



# **Clinical Report: Myopia Management**

**DEVELOPED BY THE  
EVIDENCE-BASED OPTOMETRY COMMITTEE**



**AMERICAN OPTOMETRIC ASSOCIATION**

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## INTRODUCTION

Myopia is a chronic condition of the eye that negatively impacts vision in people of all ages. It is a disorder of refraction, with uncorrected myopia being the leading cause of distance vision impairment. In the past 20 years, the prevalence of myopia has increased dramatically in many areas of the world. In the United States, the prevalence of myopia increased in people aged 12-54 years from 25% in 1971-1972 to 41.6% in 1999-2004.<sup>1</sup> Studies show variations in the prevalence of myopia and high myopia between regions and ethnic groups around the world.<sup>2</sup> However, it is projected that half the world will be myopic by 2050 with nearly 10% having myopia greater than 5.00 diopters (D).<sup>3</sup>

The dramatic increase in the prevalence and severity of myopia, as well as a decrease in the age of onset of myopia, has resulted in expanded interest in the development and application of treatments to slow the progression in children and reduce the risk of eye-related diseases and associated complications with myopia later in life. On September 30, 2016, the United States Food and Drug Administration (FDA) held a workshop titled *Controlling the Progression of Myopia: Contact Lenses and Future Medical Devices*, co-sponsored by the American Optometric Association, American Academy of Optometry, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Society of Cataract and Refractive Surgery, and the Contact Lens Association of Ophthalmologists. The FDA concluded that treatment strategies to reduce the rate of myopic progression would be beneficial in avoiding some of myopia's effects on public health.<sup>4</sup>

Doctors of optometry continue to play a primary role in diagnosis, clinical management and treatment of this increasing public health threat. Expanded myopia management services will be needed beyond the correction of myopic refractive error with current commonly prescribed spectacles or contact lenses for distance vision correction only. This report presents the current clinical evidence from published studies on the efficacy and application of myopia management procedures. It reviews evidence and provides guidance on the use of several currently available options for controlling myopia development in children: atropine, multi-focal soft contact lenses, orthokeratology with rigid gas permeable contact lenses, multifocal spectacle lenses, and behavioral modifications. Only products that have received approval from the FDA are mentioned by brand name in this report.

## WHAT FACTORS INFLUENCE THE DEVELOPMENT OF MYOPIA?

The exact mechanism for the development of myopia is uncertain. However, its development has long been viewed as the result of genetic, ethnic, and/or environmental risk factors.<sup>5</sup> The current understanding of the processes of emmetropization or how the failure of such mechanisms can lead to refractive errors is incomplete, but modulation in the amount of axial growth in relation to the initial refractive error appears to be the major factor associated with emmetropization.<sup>6</sup>

Animal studies, observational clinical studies, and randomized clinical trials have demonstrated that the retinal image can influence the eye's growth. These studies have shown that the mechanisms of optically guided eye growth are influenced by the retinal image across a wide area of the retina and not just the fovea. Such results necessitate a fundamental shift in how refractive errors are defined.<sup>7</sup>

There is a genetic component in myopia development. The risk of developing myopia increases significantly in children who have two parents with myopia compared with those whose parents do not have myopia. Additionally, ethnic background appears to play a role in myopia susceptibility. Asian children are more likely to be myopic than their Caucasian counterparts.<sup>8</sup>

The visual environment also appears to be a contributor to school-aged myopia. Children who become myopic tend to spend less time outdoors.<sup>9</sup> Myopia development and progression may also be related to reading and computer

screen viewing for long periods of time.<sup>10</sup> Additionally, many studies have shown that myopia has a higher prevalence in urban areas versus rural areas which is likely to be based on differences in near work and time outdoors.<sup>11</sup>

## HOW CAN MYOPIA BE CLASSIFIED?

Myopia can be classified in a number of ways including etiology, age at onset, pattern of progression, amount of myopia, and eye complications associated with myopia. In clinical terms, low myopia ranges between  $-0.50\text{D}$  and less than  $-6.00\text{D}$ , whereas high myopia is any refractive error  $-6.00\text{D}$  or greater. Additionally, the International Myopia Institute (IMI) developed a recommendation adopting the following three quantitative definitions for myopia in their strict mathematical sense (e.g.,  $-6.00\text{D}$  is less than  $-5.00\text{D}$ ):<sup>12</sup>

- Myopia is a condition in which the spherical equivalent refractive error of an eye is equal to or less (more myopic) than  $-0.50\text{D}$  when ocular accommodation is relaxed.
- Low myopia is a condition in which the spherical equivalent refractive error of an eye is equal to or less (more myopic) than  $0.50\text{D}$  and greater (less myopic) than  $-6.00\text{D}$  when ocular accommodation is relaxed.
- High myopia is a condition in which the spherical equivalent refractive error of an eye is equal to or less (more myopic) than  $-6.00\text{D}$  when ocular accommodation is relaxed.

Classifying myopia by age of onset as pathological or early onset (usually before age six), school-age (6-18 years of age) or adult onset (generally occurring at 19-40 years of age) may be useful in discussions with patients and parents/caregivers. Children with early onset myopia are at particular risk of complications associated with myopia, as progression over time might result in higher myopia and a greater risk of complications.

## WHAT ARE THE COMPLICATIONS ASSOCIATED WITH THE DEVELOPMENT OF MYOPIA?

Myopia, especially high myopia, presents a substantial risk for the development of sight-threatening conditions later in life, including myopic macular degeneration, retinal detachment, primary open angle glaucoma, and cataract. The most significant complication is myopic macular degeneration. Characteristics of myopic macular degeneration include lacquer cracks, Fuchs spot, choroidal neovascularization, and/or choroidoretinal atrophy.<sup>13</sup>

A  $1.00\text{D}$  increase in myopia is associated with a 67% increase in the prevalence of myopic macular degeneration. Restated, slowing myopia by  $1.00\text{D}$  should reduce the likelihood of an individual developing myopic macular degeneration later in life by 40%. Furthermore, this treatment benefit accrues regardless of the level of myopia. Thus, while the overall risk of myopic maculopathy is higher in a  $-6.00\text{D}$  myope than in a  $-3.00\text{D}$  myope, slowing their myopic progression by  $1.00\text{D}$  during childhood should lower the risk by 40% in both cases.<sup>14</sup> Although high myopia carries the highest risk of complications and visual impairment, low and moderate myopia also have considerable risks.<sup>15</sup>

The burden of blindness and visual impairment due to complications of myopia will rise significantly if no effort is made to reduce its development and progression.<sup>16</sup>

## WHAT ARE THE RISK FACTORS FOR DEVELOPMENT OR PROGRESSION OF MYOPIA?

Several factors can increase a child's chances for the development of myopia:

- Lower amounts of hyperopia than expected for a child's age can indicate a risk for future development of myopia.<sup>17</sup> Children with a refractive error of +0.50 D or less at ages 7 or 8, +0.25 D or less at ages 9 or 10, and emmetropia at age 11 are at significant risk for the development of myopia.<sup>18</sup>
- The risk of developing myopia increases threefold or more in children with two parents who have myopia compared with children with no parents with myopia.<sup>5</sup> In addition, ethnic background also plays a role in myopia susceptibility.
- The presence of binocular vision problems, including reduced accommodative responses, increased accommodative lag, and higher AC/A ratios may also influence the development or progression of myopia.<sup>19</sup>
- Spending less time outdoors and more time spent reading are also risk factors for myopia development.<sup>20</sup>

To control myopia, the rate of axial elongation of the eye must be slowed. In most children, axial length increases rapidly at younger ages and then slows and stabilizes around 16 years of age. The close association between growth and stabilization of axial length and myopia is consistent with the theory that axial elongation is the primary ocular component in myopia progression and stabilization.<sup>21</sup>

The most rapid growth in axial length appears to occur in the year before the onset of myopia. Children who become myopic have significantly more axial elongation up to 3 years before onset through 5 years after onset.<sup>17</sup> A major factor for faster progression of myopia is a younger age at onset.<sup>22</sup>

## WHAT TESTS ARE NEEDED FOR MYOPIA MANAGEMENT?

Prior to beginning a myopia control treatment program, a child should receive a comprehensive eye and vision examination.<sup>23</sup>

Key aspects of the examination include:<sup>8</sup>

- A detailed patient history, with specific emphasis on parental history of myopia; the child's age of onset of myopia; myopia progression and previous myopia control procedures (if applicable); daily visual habits (e.g., average hours spent on near work and time spent outdoors)
- Measurement of visual acuity
- Cycloplegic refraction or cycloplegic auto-refraction with tropicamide 1%<sup>4</sup> to determine baseline refractive error and at follow-up examinations
- Axial length measurement
- Binocular vision testing including, but not limited to, cover test, accommodative, and vergence assessments
- Evaluation of corneal topography and/or tomography for various modalities of contact lens therapy, corneal shape changes, and to rule out pathology such as keratoconus

(Note: Baseline corneal curvature, shape, and elevation evaluation for myopia management requires contact lens discontinuance for a minimum of 1-2 weeks prior to the initial evaluation to eliminate any contact lens induced corneal shape changes.)

- A thorough evaluation of eye health (anterior and posterior segments), including baseline retinal and/or optic nerve head optical coherence tomography, fundus photography, and visual field testing, when necessary, for patients suspected of having myopic complications like glaucoma, macular degeneration, etc.

## WHAT EQUIPMENT/INSTRUMENTATION IS NEEDED FOR PROVIDING MYOPIA MANAGEMENT SERVICES?

The clinician should have or obtain access to the following equipment/instruments:

- Standard optometric equipment for a comprehensive eye and vision examination
- Standard equipment for a complete binocular vision assessment
- Corneal topographer and/or corneal tomographer
- Amplitude Scan (A-scan) or other device to accurately measure axial length of the eye. Axial length should be assessed using an optical biometric method, such as optical partial coherence interferometry that provides non-contact measurements with high accuracy and precision.<sup>24</sup>
- Optical coherence tomography (OCT) or fundus photography (If fundus abnormalities are present, documentation is required.)<sup>25</sup>

## WHEN SHOULD MYOPIA CONTROL TREATMENT BE USED?

The most appropriate time to begin treatment should be based on the age of onset of myopia, refractive status, and a careful risk assessment. The age of myopia onset or duration of myopia progression has been found to be the most important predictor of high myopia in later childhood in myopic children. The decreased risk of complications later in life provided by even modest reduction in progression suggest treatment is advised for all young children with myopia.<sup>22</sup>

In addition, a child's binocular vision status may influence the efficacy of treatment (e.g., lag of accommodation and near esophoria). Also, clinicians must determine whether a child/parent/ caregiver can safely administer and comply with treatment (e.g., care, insertion, and removal of contact lenses; application of eyedrops).<sup>8</sup>

Myopia generally progresses most rapidly during the pre-teenage years (7-12 years of age), then slows during adolescence and adulthood.<sup>26</sup> Treatments are more likely to be effective at younger ages, when rapid progression is underway.<sup>8</sup>

Several clinical studies on the cumulative effects of myopia control therapies report a 0.30 mm reduction in axial elongation (about 0.75 D) over a two-to-three-year period.<sup>27-30</sup> Because the maximum effect observed to date is 0.44 mm (about 1.00 D) over a 7-year period, treatment should begin as early as possible.<sup>31</sup>

## WHAT FACTORS SHOULD BE CONSIDERED WHEN INITIATING A MYOPIA CONTROL PROGRAM?

No currently available myopia control treatment has been shown to completely stop or reverse the progression of myopia. The available efficacy data for myopia control treatments are generally limited to about five years or less, making it difficult to predict long-term treatment effects.

Assessment of axial elongation is the preferred method for evaluating myopia progression. If measurement of axial length is not readily available, doctors of optometry can co-manage a patient with another eye care provider that has access to an A-scan or other device that can measure axial length of the eye in a non-contact modality. Alternatively, measurement of refractive error, under cycloplegia, can be used to monitor myopia progression.

Certain devices that are used to assess individuals for cataract surgery intra-ocular lens calculations and other ophthalmic procedures may have the capability to measure axial length accurately for myopia management purposes in a non-contact modality. Additionally, each device has been shown to have statistically significant differences in measurement, concluding that the devices are accurate, but the measurement of an individual's axial length should take place on the same device at recurring follow-up examinations to accurately assess for change in overall length.<sup>32</sup>

Factors to consider when beginning a myopia control treatment program:<sup>8, 33, 34</sup>

- Overall hygiene and personal responsibility level of the child should be considered before starting a contact lens-based myopia management program to reduce risk of complications.
- Parents/guardians and patients should be extensively educated on the risks, benefits, signs/symptoms of complications, and care procedures involved with a myopia management program.
- There is insufficient evidence to suggest that faster progression or younger aged children with myopia derive greater benefit from treatment.
- The rate of reduction of axial myopia is typically greatest in the first year but may not be sustained due to the increasing age of the patient.
- Refractive surgeries such as, but not limited to, photorefractive keratectomy (PRK) or laser assisted in-situ keratomileusis (LASIK) may reduce the amount of refractive myopia but does not change the axial length of the eye. Post procedure eyes are still at risk if their axial length is outside of normal limits.
- The maximum expected myopia reduction using existing myopia control procedures is approximately 1.00 D, however in some cases it can be greater than 1.00 D.
- When treatment is stopped, some rebound, or progression of myopia may be observed.
- The long-term safety and efficacy of treatments to control myopia progression remains unresolved.

Clinicians should choose a treatment based on numerous considerations such as the child's age and rate of myopia progression, as well as the clinician's own experience and training, the preferences of parents and children, and ability of the child/parent/caregiver to adhere to the treatment plan.

## WHAT ARE THE TREATMENT OPTIONS FOR MYOPIA CONTROL?

### PHARMACOLOGIC

Muscarinic acetylcholine receptor antagonists (antimuscarinic agents) such as atropine sulfate (non-selective antimuscarinic agent) and pirenzepine dihydrochloride (selective antimuscarinic agent) are a part of a group of drugs that have been used in a topical formulation to slow or halt myopic progression successfully.<sup>35</sup> The most commonly used is atropine, which has a long history of study. According to the FDA, Atropine Sulfate Ophthalmic Solution, USP 1.0% was first approved in 2014 (although unapproved products have been used for over 100 years) and is indicated for cycloplegia, mydriasis, and penalization of the healthy eye in the treatment of amblyopia.<sup>36</sup> The use of topical ophthalmic atropine drops has been shown in numerous research studies to slow myopia progression. However, some uncertainty remains about the potential side effects and most effective dosing concentrations of atropine for the treatment of myopia in children.

Studies of atropine use to control myopia have evaluated a range of concentrations from 1.0% to 0.01%. A systematic review and meta-analysis of 44 published studies on myopia control concluded that the efficacy of atropine eyedrops was superior to other types of myopia control treatments (orthokeratology and novel multi-focal contact lenses).<sup>37</sup>

### 1.0% Atropine research studies

The Atropine for the Treatment of Childhood Myopia (ATOM) study looked at the effect of atropine versus a placebo eye drop on myopia progression. In the ATOM 1 study, after 2 years of 1.0% atropine use, the mean progression of myopia was significantly lower than in the placebo group. The atropine was then stopped, and the children were observed for one more year. During this time, a rebound effect was observed. However, despite the rebound, the amount of myopic progression remained lower in the eyes treated with atropine.<sup>29</sup>

The application of 1.0% atropine in the control of myopia progression has not been widely accepted because it results in clinically significant pupillary mydriasis and accommodative paralysis. Lower concentrations of atropine (0.5%-0.01%) have been reported to be associated with fewer symptoms, while still controlling myopia. A study was undertaken to find the highest concentration of atropine that does not result in significant symptoms from pupillary dilation and accommodative paralysis. Results indicated that atropine 0.02% is the highest concentration that did not result in clinical symptoms and findings associated with higher dosages. Mean pupillary dilation was 3 mm, and mean accommodative amplitude was 8 D with this concentration.<sup>38</sup>

### Low-concentration atropine research studies

In the ATOM 2 study, participants received either 0.5%, 0.1%, or 0.01% atropine eyedrops for two years. Treatment was stopped and participants were monitored for one year, during which a rebound effect occurred. Of particular note in ATOM 2, the rebound progression was most prominent in the 0.5% atropine group.<sup>39</sup> In a third phase of the ATOM study, children who had myopia progression of at least -0.50 D in at least one eye during phase 2 were restarted on atropine 0.01% for an additional 24 months. Over 5 years, atropine 0.01% eyedrops were reported to be more effective in slowing myopia progression with less visual side effects compared with higher doses of atropine.<sup>40</sup> However, the major limitation to this study was the absence of a defined control group.

As a result of the ATOM studies, the use of low-concentration atropine has emerged as a potential therapy for myopia progression, but its efficacy and optimal concentration remain uncertain. The Low-Concentration Atropine for Myopia Progression (LAMP) study found that the use of 0.05%, 0.025%, and 0.01% atropine eye drops all reduced myopia progression along a concentration-dependent response. All concentrations were well tolerated without an adverse effect on vision-related quality of life. Of the three concentrations used, 0.05% atropine was most effective in controlling spherical equivalent refractive progression and axial length elongation over a period of one year.<sup>41</sup> Over two years, the efficacy of 0.05% atropine was double that observed with 0.01% atropine, and it remained the optimal concentration among the studied atropine concentrations in slowing myopia progression. The LAMP study proposed the use of 0.05% atropine as an optimal dose for obtaining clinically important outcomes with minimum risk for adverse reactions including photophobia, reduction in accommodative amplitude, and pupillary dilation.<sup>42</sup>

The LAMP study also looked at the effect of age at treatment in response to atropine. Younger age is associated with poor treatment response to low-concentration atropine at 0.05%, 0.025%, and 0.01%. Among concentrations studied, younger children required the highest (0.05%) concentration to achieve similar reduction in myopic progression as older children receiving lower concentrations.<sup>43</sup> The study also found that low concentrations of atropine (0.05%, 0.025%, and 0.01%) have no clinical effect on corneal or lens power. Anti-myopic effects of low-concentration atropine act mainly on reducing axial length elongation, and therefore, could reduce the risk of subsequent myopia complications.<sup>44</sup>

A systematic review and meta-analysis published in 2017 of 19 randomized trials and cohort studies evaluating the efficacy versus the adverse effects of various doses of atropine for myopia control in children reported that all doses of atropine (1.0%, 0.5%, 0.1% and 0.01%), were found to be equally beneficial with respect to refractive error progression, however, axial elongation was arrested completely with 1.0% atropine, but 0.5% and 0.1% atropine slowed it by only 29% and 25%, respectively, with 0.01% having no effect on axial elongation.<sup>45, 46</sup> However, high-dose atropines have been associated with more adverse effects, such as the 43.1% incidence of photophobia

compared with 6.3% for low-dose atropine and 17.8% for moderate-dose atropine. While lower strength doses (i.e., 0.01%) may have fewer side effects, they may not be as effective in controlling myopia progression as higher strengths (i.e., 0.5% and 1.0%).<sup>39</sup>

A more recent meta-analysis evaluated the safety and effectiveness of atropine in controlling the progression of myopia and explored the relationship between the dose of atropine and its effectiveness. It concluded that the effectiveness of atropine in controlling the progression of myopia was dose related. The use of 0.05% atropine was likely to be the optimal dose.<sup>47</sup>

Another study of low-dose atropine eyedrops evaluated the effects of 0.01% and 0.02% atropine eye drops on myopia progression, pupil diameter, and accommodative amplitude. Results show 0.02% atropine eye drops had a better effect on myopia progression than 0.01% atropine, but 0.02% and 0.01% atropine both showed similar effects on pupil diameter and accommodative amplitude after 12 months of treatment.<sup>48</sup>

#### Effect of discontinuing atropine use

Accelerated myopia progression after stopping the use of higher strength atropine has been reported.<sup>49</sup> A study of changes in spherical equivalent refraction and other ocular parameters one year after stopping the administration of atropine in 400 myopic children, 6 -12 years of age who received atropine 0.5%, 0.1%, or 0.01% for 24 months found there was a myopic rebound, and it was greater in eyes that had received 0.5% and 0.1% atropine. The 0.01% atropine effect, however, was more modulated and sustained.<sup>50</sup>

#### Patient management

Only 1.0% atropine has been approved by the FDA for amblyopia treatment and not for indications of myopia management. Use of atropine eye drops must be considered off-label for any other indication other than amblyopia treatment. As such, doctors of optometry must make patients and parents/guardians of patients who are minors aware of its off-label use for complete informed consent for myopia management purposes. In addition, concentrations other than 1.0% are not commercially available and must be prepared by a compounding pharmacist. Potential ophthalmic side-effects attributable to the use of atropine eye drops include photophobia, glare sensitivity, and loss of accommodation. In addition, there are concerns about potential long-term systemic or ocular side effects. Doctors of optometry need to be aware that there were adverse reactions, warnings, precautions, and contraindications to the use of atropine in the FDA Pediatric Postmarketing Pharmacovigilance and Drug Utilization Review for Atropine Sulfate Ophthalmic Solution, USP 1.0%.<sup>36</sup> The most common adverse reactions that have been reported are eye pain and stinging on administration, blurred vision, photophobia, decreased lacrimation, and increased heart rate and blood pressure. It should only be used in pregnant women if clearly indicated.

The risks associated with atropine use are relatively low and the benefits may be long lasting. The course of treatment usually involves having the child/parent/caregiver apply atropine eye drops once daily at bedtime. One option is to start with a low concentration of atropine and monitor for adverse side effects and myopia progression. Increase dosage concentration as needed. Children receiving atropine treatment will need a refractive correction for distance and possibly near, as well as photochromatic lenses or additional sunglasses to relieve photosensitivity issues when outdoors.<sup>8</sup>

Since the long-term effects of atropine for the treatment of myopia have not been determined, it has been suggested that treatment be limited to two years.<sup>51</sup> It is beneficial to gradually reduce dosage or dose frequency at the end of treatment to minimize rebound effects.



## MULTIFOCAL SOFT CONTACT LENSES

A number of studies of multifocal soft contact lenses (MFSCCL) with a central distance area and increased power in the periphery (dual focus and extended focus)<sup>52</sup> have demonstrated that they can slow myopia progression. The lenses studied used either a progressive design with a gradual increase in lens power toward the periphery of the lens or a concentric ring design with distinct plus power zones in the periphery of the lens. As opposed to overnight orthokeratology lens wear, MFSCCLs are generally worn during the day.

The hypotheses proposed to explain the efficacy of these lenses are generally based on the premise that the stimulus for eye growth is a defocused retinal image with hyperopic blur either centrally or peripherally. Although the individual power profiles of the lenses vary, the contact lenses generally incorporate 'positive power' to reduce the hyperopic blur or impose myopic defocus, or in the case of the extended depth of focus lens, they have a power profile designed to optimize retinal image quality for points on or in front of the retina.<sup>53</sup>

### Research studies

A study of 8-11-year-old children sought to determine the progression of myopia and axial elongation of children fitted with commercially available distance center MFSCCL with a +2.00 D add worn for two years. The MFSCCL wear resulted in a 50% reduction in the progression of myopia and a 29% reduction in axial elongation during the two-year treatment period compared to a historical control group.<sup>54</sup>

Using a randomized controlled trial, defocus incorporated soft contact (DISC) lenses were evaluated in 221 children aged 8-13 years old. The lenses incorporated concentric rings, which provided an addition of +2.50 D, alternating with the normal distance correction. The daily wearing of DISC lens significantly slowed myopia progression and axial elongation in Hong Kong school children. The findings demonstrated that simultaneous clear vision with constant myopic defocus can retard myopia progression.<sup>55</sup>

The Myopia Control with Bifocal Contact Lenses (CONTROL) study was a one-year, prospective, randomized, clinical trial of bifocal contact lenses for control of myopia in children with esophoric fixation disparities at near. The center distance bifocal contact lenses tested in the study achieved greater control over myopia progression and axial elongation (>70%) compared with most published results with multifocal spectacles.<sup>56</sup>

In a study of primarily Asian children ages 8-11 years old, soft contact lens with spherical aberration slowed axial growth of the eye, although this did not translate into a sustained statistically significant effect on spherical equivalent refraction. The majority of the treatment effect occurred in the initial six months of wear. No evidence of rebound effect was observed after ceasing treatment.<sup>57</sup>

A systematic review evaluated studies on the effect of soft contact lens with concentric ring bifocal and peripheral add multifocal designs on controlling myopia progression in school-aged children. Compared with the control group, concentric ring bifocal soft contact lenses and peripheral add multifocal soft contact lenses showed less myopia progression and less axial elongation at 12 months. These lenses produced additional myopia control rates of 30-38% for slowing myopia progression and 31-51% for lessening axial elongation within 24 months. The study concluded that both concentric ring bifocal and peripheral add multifocal soft contact lenses are clinically effective for controlling myopia in school-aged children, with an overall myopia control rates of 30-50% over two years. The concentric ring bifocal soft contact lenses seemed to have greater effect than peripheral add multifocal soft contact lenses.<sup>58</sup>

In a retrospective case series analysis, a group of 32 children ages 6-19 years were fit with a commercially available extended depth of focus (center distance) multifocal soft contact lenses to evaluate their effect on slowing the progression of myopia over 6-25 months. Approximately 98.4% of the children showed reduction of annualized

myopic progression; 91% showed a decrease of 70% or greater. Overall, 81.25% showed complete halting of myopic progression, including 6.25% demonstrating myopic regression.<sup>52</sup>

A randomized clinical trial was conducted to determine myopia control efficacy with novel contact lenses that reduced both central and peripheral defocus and provided extended depth of focus with better global retinal image quality for points on, and anterior to, the retina and degraded for points posterior to the retina. Contact lenses that either imposed myopic defocus at the retina or modulated retinal image quality resulted in a slower progression of myopia with greater efficacy seen in compliant wearers. Importantly, there was no difference in the myopia control provided by either of these strategies.<sup>59</sup>

A double-masked randomized clinical trial evaluated whether MFSCs slow myopia progression in children and whether high add power (+2.50 D) slows myopia progression more than medium (+1.50 D) add power lenses. Among children with myopia, treatment with high add power MFSCs significantly reduced the rate of myopia progression over three years compared with medium add power multifocal and single vision contact lenses.<sup>60</sup>

A study to compare myopia progression in children randomized to MiSight® contact lenses versus children corrected with single-vision spectacles was conducted over a two-year period. The use of MiSight® contact lenses produced lower myopia progression (39.32%) and lower axial growth of the eye (36.04%) at two years compared to spectacle use.<sup>61</sup>

A randomized, double-masked clinical trial demonstrated the effectiveness of the MiSight® soft contact lens in slowing myopia progression over multiple years. The purpose of the study was to quantify the effectiveness of MiSight® daily disposable soft contact lens in slowing the progression of juvenile-onset myopia. Over the course of the study, there were no cases of serious ocular adverse events reported. Results of this clinical trial demonstrated the effectiveness of the MiSight® daily disposable soft contact lens in slowing change in spherical equivalent refraction and axial length.<sup>27</sup> The FDA has approved the use of the MiSight® (omafilcon A, Cooper Vision) dual focus contact lenses for the treatment of progressive myopia.

#### Ocular health and contact lens wear in children

Concerns have been raised about the potential for adverse ocular health problems in young children fitted with contact lenses. However, this has not been confirmed in clinical studies. A review of data from a range of studies on the incidence of complications, specifically corneal infiltrative events and microbial keratitis, was conducted for patients under the age of 18 years. The incidence of corneal infiltrative events in children was found to be no higher than in adults, and in the youngest age range of 8-11 years, it may be markedly lower.<sup>62</sup>

A more recent study was conducted to evaluate the ocular health and safety of children ages 8-12 years old fit with soft hydrogel daily disposable contact lenses and followed for 6-years in a double-masked clinical trial investigating the performance of a dual-focus contact lens designed to control myopia progression. During years 1-3, children were randomized to either MiSight® 1 day (omafilcon A, CooperVision) or Proclear® 1 day (omafilcon A, CooperVision). The lenses were identical in material and geometry except for the front optical zone design. At the end of year 3, all those wearing Proclear® 1 day were switched to MiSight® 1 day, therefore all wore MiSight® 1 day in years 4-6. After 6 years of lens wear, ocular health by biomicroscopy was similar to pre-lens wear. Across the 6 years, there were no contact lens related serious adverse events reported. Results suggest that children this age can successfully wear daily-disposable hydrogel contact lenses with minimal impact on ocular physiology.<sup>63</sup>

#### Patient Management

It is recommended that a MFSC incorporating the patient's full distance refractive error and relative +2.00 to +2.50 treatment correction be initially selected.<sup>9</sup> The add power to be used can be determined by measurement of distance and near visual acuities with contact lenses and balancing the add power with the distance visual acuity (higher adds

may blur distance vision). Also, the impact of the contact lenses on the binocular vision system should be evaluated. A higher add power may be needed to neutralize an esophoric ocular posture.

## ORTHOKERATOLOGY

Orthokeratology using specially designed reverse geometry rigid gas permeable contact lenses worn overnight has been proposed to reduce the progression of myopia. Numerous studies have looked at the efficacy and safety of orthokeratology as a myopia control strategy.

### Research studies

The Longitudinal Orthokeratology Research in Children (LORIC) study compared the changes in axial length of eyes in patients wearing orthokeratology lenses and those wearing spectacle lenses. There was a significant slowing of eye growth in the orthokeratology group. The average myopic reduction was 46%, however, there was considerable variability in the amount of eye elongation of any patient suggesting there is no way to predict the effect of orthokeratology on myopia progression of individuals.<sup>64</sup>

The Retardation of Myopia in Orthokeratology (ROMIO) study was a single-masked, randomized clinical trial to evaluate the effectiveness of orthokeratology for myopia control. On average, children wearing orthokeratology lenses had a slower increase in axial elongation by 43% compared with that of children wearing single-vision glasses. Younger children tended to have faster axial elongation and therefore may benefit from early orthokeratology treatment.<sup>65</sup>

Two studies sought to compare axial length elongation in myopic children receiving overnight orthokeratology treatment to those wearing spectacles as controls. In the first study, the increase in axial length during the two-year study period was 0.39 +/- 0.27 and 0.61 +/- 0.24 mm, respectively, and the difference was significant.<sup>66</sup> The second study found the increase in axial length during the 5-year study period was 0.99 +/- 0.47 mm and 1.41 +/- 0.68 mm for the orthokeratology and control groups, respectively, and the difference was statistically significant. The annual increases in axial length were significantly different between the groups for the first, second, and third years, but not for the fourth and fifth years.<sup>67</sup> Both studies concluded that orthokeratology can slow axial length elongation in childhood myopia.

A systematic review was conducted of published studies to compare the efficacy, safety and acceptability of orthokeratology to a control group of single vision spectacles wearers on slowing axial elongation. Orthokeratology was reported to have significantly greater efficacy in controlling axial elongation in children compared to spectacle correction. The safety and acceptability results were good, and there appeared to be a greater myopia control effect in Chinese children compared to Caucasians, and in those with higher initial myopia.<sup>68</sup>

A retrospective study investigated the effectiveness of orthokeratology in reducing the development of myopia in 141 Chinese children with low to moderate myopia. After one year, there was a significant difference in the average axial elongation between the orthokeratology lens group (0.27 +/- 0.17) mm and the control group (0.38 +/- 0.13) mm. The study concluded that orthokeratology lenses were effective in controlling myopic progression in Chinese children, particularly in younger children and in children with higher myopia.<sup>69</sup>

### Ocular health and orthokeratology in children

Orthokeratology side effects have resulted in this treatment experiencing higher dropout rates compared to other myopia interventions.<sup>37</sup> A systematic review reported that there is sufficient evidence to suggest that orthokeratology is a safe option for myopia correction and retardation. However, long-term success of orthokeratology treatment requires a combination of proper lens fitting, rigorous compliance to lens care regimen, good adherence to routine follow-ups, and timely treatment of complications. It is also worth noting that *Pseudomonas aeruginosa* and

Acanthamoeba were the most commonly reported pathogens for orthokeratology associated infectious keratitis, both of which require early diagnosis and prompt treatment to minimizing the risks of permanent vision loss.<sup>70</sup>

While rigid gas permeable contact lenses have shown to be safe and very low risk in children (including very low risk of infectious keratitis), a systematic review summarized the clinical profile of infectious keratitis in association with orthokeratology lens wear. Despite early intervention and treatment, the majority of infections resulted in the formation of corneal scars, and almost 10% of eyes needed surgical treatment. Timely awareness and treatment of keratitis should be emphasized to the lens wearers.<sup>71</sup>

A retrospective study of 66 school age children assessed whether overnight orthokeratology was effective in slowing myopia progression over a 12-year follow-up period. Compared with the control group, the orthokeratology group had a significantly lower trend of refractive error change during the follow-up periods and demonstrated a clinically acceptable safety profile.<sup>72</sup>

#### Comparison of orthokeratology to atropine

An historical control study of 247 children with myopia analyzed the efficacy of 0.125% atropine and orthokeratology in controlling myopia progression and elongation of axial length. Comparison of increases in axial length in relation to baseline myopia showed significant correlations both in the orthokeratology lens group and atropine group. High-myopia patients benefited more from both orthokeratology lenses and atropine than did low-myopia patients. The correlation of baseline myopia and myopia progression was stronger in the orthokeratology lens group than in the atropine group. The study concluded that orthokeratology is a useful method for controlling myopia progression even in high-myopia patients.<sup>73</sup>

A study comparing the efficacies of 0.02% atropine eye drops and orthokeratology to control axial length elongation in children with myopia found that orthokeratology seems to be a better method for controlling axial length elongation compared with administration of 0.02% atropine in children with higher myopia over a treatment period of two years. Faster axial length elongation was found in the 0.02% atropine group compared with the orthokeratology group at higher baseline spherical equivalent refractive error.<sup>74</sup>

#### Discontinuation of treatment

Over a 14-month period, an evaluation and comparison were made of changes in axial elongation in children who discontinued and then resumed orthokeratology lens wear with those who continued to wear their lenses or spectacles following a two-year myopia control study. It was reported that discontinuing orthokeratology lens wear at or before the age of 14 years may lead to a more rapid increase in axial length. This was comparable to those wearing spectacles during the initial two-year myopia control study, but greater than the control and orthokeratology group in this study. Axial elongation slowed again with resumed lens wear after six months.<sup>75</sup>

#### Patient management

Numerous lens designs are available for orthokeratology. However, most lenses are not approved for myopia control, therefore their use is considered off label. Recently, Acuvue® Abiliti™ overnight therapeutic contact lenses (Johnson & Johnson Vision) received FDA approved for myopia management.<sup>76</sup>

The suitability assessment and fitting process for childhood myopia control orthokeratology is generally no different than a proper fitting of contact lenses for a usual and customary myopia refractive correction. It is recommended that orthokeratology lenses be worn nightly for a minimum of eight hours to maximize correction for best unaided vision during waking hours.<sup>8</sup>

## SPECTACLE LENSES FOR MYOPIA PROGRESSION

Multifocal lenses (bifocal and progressive addition lenses) have been advocated as a possible substitute for single-vision lenses to slow myopia progression in children, but results vary across studies. Novel spectacle lens designs have also been studied for myopia control based on a peripheral defocus design with some reports of success in slowing myopia progression.

### Research studies

The Correction of Myopia Evaluation Trial (COMET) evaluated progressive addition lenses (PALs) versus single vision lenses for slowing progression of myopia. The use of PALs compared with single vision lenses slowed the progression of myopia in children by a small, statistically significant amount only during the first year.<sup>77</sup> A follow-up study found the use of PALs reduced myopia progression in children with high accommodative lag and near esophoria. However, the effect of the PALs was found to be statistically, but not clinically significant, in slowing myopia progression.<sup>78</sup>

A randomized trial was conducted to compare the effect of wearing, then ceasing to wear PALs versus single-vision lenses on myopia progression in children with high accommodative lag. The statistically significant, but clinically small PAL effect suggests that treatments aimed at reducing foveal defocus may not be as effective as previously thought in myopic children with high accommodative lag.<sup>79</sup>

A randomized trial on the effect of bifocal and prismatic bifocal spectacles on myopic progression reported after 24 months that bifocal lenses can moderately slow myopic progression in children with high rates of progression. The treatment effect of bifocals and prismatic bifocals was significant and both bifocal groups had less axial elongation (0.21 mm) than the single vision lens group. The study concluded that bifocals may be considered for slowing myopic progression in children with an annual progression rate of at least 0.50 D.<sup>80</sup> Three-year results from this study continued to show bifocal spectacles can slow myopia progression in children. The results also suggest that prismatic bifocals are more effective for myopic children with low lags of accommodation.<sup>81</sup>

A meta-analysis of nine clinical trials showed that multifocal spectacle lenses with powers ranging from +1.50 D to +2.00 D were associated with a statistically significant decrease in myopia progression in school-aged children compared with single vision lenses. The benefit was greater in children with a higher level of myopia at baseline and was sustained for a minimum of 24 months. Asian children appeared to have greater benefit from intervention with multifocal lenses than Caucasian children.<sup>82</sup>

Newer spectacle lens technology has emerged with lenses designed to reduce peripheral hyperopic defocus as a means for preventing myopia progression. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses have a 9 mm central optical zone and a 33 mm annular zone with multiple 1 mm segments having a relative positive power of +3.50 D. A two-year randomized controlled trial comparing DIMS lenses to single vision lenses found that myopia progressed 52% more slowly for children in the DIMS group compared with those in the single vision lens group. Likewise, children in the DIMS group had less axial elongation by 62% than those in the single vision lens group. The study concluded that daily wear of the DIMS lenses significantly retarded myopia progression and axial elongation in myopic children.<sup>28</sup> DIMS lenses have not yet been approved in the United States by the FDA for use in myopia management.

In a follow-up to a two-year myopia control trial, children in the original study continued to DIMS lenses or were switched from single vision to DIMS lenses for a one-year period. The myopia control effect found in the original two-year study was sustained in the third year in children who had used the DIMS spectacles in the previous two years and was also shown in the children switching from single vision to DIMS lenses.<sup>83</sup>

A study of 187 school children evaluated the efficacy of two new myopia control spectacle lenses with lenslets of different asphericity over a one-year period. The children were randomized to receive spectacle lenses with highly aspherical lenslets (HAL), spectacle lenses with slightly aspherical lenslets (SAL), or single vision spectacle lenses.

Compared with single vision lenses, the myopia control efficacy measured using spherical equivalent refraction was 67% for HAL and 41% for SAL, and the efficacy measured using axial elongation was 64% for HAL and 31% for SAL. HAL lenses resulted in significantly greater myopia control than SAL lenses for spherical equivalent refraction (difference of 0.21 D) and axial elongation (difference of 0.12 mm). All groups adapted to their lenses with no reported adverse events, complaints or discomfort. It was concluded that spectacle lenses with aspherical lenslets effectively slow myopia progression and axial elongation compared with single vision lenses. Myopia control efficacy increased with lenslet asphericity.<sup>84</sup> HAL and SAL lenses have not yet been approved in the United States by the FDA for use in myopia management.

### Patient management

Multifocal spectacles remain an option for those patients who are not suitable or not motivated for the use of other myopia control therapies. The future availability of novel spectacle lens designs may offer additional opportunities for myopia control.

With regard to prescribing spectacles, doctors of optometry should be aware that patients who are under corrected tend to myopically progress more rapidly and more severely than those who have been prescribed full distance correction. Additionally, it was shown that spectacle under correction does not slow growth of the eye in a clinically meaningful manner.<sup>85, 86</sup>

Given the association and increased risk for retinal tear and retinal detachment in patients with myopia, eye protection needs to be considered for moderate and severe levels of myopia. While many patients may elect to have their myopia progression treated with a contact lens modality, which can simultaneously correct their refractive error, that does not negate the need for impact-resistant frames and lenses to be used for high-risk activities like sports.<sup>87</sup>

## **BEHAVIORAL MODIFICATION**

Although there is a genetic component to myopia development, the visual environment appears to be a major contributor to school-aged myopia.<sup>9,88</sup> Time spent outdoors, and time spent reading or viewing computer screens and smartphones may have an impact on the development of myopia.

### Research studies

The overall findings of a systematic review and meta-analysis indicate that increasing time spent outdoors may be a simple strategy by which to reduce the risk of developing myopia and its progression in children and adolescents.<sup>89</sup>

A study of the effects of outdoor activity during class recess on myopia changes among elementary school students in Taiwan found that outdoor activities during class recess in school have a significant effect on myopia onset and myopic shift. Such activities may have a prominent effect on the control of myopia, especially in nonmyopic children.<sup>90</sup>

In a study of six-year-old children in China, the addition of 40 minutes of outdoor activity at school compared with usual activity resulted in a reduced incidence rate of myopia over the next three years. Further studies are needed to assess long-term follow-up of these children and the generalizability of these findings.<sup>91</sup>

Another systematic review concluded that outdoor exposure appears to provide protection from myopia onset in non-myopes but does not result in restriction of myopia progression in already myopic children. Increased time outdoors is effective in preventing the onset of myopia as well as in slowing the myopic shift in refractive error. But paradoxically, outdoor time was not effective in slowing progression in eyes that were already myopic.<sup>9</sup>

The results of a meta-analysis of published research suggest that there is a slightly lower risk of myopia onset and myopic shift with more hours of outdoor activities, but concluded that future clinical trials are needed to assess its long-term effect and whether the effect varies by initial myopic status.<sup>92</sup>

A systematic review published in 2020 of studies on the impact of outdoor time on myopia development included five randomized controlled trials with 3,014 children. Analysis of the studies found that new myopia cases in the outdoor group were fewer than that of the control group and the change in axial length of the outdoor group was smaller than that of the control group. It was concluded that outdoor time helps slow down the change of axial length and reduce the risk of myopia.<sup>93</sup>

The effect of near work activities on myopia in children was also evaluated in a systematic review and meta-analysis. It found that more time spent on near work activities was associated with higher odds of myopia and that the odds of myopia increased by 2% for every one diopter-hour (a weighted sum of the time spent in particular activities according to the accommodative demand required to perform the task)<sup>94</sup> more of near work per week. Therefore, the development of a strategy to reduce the impact of near work on myopia would be important for preventing myopia in children.<sup>95</sup>

### Patient management

All parents of young children should be counseled on the benefits of their child spending more time outdoors and on restricting the amount of time spent looking at smartphones or computer screens. A minimum of 8-15 hours of outdoor activity per week is recommended to achieve clinically meaningful protection from myopia development.<sup>8</sup>

## **HOW SHOULD MYOPIA MANAGEMENT PROGRAMS BE DISCUSSED WITH PATIENTS/PARENTS/CAREGIVERS?**

It is important to discuss a child's risk for myopia development and/or progression with parents and/or caregivers. Although heredity and ethnicity play an undeniable role in myopia development, it is also significantly influenced by the visual environment.

Discussion with patients/parents/caregivers should include a comprehensive review of the causes of myopia, the risks and consequences of the development and progression of myopia in children, and the treatment options currently available.

Emphasis should be on the long-term benefits of reducing myopia progression and related ocular complications. There is a need to manage parent's expectations. The goals of myopia management are to slow the progression of myopia, not to eliminate it. Children will still need to wear glasses once the myopia control therapy ends.

Providing proper informed consent is an important part of myopia management. Written materials should be used to supplement in-office education.

## **WHAT ARE THE ELEMENTS OF FOLLOW-UP CARE?**

Regular follow-up of patients undergoing myopia treatment is needed to determine whether treatment should be continued, modified, or augmented with additional treatment options or stopped altogether. Depending on treatment, patients should generally be reevaluated on a 3-6-month schedule or as indicated below.<sup>8</sup> Patients are required to be reevaluated throughout their treatment.

Note: The reevaluation schedule below is a general recommendation. Individual patient reevaluation should be at the discretion of the doctor and be based on the clinical presentation, the best indication for the patient, and on a case-by-case basis.

Elements	Days	Months
Atropine	4-7 days	1 month 3 months Then every 6 months
Orthokeratology	1 day 4-7 days	1 month 3 months Then every 6 months
Multifocal soft contact lenses	4-7 days	1 month Then every 6 months
PAL/bifocal spectacles		1 month Then every 6 months

Patients/parents/caregivers should be cautioned to seek immediate care if adverse reactions or other problems relating to the therapy develop. Additionally, it is best practice for all children, especially those of myopic parents, to have an in-person annual comprehensive eye examination prior to the beginning of a new school year.<sup>23,96</sup>

### **WHEN SHOULD TREATMENT BE CHANGED OR STOPPED?**

The impact of myopia control treatments on age of cessation of myopia progression is unknown. There are limited data on when myopia stops progressing. Progression has been noted in young adults and approximately one-third of myopic adults develop myopia after 15 years of age. The mean age of refractive error stabilization for early childhood onset myopia seems to be around 16 years of age, but there is considerable variability. Axial length seems to take much longer to stabilize, with 90% stabilizing by 21 years of age in one longitudinal study.<sup>97</sup>

Close monitoring by the clinician is important on treatment cessation, so that any apparent acceleration in progression can be quickly addressed by reinstating treatment. Furthermore, there are legal and ethical issues related to treatment intervention that might need to be considered.<sup>8</sup>

Treatment should be continued as long as the benefits outweigh the potential risks or additional costs associated with the treatment. When myopia progression is not sufficiently controlled, treatment may be stopped, switched to another form of therapy, or augmented by combining with another treatment modality. Poor tolerance of visual side effects or failure to follow treatment protocols may also warrant cessation or change of treatment.<sup>8</sup>

### **NON-RESPONDERS**

Non-responders are those children who have shown minimal efficacy of their treatment in myopia control studies. By simple virtue of having an ‘average’ efficacy for a myopia control treatment, there will be some children who fall below and above that average. Influential factors are younger age, higher myopia, and higher prior myopia progression.

### **WHAT CAN BE DONE IF AN INDIVIDUAL IS A NON/POOR RESPONDER TO INITIAL TREATMENT?<sup>98</sup>**

- **Evaluate expectations.** Consider whether the child is an ‘average’ myope likely to experience ‘average’ efficacy with their intervention strategy. Are they younger, a higher myope, a faster prior progressor, an amblyope? The usual results may not apply.
- **Revisit the treatment.** Review the compliance and treatment process (user error) issues, as well as ensuring it is still a suitable treatment for that child’s and their family’s capabilities. If there is a treatment available that has been shown to work better, then consider changing treatments. Remember that comprehensive myopia management includes discussion of visual environment, so consider this part of the ‘treatment’ as well.



- **Add atropine.** There are early studies showing a potential synergistic effect of atropine 0.01% and orthokeratology.<sup>99</sup> Baseline data has been presented on atropine 0.01% plus multifocal contact lenses (center distance +2.50 add) indicating good short-term tolerance of combination treatment, with data on efficacy to follow.<sup>100</sup>
- **Review more frequently.** This can be especially helpful in cases of non-compliance and user error. Consider follow-up examinations every 3-6 months, if you were doing so at longer intervals before.
- **Remember that some progression will occur.** In children under 10, minimal progression of 0.25 D to 0.50 D per year represents a successful treatment outcome, compared to the 0.75 D to 1.25 D of annual progression without a myopia management treatment in place. In children over 10 years of age, 0.50 D per year or more of progression likely represents a non-response to myopia control treatment. It is recommended clinicians discuss/ remind the parent or guardian of these goals.

## CONCLUSION

The most effective strategy to reduce myopia-related complications is to prevent myopia progression during childhood. Even with the limitations of myopia management using currently available treatment options, initiating some form of treatment will likely provide a better long-term outcome than prescribing single vision lenses. A major goal of myopia management in children is reducing the risk of visual impairment and blindness later in life.

While ongoing research will continue to provide additional information on the safety and efficacy of current or new therapies for myopia control, current evidence-based treatment options are available. Doctors of optometry need to take a leading role in addressing the growing public health problem of increasing prevalence and amount of myopia in children.

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