PERSPECTIVE

Controversies in Myopia Control Treatment: What Does It Mean for Future Research?

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• PURPOSE: Treatment of myopia has been informed by more than 3 decades of clinical trials and other observations. However, controversies regarding myopia control remain, such as when to stop treatment and what is the long-term efficacy of treatment. This perspective aims to describe clinically relevant and current controversies regarding myopia treatment.

• DESIGN: Perspective.

• METHODS: We reviewed clinical trial data and other studies regarding myopia control therapies.

• RESULTS: Controversies in myopia treatment are related to the efficacy of low-dose atropine eyedrops and new lens design spectacles to substantially reduce progression of myopia. In addition to efficacy, safety of therapies including soft contact lenses, orthokeratology and low-level red light remains a concern. The therapeutic role of outdoor time in reducing myopia progression also requires further investigation. More research is necessary to confirm treatment effectiveness, duration of required treatment, tapering schedules, and when to begin and stop treatment.

• CONCLUSIONS: Myopia management is evolving, and maintaining competency in the multiple approaches poses a challenge. Key challenges include identifying high-risk children who would benefit most from treatment, limited evidence supporting the effectiveness of myopia progression control treatments in certain populations, and concerns regarding availability and cost of treatment, which may create socioeconomic barriers to access. The limitations of current methods to slow or stop myopia progression highlight the need for continuing rigorous investigation of new and improved strategies to reduce the burden of myopia. (Am J Ophthalmol 2025;272: 79–86.

There has been concern regarding increased myopia prevalence. In the United States, myopia prevalence increased from 25.0% to 41.6% between 1999 and 2004 in individuals aged 12 to 54 years.[1] Approximately 4% of the population has high myopia and thus have high risk of visual loss.[2] Given both an aging and increasingly myopic population, myopic macular degeneration, retinal detachment, cataract, and open angle glaucoma[3] could become more prevalent.

Slowing myopia progression with atropine[4] and orthokeratology[5] has been recognized as somewhat effective, but can be associated with adverse events. Recent developments of a new generation of "anti-myopia" spectacles and contact lenses, as well as red-light therapy have revolutionized how patients with myopia are being treated and reinvigorated scientific research in this area.[6,7]

According to the National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) at the US Centers for Disease Control and Prevention (CDC), chronic diseases are defined as conditions that last more than 1 year and require ongoing medical attention. Myopia fits the description of a chronic disease as recognized by the National Academy of Sciences, Engineering and Medicine.[8] However, myopia has not yet been recognized as a "disease" in the United States by the CDC or the Centers for Medicare and Medicaid Services (CMS). Substantial strides have been made in the search for effective preventive treatments for high myopia, pathologic myopia, and associated complications. Of note, myopia research is expanding by more than a thousand studies per year.[9] However, controversies remain regarding the efficacy of current therapies for myopia. The intent of this perspective is to describe clinically relevant controversies regarding myopia treatment.

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ARE LOW-DOSE ATROPINE EYEDROPS A PROVEN TREATMENT TO REDUCE PROGRESSION OF MYOPIA?

Several randomized controlled trials (RCTs), including the Atropine for the Treatment Of Myopia (ATOM) and the Low-Concentration Atropine for Myopia Progression (LAMP) studies, systematic reviews and meta-analyses support the use of 0.01% atropine as safe and effective in slowing myopia progression in the short term.[4,10–12] However, a 2-year clinical trial (PEDIG MTS1) using 0.01% atropine in a primarily non-Asian population in the United States found no meaningful benefit on spherical equivalent (SE) or axial elongation.[13]

A second clinical trial (CHAMP) in the United States found 0.02% atropine to not be effective in their preplanned primary outcome of responder rate. However, following a prespecified hierarchical analysis plan, the data suggested efficacy for 0.01% atropine.[10] The results of the CHAMP study have led to a discussion of when statistically significant differences are clinically meaningful.[10] Of note, the Western Australia (WA-ATOM) and MOSAIC trials did not identify statistically significant or clinically meaningful benefits after 24 months in Australian and European cohorts, respectively.[14,15]

Several theories have emerged to explain the results of these studies, such as racial/ethnic differences (fewer Asian children; inclusion of Black children with lower myopia progression), age range (more children aged 5-7 years with lower myopia), iris color, and possible inconsistencies in the formulation of atropine that may have led to differences in bioavailability and effectiveness (of note, the same product was used by PEDIG MTS1, CHAMP, and MOSAIC). Thus, different atropine concentrations may be necessary for certain populations to observe a benefit, as the LAMP study identified a dose-dependent effect.[12]

Rebound is an increase in rate of myopia progression after stopping therapy. In the 3-year LAMP study, the rebound effects following 0.05%, 0.025%, and 0.01% atropine were clinically small, especially in older children.[12] Longer-term results were published but were not placebo controlled, because most patients had been switched to other treatments.[16] As in the ATOM 2 study, rebound was greater following use of higher atropine concentrations.

Some experts have hypothesized that the rebound effect is higher in clinical trials because of the design, which abruptly stops the treatment instead of tapering treatment for 3-6 months as is recommended by some clinicians. If true, then studies implementing treatment with low-dose atropine without tapering may observe higher rebound and varied findings regarding atropine efficacy. When assessing outcomes for the occurrence of rebound, greater myopia progression is expected in the treatment washout group than in the placebo group. The WA-ATOM study[14] included Australian children treated with 0.01% atropine for 2 years with a 1-year washout. As in LAMP, the WA-ATOM authors found that rebound was less for older children. The clinical value of tapering treatment needs to be prospectively studied.

Regarding the duration of therapy, in the LAMP study children stopped therapy at 3 years, but subsequently many children resumed 0.05% if they progressed 0.50 diopters (D) or more over the next year.[16] By 5 years, LAMP investigators had restarted therapy for most children (87.9%) in the cessation group; similar proportions of retreatments were found for the 3 atropine concentrations (0.01%, 0.025%, and 0.05%).

Recently, a first of its kind long-term follow-up study from Singapore (ATLAS) found that the use of low-dose atropine (0.01%-1.0%) for 2-4 years in children with a mean baseline age of 9 years was no better than placebo when myopia was measured many years later.[17] Although follow-up rates were low, these results are a warning that the durability of short-term treatments for myopia control is uncertain and there is need to prospectively evaluate longer periods of treatment, well beyond the 2-4 years currently prescribed, to determine if that approach will maintain long-term benefits.

Greater myopia progression was found for younger children at cessation of therapy suggesting that continuing treatment until adolescence could contribute to a sustained benefit.[16] Such an approach, without clear evidence, is being adopted by some clinicians who are continuing treatment well into the teenage years when the risk of rebound may be lower. These results in East Asia suggest that use of low-dose atropine for longer periods is needed, and resumption of treatment in those with significant myopia progression after cessation should be studied. Such approaches need confirmatory randomized studies. Future research on low-dose atropine eyedrops needs to discover the mechanism of action as it is unknown, as well as the duration of treatment, best concentration, value of tapering, progression following cessation, and longer posttreatment monitoring.

ARE NEW LENS DESIGN SPECTACLES PROVEN TO AVOID MYOPIA PROGRESSION?

The development of new spectacle lens designs to control myopia has been impressive. The efficacy of highly aspherical lenslets (HAL) lenses in reducing myopia progression was tested in an RCT in China.[18,19] At 1 year, the myopia control efficacy of HAL lenses compared with single vision lenses (SVL) was observed (SE difference of 0.53

D; axial length difference of 0.23 mm).[19] At 2 years, the HAL lenses group continued to have less myopia progression and axial elongation (difference at 2 years = 0.80 D and 0.35 mm) compared with SVL.[18] During a 1-year extension, myopia progression in the HAL group was an additional 0.38 D compared with 0.56 D in the SVL group.[20] Of note in the HAL group, axial elongation in the second and third years was greater than in the first year.

A crossover RCT of HAL lenses in Vietnamese children found minimal benefit.[21] Although, there was slowing of axial elongation in Vietnamese children, the SE benefit from baseline to 6 months was not significant. Trials regarding HAL lenses have been short-term, and longer-term randomized trials with follow-up will be important to confirm the lens performance and overall impact on myopia progression. Crossover designs have been helpful for recruitment but significantly complicate interpretation of the value of a treatment by using short treatment intervals when longer intervals are needed and the absence of a placebo control group at the end of study treatment. Additionally, trials with children with varied race/ethnicities, age ranges, duration of treatment, and assessment of rebound effects over 6 or more months after stopping HAL lens are necessary to confirm effectiveness.

A trial of defocus incorporated multiple segment (DIMS) lenses in Chinese children has provided data after 6 years of intervention.[6] At 2 years, 79 children in the DIMS group and 81 in the SVL group had SE myopic progression of –0.41±0.06 D in the DIMS group and –0.85±0.08 D in the SVL group.[22] Children were then divided into 4 groups (group 1: DIMS for 6 years; group 2: DIMS for 3.5 years and SVL afterwards; group 3: SVL for 2 years and DIMS afterwards; group 4: SVL for 2 years, DIMS for 1.5 years, and SVL afterwards). Suggesting effectiveness was the observation that the DIMS lenses in children wearing the lenses for 6 years had slow myopia progression of −0.15 D/y and axial elongation of 0.10 mm/y, but there was no SVL group for the entire 6 years. Of some concern, SE refractions at year 6 were similar between the 4 groups (group 1: −3.96 D ± 1.42; group 2: −4.28 D ± 1.15; group 3: −3.92 D ± 1.18; and group 4: − 3.87 D ± 1.53); of concern, the SE was highest in group 2 that used DIMS for 3.5 of 6 years. SE at baseline was lower in groups 3 and 4, which may account for their lower final SE. During the final years of the study, most children were reaching their teenage years, so slowing myopia progression would be expected. Although all groups were on average below the threshold of high myopia (–5.00 D or –6.00 D), progression of myopia may still occur.

Further, uncertainty remains whether wearing anti–myopia progression spectacle designs will prevent the development of retinal complications associated with myopia, even when the lenses are started in preteen years. Regarding rebound when stopping DIMS, there was a clinically minor progression of approximately 0.22 D/y and 0.12 mm/y, which may be the expected continuation of myopia progression.

A trial of 2 diffusion optics technology (DOT) lens designs that reduce contrast signaling in the retina and thereby slow myopia progression, has provided 12-month results in children aged 6-10 years.[23] The CYPRESS trial was conducted at 14 sites in North America with 2 lens designs, finding that when compared with SVL, there was less SE progression (0.32 and 0.40 D, respectively) and less axial elongation (0.10 and 0.15 mm, respectively). These short-term results showed better efficacy in slowing SE progression than axial elongation. As with all lens design trials, longer-term results are needed as it is likely such lenses will be prescribed and used for many years in childhood and adolescence. Of note, many of the studies testing new lens design spectacles for myopia control are industry-sponsored and additional independent studies would be valuable to confirm effectiveness.

ARE SOFT CONTACT LENSES FOR MYOPIA CONTROL A SAFE AND PROVEN TREATMENT TO AVOID MYOPIA PROGRESSION?

New design contact lenses (CLs) using dual-focus and extended depth of focus designs are offered as refractive correction and simultaneously to slow myopia progression. Controversies have emerged regarding the safety and efficacy of such solutions. Safety of CL in children is an important consideration as CL use is not risk free. One report calculated that lifetime risk of microbial keratitis due to CL for myopia control beginning at age 8 years (estimated 1 in 76 with daily disposable wear) is much less than the risk of vision impairment due to complications from high myopia.[24] A review found that the incidence of microbial keratitis in children who wore CL was similar to adults, although the incidence of corneal infiltrates was lower.[25]

Regarding efficacy of myopia control CL, 2 studies found significant reductions in myopia and AL progression.[26,27] The CL with longest published evidence is the MiSight (CooperVision, San Ramon, CA), a daily disposable dual-focus CL approved by the US Food and Drug Administration (FDA) for myopia control.[27] MiSight contact lenses have demonstrated a significant reduction of myopia progression after 3 years.[28] Six-year results suggest that MiSight continued to slow myopia progression.[27] Of concern, analysis at 6 years was complicated by a high loss to follow-up and no control group in years 4-6. Both factors are an increasingly common problem in the interpretation of data from clinical trials of myopia control. Of note, 10% of eyes did not respond to treatment; a similar percentage of nonresponders has been reported with other myopia control treatments.

In the MiSight Assessment Study Spain (MASS), there have been concerns that children in the intervention group were older (approximately 1 year).[29] As younger children progress faster than older children, it may be that the difference in myopia progression was in part related to having more older children enrolled in the MiSight arm. To evaluate this possibility a multivariable analysis found that age was not a factor in the outcome. In addition, the authors found that children wearing MiSight spent more time outdoors, which possibly played a role in slowing axial elongation.[30] Previous research does not consistently support the role of outdoor time in slowing myopia progression, but rather a greater impact delaying myopia onset.

IS ORTHOKERATOLOGY AN ACCEPTED TREATMENT TO SLOW PROGRESSION OF MYOPIA?

Overnight orthokeratology is an FDA-approved intervention to allow good vision without need for glasses or CLs during the daytime. However, ortho-K lenses also have been proposed to reduce myopia progression.[31] The exact mechanism for slowing myopia progression is not known, but it may involve myopic defocus from steepening the more peripheral cornea slowing axial elongation.[32] A pooled analysis of 3 prospective studies showed a treatment effect of 0.24 mm (95% CIs: 0.15-0.34 mm) following wearing of ortho-K lenses for a 2-year period.[33] Risk of microbial keratitis is an important concern with overnight orthokeratology wear in children.

Although the risk has been reported to be similar to other CLs,[34] available studies have treatment durations of 1-2 years and do not provide sufficient long-term outcomes to establish a risk profile. In a systematic review of infectious keratitis and orthokeratology lens use, the authors found that despite the treatment, most of the infections resulted in corneal scars and approximately 10% of the eyes needed surgical treatment.[5] In Taiwanese children, the rates of contact lens–related microbial keratitis have increased over time because of an increased use of overnight orthokeratology.[35] Further research regarding safety and efficacy is necessary to support the widespread use of overnight orthokeratology for myopia control.

IS LOW-LEVEL RED LIGHT A SAFE AND PROVEN TREATMENT TO AVOID MYOPIA PROGRESSION?

Repeated low-level red light (RLRL) therapy has been used for amblyopia treatment in China. Recently, RLRL of 650 nm has been proposed as a myopia control treatment. RLRL therapy is hypothesized to increase retinal blood flow and possibly reduce scleral hypoxia. However, the mechanism for myopia control is unknown. An RCT published in 2022 showed that RLRL therapy slowed myopia progression after 1 year, with mean differences between control and intervention groups of 0.26 mm for axial elongation and –0.59 D for SE progression.[36] No adverse events were reported, which was reassuring although longer-term data are needed.

However, a retinal injury was reported in a 12-year-old girl after 5 months of treatment.[37] Her visual acuity partially recovered after 3 additional months. Two RCTs published in 2023 and 1 in 2024 did not document functional or structural damage.[7,38,39] RLRL therapy also has been reported to reduce incident myopia in children with premyopia by 54.1% within 12 months.[38]

In a meta-analysis of RLRL, the authors identified 13 studies (8 RCTs, 3 non-RCTs, and 2 cohort studies).[40] They concluded that the evidence of efficacy is of low certainty, and additional RCTs with longer follow-up are necessary. Unanswered questions include long-term safety for retinal structure and function, when used for years in myopia control, and whether late effects could occur in adulthood.[41] Further studies on different races/ethnicities, treatment protocols, monitoring requirements, incidence of injury, rate of recovery, and equipment maintenance are important to confirm safety and effectiveness.

IS TIME SPENT OUTDOORS UNRELATED TO MYOPIA PROGRESSION?

RCTs have shown that more time outdoors is an important strategy to slow the onset of myopia.[42] However, the effect of more outdoor time on myopia progression is uncertain, as research has provided conflicting results.[43] Many studies did not use objective measurements of time outdoors, relying on questionnaires that are prone to recall bias. The authors of an overview that included 7 systematic reviews found insufficient evidence to support the value of increasing outdoor time in slowing myopia progression.[44] However, the authors noted the studies were marred by poor methodology and inconsistent reporting.

In a large RCT of more than 6000 children in Shanghai, China, He and associates[45] found prescribing increased outdoor time to be modestly protective against myopic progression; however, neither of the increased outdoor time groups achieved their targets for time outdoors, highlighting the need for monitoring compliance with the intervention, as well as improved strategies to achieve increased outdoor time. In a multi-area, cluster-randomized intervention-controlled trial in Taiwan, the risk of rapid myopic progression was reduced by 54% in the intervention group.[46]

FIGURE 1. Top 6 priorities for research in myopia management.

Seasonal effects on myopia progression have been reported with decreases in axial elongation and myopia progression in summer,[47] suggesting that physiological eye growth may follow a seasonal pattern associated with daylight composition and intensity. Further research into the mechanisms and risk factors for myopia development and progression including time outdoors should be a priority of our community.

CONCLUSIONS

Integral to the search for effective control of progression of childhood myopia, analysis of nonresponders to myopia control therapies will be important. It is unknown whether nonresponders will be the adults with sight-threatening complications and if any therapy would have prevented development of those complications. Sharing deidentified, curated data from multiple trials could allow investigators to expand the study of risk factors for progression, successful and unsuccessful treatments, predictive factors for success and failure of treatments, develop new or modify current treatments, or even prescribe personalized treatment.

In the Figure 1, we depict 6 controversies and suggest that those should be priorities for research in myopia management. Shortcomings of current methods to treat myopia progression are evident and new and modified strategies need to be rigorously investigated to lessen the burden of myopia without prescribing ineffective and costly therapies. Current clinical pathways prioritize managing myopia with glasses, contact lenses, and refractive surgery but need to incorporate effective treatments to control myopia, especially for those patients at risk for high myopia. Discovering effective low-burden interventions, improving the interventions we have, and making all approaches widely available remains the goal to improve the public health.

Additional controversies that need further discussion and research include the optimal age and refractive state for starting treatment, the efficacy of combination therapies, and the role of prolonged near work on myopia progression. Identifying young children at high risk for early intervention is crucial, as research suggests that the younger the child, the faster myopia tends to progress, and the greater the likelihood of developing higher levels of myopia and risk for vision loss in adulthood.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Carla Lanca: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Michael X. Repka:** Writing – review & editing, Conceptualization. **Andrzej Grzybowski:** Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization.

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