques." If used, the recommended dosage for cycloplegic refraction is two drops of 1% tropicamide or cyclopentolate given 5 minutes apart. Cycloplegic refraction should be performed 30 to 45 minutes after the first drop is instilled.[92] For more information on specific refraction techniques that have been used in myopia control studies, refer to the IMI – Clinical Myopia Control Trials and Instrumentation Report.
3. Best-corrected visual acuity.
4. Binocular vision and accommodative tests: see Section 4.3.

Table 1. Accommodative Function Tests Used in Clinical Studies

Accommodative Assessment	Clinical Tests
Accommodative accuracy (lag or lead)	Open-field autorefractors (Canon R-1,[56,77,98–102] Grand Seiko WV-500,[13,52,66,103,104] or Grand Seiko WR-5100[105,106]
	Aberrometers (Complete Ophthalmic Analysis System [COAS] aberrometer[107,108])
	Monocular estimate method (MEM) retinoscopy[82,109,110]
	Nott dynamic retinoscopy[111,112]
	Photorefractor[113,114]
Accommodative amplitude	Minus lens technique (or Sheard's technique)[109]
	Push up (or in) test[66,114]
Accommodative facility	Distance (plano/−2.00 D flippers)[13,115]
	Near (±2.00 D flippers)[13,109,110,114,115]

Table 2. Vergence Function Tests Used in Clinical Studies

Vergence Assessment	Clinical Tests
Distance and near heterophorias	Risley prism and Maddox rod[56]
	Von Graefe method[116,108]
	Alternating cover test[69,82,100,101,103]
	Howell near phoria card[104,110]
	Saladin near point balance card[81]
Near fixation disparity	Saladin near point balance card[69,108]
AC/A ratio	Calculated method[56,101,102,117]
	Gradient technique[13,116,117]

5. Anterior eye health evaluation using a slit-lamp and intraocular pressure measurement.
6. Corneal topography: if indicated (for example, for contact lens fitting).
7. Axial length (AL): although routinely employed in myopia control studies to determine the outcome of reduced axial elongation, measurement of AL is not widespread in clinical practice, and at this point, there are no established criteria for normal or accelerated axial elongation in a given individual. It is well known that during emmetropization, axial elongation is more rapid in younger (6–10 years) than older (12–16 years) children.[5] However, there is a broad range observable, with emmetropes typically showing an AL of 22 to 24.5 mm, and myopia typically associated with ALs greater than 25 mm.[57] Increases of about 0.1 mm/yr have been shown to be associated with normal eye growth, whereas 0.2 to 0.3 mm/yr is associated with increasing myopia,[7] although myopia progression can occur with smaller AL changes in an individual. This makes AL measurement currently an uncertain diagnostic factor in clinical myopia management, but a useful factor in risk of myopia pathology, where an AL approaching 26 mm in a myopic child, where further axial growth is still expected due to emmetropization, could increase the index of concern for the practitioner.[57]

Where available, measurement with a noncontact device, for example, IOL Master (Zeiss, Oberkochen, Germany) or LENSTAR (Haag-Streit, Köniz, Switzerland) is ideal. The mean and SD of multiple measurements should be recorded.

1. Fundus examination and imaging: examination of both the central and peripheral retina under dilation, annually in high myopes and in others as indicated. If retinal findings are noted, Optical Coherence Tomography (OCT) images and/or fundus photos may be taken to objectively document retinal features and/or abnormalities. Practitioners may also grade and scale any retinal changes in fundus photos (e.g., chorioretinal atrophy, staphyloma, peripapillary atrophy, titled disc).[93] More detail on macular and nonmacular structural complications of myopia, including the Meta-analysis for Pathological Myopia (META-PM) classification system for myopic maculopathy, can be found in the IMI – Defining and Classifying Myopia Report.

4.2 Visual Habits and Environment Evaluation

Given the association between near work and outdoor time to myopia, it is preferred to obtain and record the visual habits of the individual such as information about daily average hours of time spent on near work and time spent outdoors.

4.3 Binocular Vision Evaluation

Assessment of binocular vision involves evaluation of both the accommodative and vergence systems.[94–96] The two primary tests of accommodation are accommodative accuracy, clinically measured as lead or lag of accommodation, and accommodative amplitude or the maximum accommodative ability (Table 1). In addition, accommodative facility is often measured to assess an individual's ability to adapt to rapid changes in accommodation (Table 1). Accommodation can be assessed under monocular (response driven by blur and proximal stimuli) or binocular conditions (response to blur, proximal and convergent stimuli). Tests adopted to assess the vergence system include those evaluating the accuracy of fixation in associated and dissociated conditions (Table 2). Heterophoria is a misalignment of the eyes during the absence of fusion (partial dissociation), whereas fixation disparity is misalignment of the eyes during fusion.[96] The primary evaluation of the interaction of the accommodative and vergence systems is accommodative convergence over accommodation ratio (AC/A; Table 2), which is a measure of the convergence per diopter change in accommodation.

Currently, there is no consensus on the gold standard techniques for assessing binocular vision function, and various methods have been used in clinical studies of myopia and myopia control as outlined in Tables 1 and 2. It is recommended that the baseline examination for myopia control should include, as a minimum, tests that assess the various elements of accommodation and vergence as listed in Tables 1 and 2. Furthermore, the same tests need to be used in follow-up consultations to monitor for changes. Previous studies have suggested that not only atropine, but MFSCL and OK can affect pediatric accommodative and binocular function.[81,97]

4.4 Dry Eye Evaluation

In myopic eyes, symptoms of dry eye–related disorders can surface or be exacerbated in response to myopia control treatments or exposure to environmental risk factors. These are detailed below. It is therefore advisable that practitioners monitor the ocular surface in children with myopia, as well in those undergoing myopia control treatments.

Contact lens wear has been associated with dry eye, either as a contributing factor to dry eye[118,119] or because contact lens discomfort and drop out is largely linked to dry eye.[120–124]

Thus, the ocular surface should be regularly evaluated in an individual wearing contact lenses.

Atropine in low doses for myopia control is often limited to compounded formulations, often preserved with benzalkonium chloride (BAK). BAK has been shown to be toxic to the corneal epithelium, is implicated in dry eye particularly with long-term use as in glaucoma therapy, and may have toxic effects in the retina.[125,126] In addition to the suggestion that an upper limit of 2 years of atropine treatment is recommended for children,[127] long-term use of eye drops with BAK may pose an unacceptable risk of corneal toxicity and dry eye.

With evidence mounting that dry eye affects younger populations[119,128] potentially exacerbated by digital device use,[129–132] practitioners should consider a dry eye evaluation at the baseline myopia control examination and monitor for dry eye and meibomian gland dysfunction (MGD). Training children in proper contact lens use, and avoiding preserved eye drops or lens cleaning solutions by fitting daily disposable contact lenses, may help to reduce the impact of myopia control treatment on the ocular surface. For detail on dry eye evaluation and treatment, refer to the Dry Eye Workshop (DEWS II) series of reports, published in 2017.[133]

4.5 Exploratory Tests

4.5.1 Relative Peripheral Refraction (Uncorrected Eye). The relation between peripheral refraction and refractive errors in humans has been studied for nearly 50 years. Hoogerheide evaluated 375 pilots and suggested that relative peripheral hyperopia in the horizontal meridian could be a risk factor for myopia development.[134] Several cross-sectional studies similarly illustrated an association between relative peripheral hyperopia and central refraction, where greater relative peripheral hyperopia was found in myopia, with relative peripheral myopia found in hyperopes and emmetropes.[135–137] There is conjecture, however, as to whether this peripheral refraction pattern is more a consequence rather than a cause of myopia development and whether it could be used to predict a future myope or not.[138,139]

MFSCLs that are based on generating peripheral myopic defocus have been shown to reduce myopia progression,[68] and similarly, OK has been shown to alter peripheral refraction from relative hyperopia to myopia,[140,141] consistent up to 1 year of wear.[142] There is no clear evidence yet, however, linking changes to peripheral refraction induced by MFSCL or OK to myopia control or progression, so more understanding of this proposed mechanism is required.

Peripheral refraction can be measured with an open field autorefractor with targets positioned in the nasal and temporal visual field across the horizontal meridian. This can also be measured during MFSCL wear or in OK wear after the initial fitting process has been completed. As research continues, measuring peripheral refraction may be a clinical test used in future.

4.5.2 Higher-Order Aberrations. It appears that there may be some relationship between higher-order aberrations and myopia control, but this is yet to be fully understood, and use of aberrometers in clinical practice is uncommon. Higher levels of total corneal higher order aberrations induced with OK wear appear to be associated with a slower progression of myopia and a smaller axial elongation. A significant shift in positive spherical aberration appears to be a key correlation,[143] whereas increased coma after OK treatment has been shown not to be associated with its myopia control effect.[144]

4.5.3 Pupil Size. Based on available data, it is difficult to ascertain the contribution of pupil size to myopia control. A single study reported that pupil size is related to myopia progression in OK treatment, where children with an "above average" scotopic pupil diameter, defined as greater than 6.4 mm by the group mean, exhibited a greater myopia control effect than children with a "below average" scotopic pupil diameter.[145] Within normal refractive development, however, there is no consistent link between pupil size and myopia progression. Further studies are needed to explore a potential relationship between pupil size and myopia control efficacy.

4.5.4 Subfoveal Choroidal Thickness. A number of studies have reported an association between choroidal thickness changes and myopia progression,[146] induced myopic and hyperopic defocus,[147] and myopia control intervention.[148] Ongoing research is aimed at exploring the relationship between myopia onset and progression with subfoveal choroidal thickness (SFCT) at the macular region and in other areas of the retina.

4.5.5 Wearable Devices to Track Visual Habits and Environment. The association between development of myopia and increased time spent in near work, or prevention by increased time outdoors, has been largely determined by questionnaire.[54,149–153] More recently, light data loggers (LDLs) have been used to make objective measures of ambient light levels, including the HOBO Pendant (Onset Computer Corporation, Bourne, MA, USA),[154–156] and Actiwatch 2 (Philips Respironics, Murrysville, PA, USA).[27,157,158] A cutoff measure of 1000 lux has been suggested to differentiate indoor and outdoor environments based on diary records,[154,155,158] although there is some conjecture.[159,160] Objective measures of light intensity continue to show an association between time spent outdoors and protection from myopia.[155,161] In addition, current generation wearable devices are also able to determine the working distance at near and posture and could shed further light on the impact of visual habits on onset and progression of myopia.

5. Selecting a Treatment Strategy

5.1 Predicting Progression Rate

In attempting to control progression of myopia, an understanding or estimation of the rate at which myopia progresses for a given individual may help identify an appropriate strategy to control the rate of progression. In this respect, it is recognized that myopia will progress at a faster rate in those that are of younger age,[162] have higher baseline myopia,[163] and have experienced past myopia progression of >0.50 D/yr.[164] Myopia can also progress more over winter than summer seasons.[165] However, although it may be possible to determine the risk of progression, determination of the rate of progression in an individual is difficult as it can be influenced by a multitude of other factors.

While acknowledging these individual variations, it still is reasonable to estimate likely progression based on average population-based progression rates. Donovan et al.[61] conducted a meta-analysis of data of single vision distance spectacle-corrected children who participated as control groups from 20 myopia control studies. Based on the meta-analysis, annualized progression rates for myopic children of Asian and Caucasian ethnicities ranged from about 0.50 to 1.00 D and varied by age and sex. These data were used in the development of the Brien Holden Vision Institute myopia calculator, which predicts level of myopia at age 17 years based on inputs of a child's current age and level of myopia, if a single vision treatment was used, and then illustrates the impact of various treatment strategies on myopia progression (https://calculator.brienholdenvision.org, in the public domain). Given that the calculator estimates long-term progression based on study data of only 2-year duration, parents should be cautioned that the calculator is for

illustrative purposes and that the child's actual myopia progression and myopia control efficacy may vary.

5.2 Selecting a Treatment

To date, there have been no published clinical trials that have tested specifically the appropriate point of intervention based on either age or refractive status, to either prevent or delay the onset or control the progression of myopia. Nevertheless, once a myopic child has been identified, an appropriate treatment to manage myopia progression must be selected based on numerous patient specific factors. As described in Section 1, there are important risk factors relating to myopia development and progression. Children who possess multiple risk factors may require more strategic management and frequent review compared with those with little or no associated risk factors. Other patient and treatment factors will also influence treatment selection as described below.

5.2.1 Baseline Refractive Error. Earlier onset of myopia often results in higher degrees of myopic refractive error.[15,166,167] Although the progression rates across children with different ages of onset may be similar, longer duration of myopia progression results in a greater magnitude of myopia.[15] Thus, a child's age and baseline refractive error must be considered together in the selection of treatment. Due to the inherent risks of any treatment (contact lens, pharmaceuticals), treatment is not generally advisable until the myopia is visually significant; the IMI – Defining and Classifying Myopia Report defines myopia as equal or more than −0.50 D.

Baseline refractive error will determine the availability of treatment. For example, different MFSCL designs have varying power ranges. Myopic children with low astigmatism may be prescribed spherical MFSCLs, although practitioners must consider the impact of the residual astigmatic refractive error on visual acuity as uncorrected refractive astigmatism over 0.75 DC can lead to visual compromise.[168] In these cases, residual astigmatism can also be corrected by spectacles worn in addition to MFSCLs, provided compliance can be assured. Currently, there are no studies investigating toric MFSCLs for myopia control.

Spherical OK lenses are typically fitted to myopes with mild astigmatism.[169] Spherical OK lenses are generally fitted to children with <1.50 D of corneal toricity. Toric periphery or other lens designs may be available to those with higher corneal toricity (based on differences in corneal elevation across the two major meridians) and have also shown efficacy for myopia control.[170] Myopes with higher baseline myopia may elect for partial correction with OK.[171] Studies have suggested individuals of younger age[172,173] and higher degrees of baseline refractive error may benefit most from OK.[174,175]

5.2.2 Binocular Vision Status. Studies have reported differences in myopia control effects related to accommodative and vergence factors. Thus, a child's binocular vision status may influence the efficacy of treatment. Greater myopia control effects with progressive addition (spectacle) lenses (PALs) were reported in children with larger lags of accommodation and near esophoria.[100] Children with lower lags of accommodation (<1.01 D) have been found to experience greater myopia control effects with prismatic bifocals (+1.50 D add and 3 prism diopters base-in in the near segment of each lens) compared with standard executive bifocal spectacle lenses (+1.50 D add).[176] In addition, children with lower baseline accommodative amplitude have greater myopia control response to OK wear than those with higher baseline accommodative amplitude.[177]

5.2.3 Ethnicity. There are limited studies investigating the influence of ethnicity on treatments. A recent meta-analysis suggested greater myopia control with atropine treatment in children of Asian compared with European ethnicity[178]; however, further prospective studies with appropriate simple sizes are needed. Cultural and regional preferences for particular treatments may need to be taken into account by the practitioner. In time, as mechanisms underlying myopia are better understood, research may help determine whether certain treatments work better in particular populations.

5.3.4 Safety, Compliance and Cost Considerations. Clinicians must determine whether children can safely self-administer and comply with the treatment. For any contact lens treatment, children (and/or parents/guardians) must demonstrate appropriate contact lens handling skills for safe and successful lens wear and maintenance. Clinicians must be aware of contraindications to atropine eye drop use so that it can be safely administered.

The annual cost of professional management and lens materials or drug costs should be discussed with parents prior to initiating treatment.[179] Until these services are covered by medical or vision insurance, costs incurred will be an out-of-pocket expense. Due to the length and number of visits required to appropriately manage these patients and the cost of specialty contact lens materials, these treatments can come at a significant cost. Parents and eye care practitioners should work together to determine which modality may be best suited for a particular child, based on the above factors.

5.3 Add Powers in MFSCL

Previous studies investigating myopia control with MFSCLs have used several different lens designs.[66,180–188] There are two main categories of MFSCL designs: concentric ring or bifocal lens design and progressive power or peripheral add lens design. Concentric ring lens designs incorporate alternating distance correction and treatment (plus power) zones to provide two focal planes or simultaneous distance correction and retinal myopic defocus. Progressive power lens designs have a gradual change in curvature to provide a central zone of distance correction with a progressive change to include a relative plus power in the periphery. The majority of investigated MFSCLs for myopia control incorporate a relative +2.00 D treatment correction creating simultaneous images on the retina. Termed the "add", this power has some influence on both peripheral and central optics of the eye.[81,108,189,190]

Some commercially available MFSCLs that were originally designed for presbyopia correction have been used for off-label myopia control treatment owing to studies that have shown that these MFSCLs induce relative peripheral myopic defocus.[189–192] In clinical practice, it is recommended that a MFSCL incorporating the patient's full distance refractive error and relative +2.00 to +2.50 D treatment correction be initially selected, regardless of the design. Although MFSCLs that manipulate optical defocus across larger areas of the visual field have been suggested to result in greater myopia control,[193] to date, there has been no systematic investigation comparing the efficacy of myopia control associated with different add powers; however, studies are underway.[194] Further discussion of this can be found in Section 8b. As currently available MFSCLs, particularly lenses with higher add powers, can significantly reduce quality of vision,[195,196] it is essential that visual acuity and quality of vision are monitored. In cases where the patient experiences significant reduction in visual acuity and/or subjective quality of vision with the selected MFSCL, an over-refraction should be conducted and incorporated into the lens power.[197] Alternatively, the add power may be reduced until acceptable vision is achieved, or a different lens design may be trialed. The impact of the add power on binocular vision function should also be evaluated.

5.4 Clinical Spectacle Myopia Control

Evidence on the efficacy of spectacle lenses with various optical designs for myopia control are not as homogeneous as that observed with contact lens options.[193] The discrepancy between the strong myopia control effects of plus defocus observed in animal models versus the weaker and less consistent effects in human myopia with spectacles could be partially explained by noncompliance, limited amounts of defocus, reduced wearing time due to visual distortion, and restricted peripheral vision. As a result, myopia control spectacles are generally reserved as a second-line treatment for those who are either not suitable, not yet ready, or are lacking motivation for myopia control contact lenses.

Undercorrection of myopia is still practiced in some countries,[179] although it has been shown to either have no effect on progression or possibly even increases the rate of myopia progression.[198,199] Interestingly, a paper on delaying correction of low myopia (<1 D) in 12-year-old Chinese children found that those who were uncorrected showed 0.25 D less progression over 2 years than those who were fully corrected.[200] This relationship held even when controlling for numerous genetic, refractive, and environmental factors, indicating the large influence of optical correction. Caution should be exercised in incorporating these results in clinical care as they are modest, and priority should be to correct ametropia and maximize acuity. It is likely the poor uncorrection results are related not only to wearing time compliance, but amount of peripheral defocus and the effect on the binocular vision system.[201]

Myopia control studies evaluating bifocal or PAL spectacle lenses have used either a +1.50[202] or +2.00 Add.[76,77,105,203,204] In clinical practice, it may be more practical to prescribe the near addition required to manage any evident accommodation or vergence disorder[205] to ensure visual comfort. Although there is indication from one study that bifocal spectacle lenses show better efficacy than PAL spectacles,[76] the practitioner should consider any esthetic issue with bifocal lenses, or compliance and frame fitting issues with PALs in the prescribing choice. The fitting seg line of bifocals should be higher than that for presbyopic correction to ensure the add is easily accessed and that enough myopic defocus is imposed on the retina.[52] Additionally, the frame should be regularly adjusted to ensure that is appropriated fitted on the nasal bridge, which is especially important in Asian children who have lower nose bridges that results in frame slippage. Regular adjustments to spectacle frames are recommended, as downward slippage of PALs may reduce myopia control effects of the near addition.[43] Selecting PAL lens designs with shorter corridors will similarly ensure the child is looking through the near addition as much as possible.

Novel spectacle lens designs have been developed for myopia control based on a peripheral defocus design and have been found to be moderately successful in younger Asian children with a family history of myopia.[206] Other designs are currently under development including multiple lenslet designs.[207]

6. Guidelines for Advice and Clinical Care

6.1 Refractive Correction and Wearing Time

Children should be encouraged to wear their myopic correction full time, as undercorrection of myopia has been shown in some studies to increase myopia progression.[198] The younger myopic child has a higher risk of progression,[15,61] and consideration should also be given to correcting any amblyogenic or strabismic risk factors such as significant astigmatism, anisometropia, and binocular vision anomalies, or the risk of developmental problems due to insufficient functional vision.[205] Although removing full distance myopic refractive error correction during near work will reduce accommodative demand and accommodative response during near viewing, there have been no studies comparing myopia progression in children wearing distance correction and removal of distance correction during near work on myopia progression.

OK wear should be encouraged every night for a minimum of 8 hours per night to maximize correction for best unaided vision during waking hours. Treatment effect of MFSCL is likely to be positively correlated with wearing time; a study of novel Defocus Incorporated Soft Contact (DISC) lenses reported an inverse relationship between myopia progression and lens wearing time. For the DISC lens design, a minimum of 5 hours per day of lens wear was recommended to slow myopia progression, with increasing efficacy up to 8 hours a day of wear.[182] For visual consistency, including ongoing acceptance of MFSCL, a child should be recommended to wear MFSCLs during school hours and for school work at home, with a backup spectacle option (Section 6.6).

6.2 Indoor and Near Work Activity

As mentioned in Section 1.1, parents should be informed that greater near work (hard copy or digitial) may influence the development and progression of myopia[36,37,39] Close reading distance (≤20 cm) and continuous reading (>45 minutes) have been associated with greater odds of myopia.[22] Outdoor activity is associated with reduced incidence of myopia in children, including those who usually perform large amounts of near work.[21,152] This suggests that children should not be prevented from participating in near work activity, but rather that regular breaks, appropriate reading distances, and near-to-distance fixation changes while reading and spending time on screens are taken, with sufficient time outdoors also encouraged.

6.3 Outdoor Activity and Lighting

There is growing evidence that outdoor activity is associated with lower incidence of myopia.[21] Spending time outdoors without requiring physical activity or direct sunlight exposure appears to have a protective effect against myopia onset but not for myopic progression, although the mechanism underlying this effect is not well understood.[21] An increase in time spent outdoors may result in greater protection, and studies involving school-aged children have suggested a minimum of 8 to 15 hours of outdoor activity per week is required to achieve clinically meaningful protection from myopiagenic stimuli.[152,161,208–210]

The protective effect of outdoor time for the onset of myopia in humans is supported by animal studies that have reported reduced eye growth with exposure to bright light and the opposite effect, axial elongation, and myopia, resulting from reduced light levels.[211,212] High ambient lighting has been shown to have protective effects against the development of form deprivation myopia in Rhesus monkeys.[213]

Although good lighting should always be recommended for any visual task, current advice to patients who are at risk of developing myopia should be aimed at maximizing both indoor and natural lighting and increasing outdoor time.[26,27]

6.4 Nutritional Advice

There is currently no conclusive evidence supporting any definite link between myopia and nutrition or malnutri-

tion.[214,215] Some studies have linked myopic progression to low-fat and low-carbohydrate intake,[216] whereas diets high in saturated fat and high cholesterol levels have also been linked to increased axial length.[217]

A placebo-controlled clinical trial showed that the caffeine metabolite 7-methylxanthine (7-MX) has the potential to reduce eye growth in children.[218] This medication is approved as a treatment for myopia progression, but only in Denmark, where these studies were undertaken. Although caffeine-like stimulants may be part of nutritional advice for myopes in the future, there is no current evidence to support nutritional treatments for myopia control.[219] Further detail on 7-MX can be found in Section 7.2.

6.5 Advice to Patients on Minimizing Risk With Contact Lenses or Atropine

Proper use of the prescribed treatment should be reviewed at each visit, and patients should be educated on ways to minimize risks of complications.

Contact Lens Wear:

- Always wash your hands before applying or removing contact lenses.[220,221]
- Never swim or shower with contact lenses or expose the contact lenses or lens storage case to water.[222,223]
- Don't wear your contact lenses if you have a cold or are unwell.[224,225]
- Daily disposable lenses are strongly encouraged. If you wear reusable contact lenses, use new lens cleaning solution each day[226,227] and use a nonpreserved care cleaning regimen such as hydrogen peroxide, if possible. Replace your lens case at least every 3 to 6 months.[225,228] Rinse the case with contact lens cleaning solution, rub, tissue wipe, and air dry casing facing down.[227]
- Unless directed by your doctor (for OK), don't sleep or nap in your lenses.[79,229]

Atropine Use:

- Where available, unit dose atropine preparations are preferable. In a multiuse bottle, to avoid contamination, never touch the tip of the bottle to the eye or any other surface and do not use the bottle past the expiration date.[230]

6.6 Backup Corrections for Contact Lens Wear

For patients wearing daytime MFSCLs, it is recommended that they use their contact lenses full time. As mentioned in Section 6.1, increasing lens wear time may provide greater myopia control efficacy.[182] Bifocal, PAL, or single-vision spectacles may be prescribed for when children are not wearing contact lenses. This prescribing decision may depend on the individual's intended wearing time, refraction, and binocular vision status in single-vision distance correction.

6.7 Review Schedule and Clinical Considerations

The follow-up schedules for patients receiving myopia control treatments are determined by multiple factors such as the risks of complications related to each option, the efficacy of treatment in myopia control, and the patients' compliance to the treatments. Generally, patients undergoing any myopia control treatment should be assessed at least every 6 months to monitor safety and efficacy of treatment.

As discussed in Section 4.1, although cycloplegic autorefraction is typically measured in research studies, it can be used in clinical practice on indication, at the practitioner's discretion, and where consistent with evidence-based best practice. Consistent refraction techniques should be used to ensure comparable clinical data. Similarly, axial length measurement is an expected outcome measure of myopia control research studies but is not used in widespread clinical practice. Axial length measurement is a somewhat problematic diagnostic factor in clinical myopia management but a useful diagnostic factor in risk of myopia pathology. If available, axial length measurements should be taken at least every 6 months.

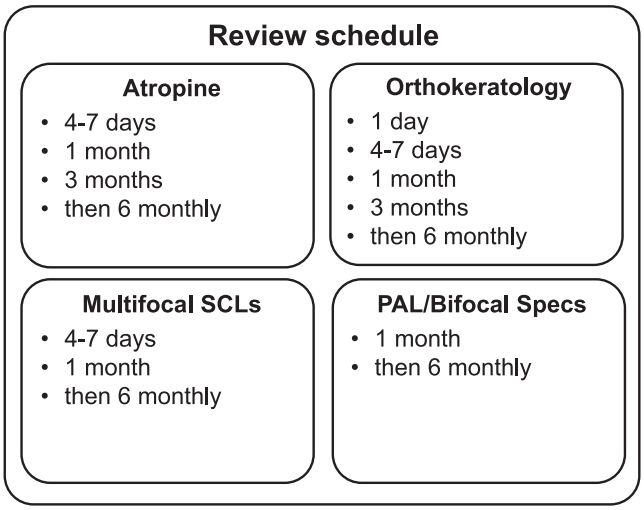

FIGURE 1. Review schedule for myopia management based on treatment type.

The minimum recommended review schedule by treatment type is shown in Figure 1, and clinical tests for myopia management with low dose atropine eye drops, OK, MFSCLs, and PAL/bifocal spectacles are detailed in Figure 2. Additional aftercare visits are likely to be required for patients undergoing OK or MFSCL treatment to optimize lens fit and to manage any issues relating to quality of vision.

6.7.1 Atropine Eye Drops. A major clinical consideration is the availability of atropine eye drops; currently, low dose atropine eye drops are not commercially available and need to be compounded by pharmacists who have appropriate sterile laboratories. Facilities in laboratories will also dictate whether clinicians have access to preserved and unpreserved formulations of atropine.

Patients undergoing atropine therapy will require distance refractive error correction. It is recommended that patients are prescribed their full distance refractive correction; however, single vision correction may not be suitable due to the cycloplegic side effects of atropine. Patients may require near addition correction to alleviate near visual symptoms (such as PAL or bifocal spectacle lenses) and photochromic lenses or additional sunglasses to relieve glare issues. The Atropine for the Treatment of Myopia 2 (ATOM2) atropine study provided photochromic lenses to all participants and offered PALs to subjects who complained of near vision issues. They found that only 7% of children on 0.01% atropine requested glasses.[231] Although accommodative amplitude was only reduced by 2 to 3 D, further detail of the effect of low dose atropine on accommodative lag, facility, and binocular vision function has not yet been researched. Due to the potential impact of atropine on accommodation, this should be assessed, and appropriate management should be prescribed if there is evidence of any accommodation and binocular vision dysfunction. Furthermore, studies establishing that low dose (0.01%)

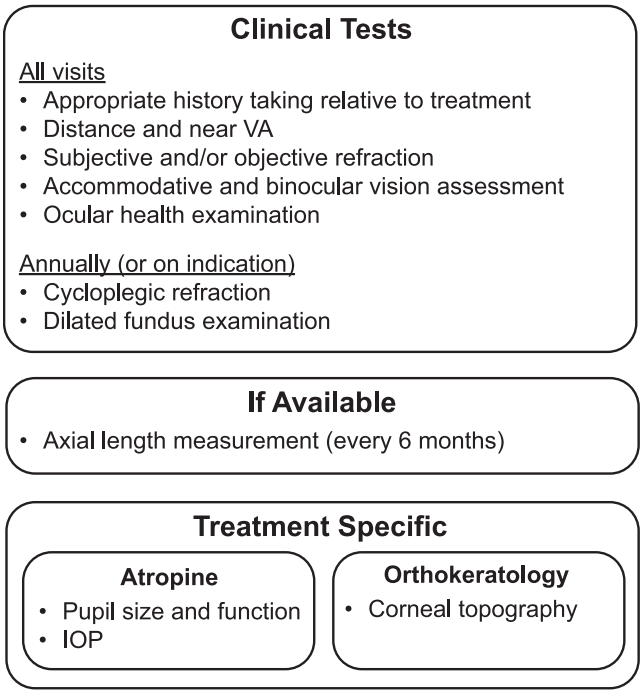

FIGURE 2. Clinical tests for myopia management.

atropine slows axial elongation to a clinically relevant level are needed.[75]

6.7.2 OK. Numerous OK lens designs are available to clinicians depending on their country of practice. To date, there has been no systematic investigation comparing the efficacy of myopia control induced by different OK lens designs. If the full refractive error is not treated by OK correction, single vision spectacle lenses for residual refractive error correction will be required—this has shown efficacy for myopia >6 D, where only 4 D was corrected with OK.[171] Soft contact lens wear for residual correction could be considered in special cases where spectacle wear is not possible, or compliance will not be achieved. In these cases, ocular health should be monitored closely considering the resultant near-constant contact lens wear. The suitability assessment and fitting process for childhood myopia control OK is generally no different than fitting for myopia correction, although in time the lens designs used may differ—discussion of current and future research on modifying OK lens designs for improved myopia control efficacy can be found in Section 7.1.

6.7.3 MFSCL. There are various MFSCL designs used for myopia control, and different designs will be available to clinicians depending on their country of practice. Detail on add power selection is provided in Section 5c. Currently one study is underway evaluating distance center designs MFSCLs with a representative low (+1.50 D) and high add (+2.50 D) on myopia and axial length progressions in children with results expected in the next year.[194] Similar to OK, there are no studies to date that have directly compared the efficacy of myopia control induced by different MFSCL designs.[232] Discussion of current and future research on modifying MFSCL lens designs for improved myopia control efficacy can be found in Section 7.1.

6.8 Treatment Duration

Regular review of patients undergoing myopia treatment should be undertaken to consider whether myopia treatment should be continued, modified, augmented with additional treatment options, or halted altogether. Parents need to appreciate when and why these different options may be indicated, and when embarking on treatment, they should be counseled as to the expected "life span" of different treatments and the relative importance of a child's age in relation to the success or efficacy of treatments aimed at slowing myopic progression.

Although influenced by many factors, myopia generally progresses most rapidly during preteenage years (7–12 years), subsequently slowing through adolescence and adulthood.[9,61,233–235] Treatments are likely to be most effective at younger ages when rapid progression is underway, and the efficacy of some treatments may wane after the first 6 months to 2 years of treatment.[62,72,172,184,236] Further research is required to fully support clinicians in determining when to cease an individual's treatment and the relative importance of factors such as age, ethnicity, rate of progression, and level of myopia when making this decision.

Long-term use of atropine may not be appropriate, as long-term side effects have not been evaluated—the World Health Organization currently recommends limiting treatment to 2 years.[127] Most studies evaluating the effect of atropine have been limited to 2-year periods (or less) of daily use,[237] and it may be beneficial to tail off dosage or dose frequency at the end of treatment to minimize rebound effects (see Section 6.10).

MFSCLs and OK act as a spectacle-free form of vision correction, and long-term use of MFSCLs and OK is not contraindicated if ocular health is maintained.[180,238]

PALs can also be used for vision correction, but the long-term, clinically meaningful myopia control treatment effect of such lenses is small compared with contact lens corrections, except in specific populations (see Section 5.4 and the IMI – Interventions for Myopia Onset and Progression Report).[105,176,239] Bifocal spectacle lenses may show better longevity of treatment.[76]

6.9 When to Change Treatment

Treatment may be stopped, switched to another form of therapy, or augmented by combining with another treatment modality when myopia progression is not sufficiently controlled, in comparison to expected progression in single-vision correction and when the average efficacy of the specific treatment has been considered.

Judgement regarding what constitutes effective reduction in progression in an individual patient is likely to depend on ethnicity, age, level of myopia, and other factors. Data on the child's previous rate of progression is valuable, but not always available, and growth curves for myopic children wearing single vision spectacles or contact lenses may be used as a reference.[61,233,240] Where treatment is failing to sufficiently control myopia progression, adjunct or combined therapies may be warranted such as MFSCLs or OK combined with low dose atropine to increase treatment effects, although there is currently limited evidence of the beneficial effect of combination treatment.[241,242] Until further studies are undertaken, practitioners should be cautious not to overpromise the value of this combination therapy.

Compliance and safety issues may also require a change in treatment modality or a halting of treatment. Poor tolerance of visual side effects and/or treatment protocols may also prompt cessation or change of treatment. Success rates in persisting with treatment are likely to be related to motivation and quality of pretreatment instruction and management of expectation.

6.10 Long-Term Efficacy and Rebound Effects

Concern has been raised about long-term efficacy and potential rebound effects for both optical and pharmaceutical interventions. In the ATOM atropine studies, after cessation of treatment, a rebound growth followed in the highest dosages, and this rebound growth was limited in the other groups.[231] In European children, the effect of high dose atropine was comparable to results from the ATOM study[72] in the first year of use.[243] Parents and patients should be made aware that myopia progression may accelerate after stopping atropine treatment, but that despite this rebound effect the level of myopia post-treatment will be, on average, less than it would have been without treatment.[74,231] Recommencement of atropine treatment if post-treatment progression rates prove unacceptable may be appropriate. In the ATOM study, Chia et al.[231] demonstrated that reintroduction of low dose atropine (0.01%) after 1 year without treatment is effective in curbing myopia progression and axial elongation in Chinese children. Currently, no comparable studies on long-term use are available, and it is yet to be investigated whether a decrease in dosage, after starting with high dose atropine, has both the beneficial effect of the high reduction in the first year and stabilization afterward.

Evidence of rebound effects in optical devices has been equivocal. A study of children wearing PALs for 1 year who were then switched to single vision glasses for 1 year showed no rebound compared with those wearing single vision alone.[52] Cheng et al.[184] suggested no rebound effect with a MFSCL for myopia control that was worn for 1 to 2 years compared with the control group after a subsequent 1.5 years of SV SCL wear, although the myopia control effect was limited to the first 6 months of treatment. On the other hand, discontinuation of OK lens wear before age 14 has been shown to lead to a more rapid increase in axial length over a 7-month period, faster than concurrent single vision spectacle wearing controls; however, this slows again with resumed lens wear after another 6 months.[244] This likely indicates that OK wear should not be discontinued before age 14.

Although the efficacy over more than 5 years of myopia control treatment, plateau, and rebound effects has not been established, current evidence still suggests that initiating some form of myopia control treatment is better than single vision correction.

6.11 When to End Treatment

Goss and Winkler reported that the mean age of myopia stabilization is around 14 to 16 years of age.[245] A later study in an ethnically diverse population confirmed this finding, with a mean (±SD) age of stabilization of 15.6 ± 4.) years.[246] Although these figures support a commonly held belief that myopia usually progresses until the mid-teens, the large SD of the latter study suggests that a sizeable proportion of the community will continue to progress into their 20s (the Comet study showed that 95% of myopes stabilized by 24 years of age).[246] Indeed, mean (±SD) myopia progression over an average of 8 years in a Scandinavian case series cohort with age of 20 to 24 was –0.45 ± 0.71 D. In 45% of cases, progression was ≥0.5 D. Although the average annual change is small, these data support the notion of continued potential for progression into adulthood. However, there is a scarcity of longitudinal data showing the normal course of myopia progression after the age of 18, in both Western and Eastern populations (see Section 6.12 on late-onset myopia).

Thus, at this time, the impact of myopia control treatments on age of cessation of myopia progression is unknown. This question has multiple ramifications. For example, would a child likely to progress without treatment until the age of 15 cease progression, albeit at a slower rate, at say age 12? If a clinician decided, from successive refractive error measurements, that the child had ceased progression at age 12, and therefore stopped treatment and returned the child to simple corrective myopia lenses, would we expect the refraction to remain stable? Ideally, cessation of treatment would also encompass a subsequent period of observation to evaluate the risk of further progression, with a view to reinstituting treatment if necessary.

Close monitoring by the clinician is important on treatment cessation, so that any apparent acceleration in progression can be quickly addressed by reinstituting treatment. Furthermore, there are legal and ethical issues related to treatment intervention that might need to be considered. For more detail see the IMI – Industry Guidelines and Ethical Considerations for Myopia Control Report.

6.12 Late-Onset Myopia

As noted above, there are scarce population-based longitudinal data characterizing progression of myopia after the school years. In one large study from the United Kingdom, it was observed that 49% of 44 year olds were myopic, with a surprising 81% being late onset (16 years or older).[247] There is also considerable evidence of myopia onset and progression among specific occupational groups during demanding university education courses. Medicine, law, and engineering are a few examples.[248–250]

The rationale for attempting progression control in late-onset myopia is somewhat different than younger ages, where the key risk is to avoid high myopia, with its attendant sight-threatening risks. It is unlikely that late-onset myopes will progress to high myopia; however, any increase in myopia is associated with increasing risk of disease, and this should be borne in mind.[30] The same treatments and protocols as applied to children and described above will generally be applicable to later-onset myopes.

Of concern, and having received little attention in the literature to date, is the moderate myope who undertakes an intense course of study and is at risk of progressing to high myopia. Anecdotally, it would seem that the numbers of individuals at risk of developing pathologic myopia is relatively low, but application of myopia control treatments for this group is potentially of equal importance to young age groups. Appropriate management requires judicious attention and follow-up by clinicians. It is evident that more research is needed to better quantify adult myopia progression.

6.13 High Myopia: Special Considerations

High myopia (>5.00–6.00 D) poses a greater risk of ocular complications that may lead to visual impairment or even blindness. Higher incidences of cataracts,[251,252] glaucoma,[253,254] and retinal abnormalities including chorioretinal atrophy and posterior staphyloma[255,256] have been reported.

Although these pathologies are typically observed in adulthood, children too can be affected by retinal pathologies.[257,258] A retrospective chart review of children aged 10 years or younger with high myopia found peripheral retinal changes in 33% of eyes including lattice degeneration (20%), white without pressure (11%), retinal holes with subretinal fluid (4%), and vitreoretinal tuft (2%).[259] In young teenage myopes with mean spherical equivalent refraction of –8.41 ± 1.60 D, the most frequent retinal lesions were optic nerve crescents (52.5%), white without pressure (51.7%), lattice degeneration (5.8%) microcystoid degeneration (5%), and

pigmentary degeneration (4.2%). Axial length longer than 26 mm was a significant risk factor for peripheral lesions, optic nerve crescents, and white without pressure.[260]

Patients should be advised that myopia, especially high myopia or when axial length is longer than 26 mm, may have a higher risk of developing a retinal detachment.[260] Patients with such characteristics should be provided with the warning signs and symptoms of retinal detachment and reviewed with annual fundus examination through dilated pupils, as described in Section 4.1. Further detail on the pathologic complications of myopia can be found in the IMI – Defining and Classifying Myopia Report.

7. Future Research Directions on Intervention and Treatment

7.1 OK and MFSCL Optimization

Studies have suggested the potential benefits of increasing the degree and extent of peripheral myopic defocus to improved efficacy of myopia control.[261] An association between greater myopic defocus on the superior retina, in children wearing PALs, and slower myopia progression has been reported.[262] Larger reductions in myopia progression in children fitted with MFSCLs compared with PALs may be attributable to greater peripheral defocus changes induced by MFSCLs.[193] This has motivated the use of customised OK and MFSCLs for myopia control in clinical practice.

A previous study attempted to increase the amount of midperipheral corneal steepening induced by OK to induce greater myopic defocus onto the peripheral retina. Reduction of the optic zone diameter of OK lenses from 6 to 5 mm to increase the retinal exposure to myopia defocus was investigated. However, these OK lens parameter changes did not cause significant changes to corneal topography.[263] More recently, a retrospective study found that participants fit with a four-curve OK lens design demonstrated a significantly larger central distance zone of treatment compared with a five-curve lens design, but there was no difference in the power or width of the midperipheral steepened zone, and the effect on relative peripheral refraction was not measured.[264] This is an area for further research.

There are several software tools available to customize OK lens designs, which are provided in the Supplementary Material. Practitioner training is recommended to understand the limits of each program. Compatibility with topographic equipment, the ease of use, and the possibility to work with a local laboratory may influence which of the following must be selected in practice. However, more research is needed to understand if and how we can modify OK lens designs to improve efficacy of myopia control.

Similar to OK lenses, investigations to increase the degree and extent of peripheral myopic defocus induced by soft contact lens designs in an attempt to improve myopia control efficacy are currently underway. Using commercially available distance-centered designs, it has been shown that only higher adds of +3.00 and +4.00 can significantly modify the peripheral refractive pattern to relative myopia compared with the central refraction,[192] but unfortunately, the visual outcomes in these currently available higher add MFSCLs have been shown to be poorly tolerated in children.[196] The Bifocal Lenses in Nearsighted Kids (BLINK) study is the first clinical trial to evaluate distance center design MFSCLs with a representative low (+1.50 D) and high add (+2.50 D) on myopia and axial length progression in children with results expected in the next year.[194]

7.2 7-MX, Scleral Reinforcement, Circadian Rhythms, and Other Future Treatments

As mentioned in Section 6.4, 7-MX has been shown to slow myopia in children and to suppress axial elongation in form deprivation myopia in the rabbit and the guinea pig[265–267] and lens-induced myopia in Rhesus monkeys.[268] An adenosine-antagonist, 7-MX is a metabolite of caffeine and theobromine, was theorized by the authors to control axial elongation by thickening and strengthening collagen fibrils in the sclera, and is approved for treatment of progressive myopia in Denmark. Intriguingly, others have speculated that if a metabolite of caffeine in the form of oral 7-MX has shown myopia control efficacy, perhaps caffeine in the form of an eye drop might have a beneficial effect on myopia progression. Results on topical treatment to date are limited to a paper from the 2017 International Myopia Conference showing both a thickening of the choroid and a reduction in myopia progression in the Rhesus monkey.[269]

If ocular pathologies such as retinal detachment and myopic maculopathy, associated with myopia progression, are due to the thinning of the sclera and the stresses created by the stretching of the eye, then there may be some role for strengthening the sclera. Although there have been attempts to strengthen the sclera via scleral reinforcement surgeries,[270] cross-linking,[271,272] and with injectables,[273] none of these methods have a long record of success in humans. Posterior scleral buckling has been reported in a large case series to slow axial elongation and to reduce vision loss, but it has yet to be duplicated by other researchers.[274,275]

Future treaments may also be designed to interact with circadian rhythms and night time light exposure. In the chick model, it has been shown that not only does disruption of circadian rhythms by light exposure at night lead to abolition of diurnal variations in ocular structures and promote myopic eye growth, but that the control of eye growth is influenced differentially by the time of day during which the eye is exposed to hyperopic and myopic defocus.[276] In humans, several recent studies have reported an association between myopia and poor or disrupted sleep,[277–279] and significant differences in serum melatonin, a key biomarker of circadian rhythm, has been found in myopic compared with nonmyopic young adults.[280] Further research is required to fully appreciate the role of ocular and systemic circadian rhythms in controlling eye growth and how timing of antimyopia interventions may interact with the circadian system. However, current knowledge supports practitioners advising parents on the benefits of encouraging natural circadian rhythms as part of a myopia intervention strategy.

The coming years are likely to result in a number of studies on various methods to control myopia, including novel medications, novel spectacle, and contact and OK designs, as well as combination treatments. The ideal contact lens for myopia control will likely include modification to all mechanisms postulated in myopia progression—relative peripheral hyperopia, higher-order aberrations, accommodation, and binocular vision—and may additionally include low dose atropine delivery, modification to indoor lighting,[281] and even biometric feedback on near working distance and time spent outdoors.[187] Nutritional and lifestyle interventions may play a bigger role, as described above. Practitioners will have to stay informed on future developments and incorporate these treatments into their practice as the evidence is revealed.

8. Clinical References, Education and Communication

8.1 Key Papers, Websites, and Courses for Practitioner Reference

Keeping up to date with the latest literature can be a challenge for the clinician—key meta-analysis papers and systematic reviews can help to summarize research results. Open access articles are freely available for both the practitioner and the research-interested parent to download. Links for these papers are available in the Supplementary Material, along with detail of online practitioner resources, forums, and relevant clinical conferences for further information and support.

8.2 Recommendations for Communication Tools

A key challenge when communicating the impact of myopia is explaining the long-term risks such as the higher risk of pathologies associated with increasing levels of myopia, as well the short-term choices, such as altering the visual environment to increasing outdoor time for premyopes or fitting a child with myopia-controlling contact lenses. This is particularly complex when the short-term choices may include additional risk, such as those associated with pediatric contact lens wear. Practitioners also report difficulty in communicating a research-based message that may conflict with the more conservative messages from other health professionals such as pediatricians, general practitioners, and eye care providers. Development of communication tools for practitioners that strongly communicate the benefits of myopia management, balanced with the risks and the currently unanswered research questions, will assist in providing evidence-based information to the parent to inform health choices for their myopic children.

8.3 Continuing Education and Accreditation of Practitioners

Research in myopia and myopia control is a continually evolving field. To be able to provide current evidence-based myopia management, clinicians need to be informed of the most up-to-date research. It is therefore important that clinicians stay current with their continuing education, particularly in the area of myopia and myopia control. The IMI – Industry Guidelines and Ethical Considerations in Myopia Control Report describes "an urgent need to create standardized educational materials on myopia risk and myopia control treatments. Such educational materials should cover areas such as epidemiology, the public health burden due to myopia, contemporary research in myopia control, interventional options and best clinical practices for myopia control." The IMI suite of reports and several other groups are expending efforts to provide this information to clinicians.

The IMI – Industry Guidelines and Ethical Considerations in Myopia Control Report discusses potential accreditation or training of eye care practitioners in prescribing myopia control treatments. Ensuring a comprehensive understanding of myopia complications, treatment complications, expected clinical results, and fitting assistance is worthwhile for both industry and prescribers to ensure best outcomes for pediatric patients.

In some countries, eye care providers may require endorsement to prescribe drugs, including atropine eye drops. Similarly, certification examinations may be required before practitioners are allowed to order and fit OK or other contact lenses. When providing myopia management services, it is expected that eye care providers have the appropriate training and necessary certification to care for children and fit contact lenses and/or prescribe ocular medications. It is also important to be able to manange or comanage potential adverse events. Continuing professional development is not mandatory across the global eye care profession, and consideration of best practice educational principles is important to ensuring evidence-based patient care.

Key papers for practitioner reference and various tools to assist with clinical issues such as treatment selection and clinician–patient communication have been detailed in the Supplementary Material. Short courses in myopia management are increasingly popular, and there may be a need for university-affiliated postgraduate courses in myopia management.

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