IMI – Clinical Management Guidelines Report

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ABSTRACT

Best practice clinical guidelines for myopia control involve an understanding of the epidemiology of myopia, risk factors, visual environment interventions, optical and pharmacological treatments, as well as skills to translate the risks and benefits of a given myopia control treatment in 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.

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.\(^4\) While 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 three years before onset and through to five 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 to age matched counterparts who stayed emmetropic.\(^7\) In an ethnically diverse, USA based study that included over 4500 children, first grade (age 6) children
measuring +0.75D or less by cycloplegic refraction had increased risk of becoming myopic between second and eighth grades (ages 8-14 years), compared to those with +0.75D or greater refraction, with the risk of myopia increasing with number of myopic parents.\textsuperscript{8,9} Additional cut-off points for age-normal hyperopia, below which myopia risk is significant, are suggested to be +0.50D or less for ages 7-8 years, +0.25D or less for ages 9-10 years and emmetropia for age 11 years.\textsuperscript{10}

1.1.2 Age

Myopia can be classified by age as childhood or ‘school’ myopia\textsuperscript{6} and late onset (after 15 years of age).\textsuperscript{11,12} The major factor contributing to faster childhood myopia progression is younger age at myopia onset, with this factor being independent of gender, ethnicity, school, time spent reading and parental myopia.\textsuperscript{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 to children with no myopic parents.\textsuperscript{1,2,16,17} Additionally, ethnic background also plays a role in myopia susceptibility. In Australia, East Asian children aged 11-15 years are eight times more likely to be myopic than their Caucasian counterparts.\textsuperscript{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%.\textsuperscript{19}

There is debate on whether childhood myopia is inherited as a genetic susceptibility, or 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,\textsuperscript{20} both of which are associated with myopia onset and progression.
Although there is a genetic component in myopia development, the visual environment appears to be a major contributor to school-aged myopia. Children who become myopic appear to spend less time outdoors as compared to their non-myopic counterparts. Additionally, the risk of myopia development and progression is significantly associated with reading at very close distances (<20cm) and for continuous periods of time (>45 min), rather than being associated with total time spent on all near activities. These factors may be related to short term changes in central axial length which have been shown to occur in progressing and higher (early-onset) young adult myopes after both short term, high (6D) demand and prolonged, standard working distance (3D) near work demand. 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, increased short-wavelength (360-400nm) and UV light exposure, the more uniform dioptric field of view across the retina when outdoors compared to indoor environments, or other mechanisms. While 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. More detail on visual environment interventions can be found in the IMI – Interventions for Myopia Onset and Progression report.

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. Examples include test driven, highly competitive education systems in Asia and Asian communities and the high prevalence of myopia in Orthodox Jewish boys compared to girls in Jerusalem, where the boys spend much longer reading religious texts at close working distances.
A number of reports have indicated that a school curriculum consisting of greater
near work demands is associated with a higher rate of myopia\textsuperscript{36, 37} and a faster
rate of myopia progression.\textsuperscript{38} There have also been suggestions that extensive
engagement in after-school tutorials may impose additional workload to the school
children, and is associated with a high prevalence rate of myopia.\textsuperscript{39} Mendelian
randomisation analyses have shown that every additional year of education is
associated with a more myopic refractive error of -0.27D.\textsuperscript{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.\textsuperscript{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 as compared to
emmetropes.\textsuperscript{42-45} Myopic children and young adults also show reduced
accommodative facility\textsuperscript{45, 46} and enhanced accommodative convergence
(elevated AC/A ratios) compared to age-matched emmetropes.\textsuperscript{47-49} Conjecture
exists, though, 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\textsuperscript{45, 50} while others do not.\textsuperscript{51-53}

1.2 Identifying and managing the pre-myope

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.\textsuperscript{27, 54, 55} The pre-myope 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.\textsuperscript{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 which appears effective in reducing the incidence of myopia across numerous studies.\textsuperscript{21}

\section*{2. Discussing myopia and associated risks with parent and patient}

\subsection*{2.1 Lay terminology discussion of causes}

Patients and parents must be informed on the probable causes and risk factors for myopia in order 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 in order 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 non-myopic parents, it is important to discuss a child’s risk for myopia development and/or progression with the parents and/or carers.

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, in order to encourage healthy visual habits, such as spending more time outdoors and reducing near work demand, in order 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. The higher the myopia and the longer axial length becomes, the higher the lifetime risk of developing these comorbidities. 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 in order 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 exam findings. For more detail on the evidence of specific treatment types, see the IMI – Interventions for 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 exam 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 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). 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 focussing light at the periphery of the eye in alignment or in front of the retina.

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.

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 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 about 0.50 to 1.00 diopters (units of measurement) per year, as accelerated eye growth occurs.\textsuperscript{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, is based on numerous factors, and the long-term effectiveness is not fully understood as the available data only extends to 1 to 5 years of treatment.

OK lenses are expected to slow myopia progression by about 30-60\%\textsuperscript{,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 30-50\%, although studies have investigated several different lens designs, some of which have shown higher results.\textsuperscript{66-70} This correction also allows part-time wear, but this may reduce the myopia control effect.\textsuperscript{67}

Children wearing soft contact lenses have been shown to have improvements in self-perception and self-esteem compared to children wearing glasses.\textsuperscript{71} Although not studied, it is expected that similar improvements would be found with OK contact lenses since 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 about 30-80\%, although significant adverse effects (light sensitivity and reduced near vision) can occur with stronger dosages.\textsuperscript{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\%),\textsuperscript{73}
although rebound effects – accelerated myopia progression – after cessation of higher strength atropine treatment have been found.\textsuperscript{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.\textsuperscript{75}

Specific spectacle lens options can also provide treatment effects for some children of around 20-50\%, in specific populations.\textsuperscript{76, 77}

\section*{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 of 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.\textsuperscript{78} For soft contact lenses, the rate of corneal infiltrative events is about 15 per 10,000 per year for children age 13-17 years.\textsuperscript{79} The rate of microbial keratitis for children 8-12 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.\textsuperscript{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 to glasses, children may notice mildly blurred vision or changes in their focusing with either OK or MFSCLs.\textsuperscript{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.\textsuperscript{83} Lower strength doses may cause less of these side effects.\textsuperscript{73, 84}

While generally showing lower efficacy than other options,\textsuperscript{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 United States (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 authorities 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 digital content 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 USA, off-label treatment is defined as “FDA approved drugs/medical devices used for non-approved indications”, which is considered legal as long as there is sufficient evidence supporting the efficacy and safety in such application.\(^8^6\)

In the UK, optometrists with ‘additional supply’ or independent prescribing qualifications are able to use and supply 0.5% and 1.0% doses, for indications involving temporary cycloplegia or mydriasis. The use of lower doses (ie. 0.01%) for myopia control is not currently listed on the Optometrists’ Formulary\(^8^7\) and so 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.”\(^8^8\)

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.”

Similar advice is provided for New Zealand practitioners, 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. 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 summarises the standard procedures for examination of myopes:

a) History taking

Age, gender, history of ocular and general health, ocular surgery, ocular and general health parental history of myopia, age of onset of myopia, past history of myopia progression (if available), previous myopia control treatments if any.

b) Refraction

Non-cycloplegic 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 employed, the recommended dosage for cycloplegic refraction is 2 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. For more information on specific refraction techniques which have been employed in myopia control studies, refer to the IMI - Clinical Myopia Control Trials and Instrumentation report.

c) Best-corrected visual acuity
d) Binocular vision and accommodative tests: see section 4.3.
e) Anterior eye health evaluation using a slit-lamp and intraocular pressure measurement (preferable).
f) Corneal topography: if indicated (for example, for contact lens fitting) and preferably measured with corneal topographer.
g) 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. However, there is a broad range observable, with emmetropes typically showing an AL of 22-24.5mm, and myopia typically associated with ALs greater than 25mm. Increases of about 0.1 mm/year have been shown to be associated with normal eye growth, while 0.2 to 0.3 mm/year is associated with increasing myopia, 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 26mm in a myopic child, where further axial growth is still expected due to emmetropization, could increase the index of concern for the practitioner. Where available, measurement with a non-contact device, for example, IOL Master (Zeiss) or LENSTAR (Haag-Streit) is ideal. The mean and standard deviation of multiple measurements should be recorded.

h) 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, 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). More detail on macular and non-macular structural complications of myopia, including the 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. 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) while fixation disparity is misalignment of the eyes during fusion. 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 employed in clinical studies of myopia and myopia control as outlined in Table 1 and Table 2. It is recommended that the baseline exam for myopia control should include as a minimum, tests that assess the various elements of accommodation and vergence as listed in Table 1 and Table 2. Furthermore, the same tests need to be employed 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.

Table 1: Accommodative function tests used in clinical studies

<table>
<thead>
<tr>
<th>Accommodative assessment</th>
<th>Clinical test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accommodative accuracy (lag or lead)</td>
<td>Open-field autorefractors (Canon R-1, 56, 77, 98-102 Grand Seiko WV-50013, 52, 66, 103, 104 or Grand Seiko WR-5100105, 106</td>
</tr>
</tbody>
</table>
• Aberrometers (Complete Ophthalmic Analysis System (COAS) aberrometer\textsuperscript{107, 108})
• Monocular Estimate Method (MEM) retinoscopy\textsuperscript{82, 109, 110}
• Nott dynamic retinoscopy\textsuperscript{111, 112}
• Photorefractor\textsuperscript{113, 114}

<table>
<thead>
<tr>
<th>Accommodative amplitude</th>
<th>Minus lens technique (or Sheard’s technique)\textsuperscript{109}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Push up (or in) test\textsuperscript{66, 114}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Accommodative facility</th>
<th>Distance (plano/-2.00D flippers)\textsuperscript{13, 115}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Near (±2.00 D flippers)\textsuperscript{13, 109, 110, 114, 115}</td>
</tr>
</tbody>
</table>

**Table 2: Vergence function tests used in clinical studies**

<table>
<thead>
<tr>
<th>Vergence assessments</th>
<th>Clinical tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance and near heterophorias</td>
<td>• Risley prism and Maddox rod\textsuperscript{58}</td>
</tr>
<tr>
<td></td>
<td>• Von Graefe method\textsuperscript{116, 108}</td>
</tr>
<tr>
<td></td>
<td>• Alternating cover test\textsuperscript{69, 82, 100, 101, 103}</td>
</tr>
<tr>
<td></td>
<td>• Howell Near phoria card\textsuperscript{104, 110}</td>
</tr>
<tr>
<td></td>
<td>• Saladin Near Point Balance Card\textsuperscript{81}</td>
</tr>
<tr>
<td>Near Fixation disparity</td>
<td>Saladin Near Point Balance Card\textsuperscript{69, 108}</td>
</tr>
<tr>
<td>AC/A ratio</td>
<td>• Calculated method\textsuperscript{101, 102, 117, 56}</td>
</tr>
<tr>
<td></td>
<td>• Gradient technique\textsuperscript{13, 116, 117}</td>
</tr>
</tbody>
</table>

**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 two 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

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, though,
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.\textsuperscript{138, 139}

MFSCL which are based on generating peripheral myopic defocus have been shown to reduce myopia progression\textsuperscript{68} and similarly, OK has been shown to alter peripheral refraction from relative hyperopia to myopia,\textsuperscript{140, 141} consistent up to one year of wear.\textsuperscript{142} There is no clear evidence yet, though, 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.

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,\textsuperscript{143} while increased coma after OK treatment has been shown not to be associated with its myopia control effect.\textsuperscript{144}

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 6.4mm by the group mean, exhibited a greater myopia control effect than children with a ‘below average’ scotopic pupil diameter. Within normal refractive development, though, 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.

Sub-foveal choroidal thickness (SFCT)
A number of studies have reported an association between choroidal thickness changes and myopia progression, induced myopic and hyperopic defocus and myopia control intervention. Ongoing research is aimed at exploring the relationship between myopia onset and progression with SFCT at the macular region and in other areas of the retina.

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. More recently, light data loggers (LDL) have been employed to make objective measures of ambient light levels, including the HOBO Pendant (Onset Computer Corporation, USA), and Actiwatch 2 (Philips Respironics, USA). A cut-off measure of 1000 lux has been suggested to differentiate indoor and outdoor environments based on diary records, though there is some conjecture. Objective measures of light intensity continue to show an association between time spent outdoors and protection from myopia. 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, have higher baseline myopia, and have experienced past myopia progression of >0.50D/year. Myopia can also progress more over winter than summer seasons. However, while 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 (2012) 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, annualised progression rates for myopic children of Asian and Caucasian ethnicities ranged from about 0.50 to 1.00D and varied by age and gender. These data were employed 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 employed, and then illustrates the impact of various treatment strategies on myopia progression. (https://calculator.brienholdenvision.org/) Given that the calculator estimates long-term progression based on study data of only 2 years 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 to those with little or no associated risk factors. Other patient and treatment factors will also influence treatment selection as described below.

Baseline refractive error

Earlier onset of myopia often results in higher degrees of myopic refractive error. 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. 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 -0.50D.

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 0.75DC can lead to visual compromise. 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.\textsuperscript{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.\textsuperscript{170} Myopes with higher baseline myopia may elect partial correction with OK.\textsuperscript{171} Studies have suggested individuals of younger age \textsuperscript{172, 173} and higher degrees of baseline refractive error may benefit most from OK.\textsuperscript{174, 175}

**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 PALs were reported in children with larger lags of accommodation and near esophoria.\textsuperscript{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 PD BI in the near segment of each lens) compared to standard executive bifocal spectacle lenses (+1.50 D add).\textsuperscript{176} In addition, children with lower baseline accommodative amplitude have greater myopia control response to OK wear than those with higher baseline accommodative amplitude.\textsuperscript{177}

**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 to European ethnicity;\textsuperscript{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 if certain treatments work better in particular populations.
Safety, compliance and cost considerations

Clinicians must determine if 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. 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.\textsuperscript{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 $+2.00D$ 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.\textsuperscript{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.\textsuperscript{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. While MFSCLs that manipulate optical defocus across larger areas of the visual field have been suggested to result in greater myopia control,\textsuperscript{193} to date, there has been no systematic investigation comparing the efficacy of myopia control associated with different add powers, however studies are underway.\textsuperscript{194} Further discussion of this can be found in Section 8b. As currently available MFSCLs, particularly lenses with higher treatment powers, can significantly reduce quality of vision,\textsuperscript{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.\textsuperscript{197} Alternatively, the add power may be reduced until acceptable vision is achieved, or a different lens design may be trialled. 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.\textsuperscript{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 non-compliance, 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\textsuperscript{179} although it has been shown to either have no effect on progression or possibly even increases the rate of myopia progression.\textsuperscript{198, 199} Interestingly, a paper on delaying correction of low myopia (<1D) in 12 year old Chinese children found that those who were uncorrected showed 0.25D less progression over 2 years than those who were fully corrected.\textsuperscript{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.\textsuperscript{201}

Myopia control studies evaluating bifocal or PAL spectacle lenses have employed either a +1.50\textsuperscript{202} or +2.00 Add.\textsuperscript{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\textsuperscript{205} to ensure visual comfort. While there is indication from one study that bifocal spectacle lenses show better efficacy than PAL spectacles,\textsuperscript{76} the practitioner should consider any aesthetic 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.\textsuperscript{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 is recommended, as downward slippage of PALs may reduce myopia control effects of the near addition.\textsuperscript{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. Other designs are currently under development including multiple lenslet designs.62

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. The younger myopic child has a higher risk of progression 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. 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. 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 back up 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 digital) may influence the development and progression of myopia. Close reading distance (<20cm) and continuous reading (>45 min) have been associated with greater odds of myopia. Outdoor activity is associated with reduced incidence of myopia in children, including those who usually perform large amounts of near work. This suggests that children should not be prevented from participating in near work activity, but rather that regular breaks, appropriate reading distances and near fixation changes whilst 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. 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. An increase in time spent outdoors may result in greater protection and studies involving school-aged children have suggested a minimum of 8 – 15 hours of outdoor activity per week is required to achieve clinically meaningful protection from myopiogenic stimuli.

The protective effect of outdoor time for the onset of myopia in humans are supported by animal studies which have reported reduced eye growth with exposure to bright light and the opposite effect, axial elongation and myopia, resulting from reduced light levels. High ambient lighting has been shown to have protective effects against the development of form-deprivation myopia in Rhesus monkeys.
While 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 maximising both indoor and natural lighting, and increasing outdoor time.\textsuperscript{26, 27}

6.4 Nutritional advice

There is currently no conclusive evidence supporting any definite link between myopia and nutrition or malnutrition.\textsuperscript{214, 215} Some studies have linked myopic progression to low-fat and low-carbohydrate intake,\textsuperscript{216} while diets high in saturated fat and high cholesterol levels have also been linked to increased axial length.\textsuperscript{217}

A placebo-controlled clinical trial showed that the caffeine metabolite 7-methylxanthine (7-MX) has the potential to reduce eye growth in children.\textsuperscript{218} This medication is approved as a treatment for myopia progression, but only in Denmark, where these studies were undertaken. While 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.\textsuperscript{219}

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:

\begin{itemize}
  \item Always wash your hands before applying or removing contact lenses\textsuperscript{220, 221}
  \item Never swim or shower with contact lenses or expose the contact lenses or lens storage case to water\textsuperscript{222, 223}
  \item Don’t wear your contact lenses if you have a cold or flu\textsuperscript{224, 225}
  \item Daily disposable lenses are strongly encouraged. If you wear reusable contact lenses, use new lens cleaning solution each day\textsuperscript{226, 227} and use non-preserved care cleaning regimen such as hydrogen peroxide, if possible.
\end{itemize}
Replace your lens case at least every 3-6 months. Rinse with contact lens cleaning solution, rub, tissue-wipe and air-dry casing facing down.

- Unless directed by your doctor (for OK), don't sleep or nap in your lenses.  

Atropine Use:

- Where available, unit dose atropine preparations are preferable. In a multi-use bottle, to avoid contamination, never touch the tip of the bottle to the eye or any other surface and don't use the bottle past the expiration date.

6.6 Back up corrections for CL wear

For patients wearing daytime MFSCL, 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. Either 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, while cycloplegic refraction is typically measured in research studies, it can be employed in clinical practice on indication, at the practitioner’s discretion, and where consistent with evidence-based best practice. Consistent refraction techniques should be employed to ensure comparable
clinical data. Similarly, axial length measurement is an expected outcome measure of myopia control research studies, but is not employed 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.

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 in order to optimize lens fit and to manage any issues relating to quality of vision.

Figure 1: Follow-up schedule for myopia management based on treatment type.
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 cycloplegic and mydriatic side effects of atropine. Patients may require near addition correction to alleviate near visual symptoms (such as PAL or bifocal lenses) and photochromic lenses or additional sunglasses to relieve glare issues.

Figure 2: Clinical tests for myopia management.
The 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.\textsuperscript{231} While accommodative amplitude was only reduced by 2-3D, 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 prescribed if there is evidence of any accommodation and binocular vision dysfunction. Furthermore, studies establishing that low dose (0.01%) atropine slows axial elongation is needed.\textsuperscript{75}

**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 >6D where only 4D was corrected with OK.\textsuperscript{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 employed may differ – discussion of current and future research on modifying OK lens designs for improved myopia control efficacy can be found in Section 8.1.

**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 MF SCLs 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. Similar to OK, there are no studies to date which have directly compared the efficacy of myopia control induced by different MFSCL designs. Discussion of current and future research on modifying MFSCL lens designs for improved myopia control efficacy can be found in Section 8.1.

6.8 Treatment duration

Regular review of patients undergoing myopia treatment should be undertaken to consider if 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 counselled 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 pre-teenage years (7 to 12), subsequently slowing through adolescence and adulthood. 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. 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 two years. Most studies evaluating the effect of atropine have been limited to two year periods (or less) of daily use and it may be beneficial to tail off dosage or dose-frequency at the end of treatment in order 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.\textsuperscript{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 to contact lens corrections, except in specific populations (see section 5.4 and the IMI - Interventions for Myopia Onset and Progression report).\textsuperscript{105, 176, 239}

\textbf{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.\textsuperscript{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.\textsuperscript{241, 242} Until further studies are undertaken, practitioners should be cautious not to overpromise to their patients about 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 pre-
treatment 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. In European children, the effect of high dose atropine was comparable to results from the ATOM study in the first year of use. 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. Re-instigation of atropine treatment if post-treatment progression rates prove unacceptable may be appropriate. In the ATOM study, Chia, Lu and Tan demonstrate that re-introduction of low dose atropine (0.01%) after one 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 afterwards.

Evidence of rebound effects in optical devices have been equivocal. A study of children wearing PALs for one year who were then switched to single vision glasses for one year showed no rebound compared to those wearing single vision alone. Cheng et al (2016) suggested no rebound effect with a MFSCL for myopia control which was worn for 1-2 years, compared to 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 seven month period, faster than concurrent single vision
spectacle wearing controls; however this slows again with resumed lens wear after another six months.\textsuperscript{244} This likely indicates that OK wear should not be discontinued before age 14.

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

\textbf{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.\textsuperscript{245} A later study in an ethnically diverse population confirmed this finding, with a mean (± SD) age of stabilization of 15.6 (± 4.2) years.\textsuperscript{246} Although these figures support a commonly held belief that myopia usually progresses until the mid-teens, the large standard deviation of the latter study suggests that a sizeable proportion of the community will continue to progress into their twenties (the Comet study showed that 95% of myopes stabilized by 24 years of age).\textsuperscript{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 D (± 0.71). In 45% of cases, progression was ≥0.5 D. While 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 MC 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 re-instituting 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). 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.

The rationale for attempting progression control in late onset myopia is somewhat different to 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. 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 pathological 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 (greater than 5.00 to 6.00D) poses a greater risk of ocular complications that may lead to visual impairment or even blindness. Higher incidences of cataracts, glaucoma and retinal abnormalities including chorioretinal atrophy and posterior staphyloma have been reported. While these pathologies are typically observed in adulthood, children too can be affected by retinal pathologies. 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%). 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 26mm was a significant risk factor for peripheral lesions, optic nerve crescents and white-without-pressure.

Patients should be advised that myopia, especially high myopia or when axial length is longer than 26mm may have a higher risk of developing a retinal detachment. 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 pathological 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. An association between greater myopic defocus on the superior retina, in children wearing PALs, and slower myopia progression has been reported. Larger reductions in myopia progression in children fitted with MFSCLs compared to PALs may be attributable to greater peripheral defocus changes induced by MF SCLs. This has motivated the use of customised OK and MF SCLs for myopia control in clinical practice.

A previous study attempted to increase the amount of mid-peripheral corneal steepening induced by OK to induce greater myopic defocus onto the peripheral retina. Reduction of the optic zone diameter of OK lenses from 6mm to 5mm, to increase the retinal exposure to myopia defocus was investigated. However, these OK lens parameter changes did not cause significant changes to corneal topography. More recently, a retrospective study found that participants fit with a 4-curve OK lens design demonstrated a significantly larger central distance zone of treatment compared to a 5-curve lens design, but no difference in the power or width of the mid-peripheral steepened zone, while the effect on relative peripheral refraction was not measured. This is an area for further research.

There are several software tools available to customize OK lens designs, which are provided in the supplementary digital content. 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 lab 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.

Similarly for 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-centred 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 to the central refraction, but unfortunately the visual outcomes in these currently available higher add MFSCLs have been shown to be poorly tolerated in children. The Bifocal Lenses in Nearsighted Kids (BLINK) study is the first clinical trial to evaluate distance center design MF SCLs 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.

7.2 7-MX, scleral reinforcement, circadian rhythms and other future treatments

As mentioned in section 6.4, 7-methylxanthine (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 and lens-induced myopia in Rhesus monkeys. An adenosine-antagonist, 7-MX is a metabolite of caffeine and theobromine, and 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.\textsuperscript{269}

If ocular pathologies like 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. While there have been attempts to strengthen the sclera via scleral reinforcement surgeries,\textsuperscript{270} cross-linking,\textsuperscript{271, 272} and with injectables,\textsuperscript{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.\textsuperscript{274, 275}

Future treatments 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.\textsuperscript{276} In humans, several recent studies have reported an association between myopia and poor or disrupted sleep,\textsuperscript{277-279} and significant differences in serum melatonin, and key biomarker of circadian rhythm, has been found in myopic compared to non-myopic young adults.\textsuperscript{280} Further research is required to fully appreciate the role of ocular and systemic circadian rhythms in controlling eye growth and how timing of anti-myopia 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, 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\textsuperscript{281} and even biometric feedback on near working distance and time spent outdoors.\textsuperscript{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 summarise 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 digital content, 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 pre-myopes, 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 which 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 which 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 for 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 for 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 exams 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 manage or co-manage 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 digital content. Short courses in myopia management are increasingly popular and there may be a need for university affiliated post-graduate courses in myopia management.

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ACRONYMS
AC/A - accommodative convergence to accommodation
BAK – benzalkonium chloride
MFSCL – multifocal soft contact lens
OK – orthokeratology
PALs – progressive addition (spectacle) lenses
7-MX – 7-methylxanthine

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