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Review Article

Advances in optical and pharmacological strategies for myopia correction in children

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Abstract: Myopia in children has become a global public health concern due to its increasing prevalence and potential long-term complications. Optical interventions, including single-vision lenses (SVL), bifocal/progressive addition lenses (PALs), peripheral defocus-incorporated multiple segments (DIMS) glasses, and orthokeratology (OK) lenses have shown varying success in slowing progression, though long-term safety and efficacy remain under investigation. Pharmacological treatments, including low-dose atropine (0.01%), pirenzepine, apomorphine, and 7-methylxanthine (7-MX), offer additional options. Low-dose atropine is the most effective, significantly reducing myopia progression with minimal side effects. Pirenzepine, though promising in animal models, faces challenges due to poor corneal permeability. Apomorphine shows potential but requires further clinical testing. 7-MX has demonstrated dose-dependent effects in slowing progression, yet its efficacy needs validation in broader populations. Emerging therapies like low-level red-light therapy (LLRT) and Diffusion Optics Technology (DOT) lenses also show promise, reducing axial elongation and refractive progression. However, their long-term safety and mechanisms remain unclear. In conclusion, while several interventions show potential, further long-term studies and personalized treatment strategies are needed to optimize outcomes. Future research should focus on new drug targets, technologies, and global collaboration to address the myopia crisis in children.

Keywords: Children, myopia, myopia control

Introduction

Myopia, affecting millions of children and adults worldwide, not only diminishes quality of life but also imposes significant social and economic burdens. By 2050, it is projected that 4.758 billion people will be affected by myopia [1]. High myopia increases the risk of serious complications, including myopic macular disease, glaucoma, and cataracts [2]. In China, especially in urban areas, myopia has become a critical public health issue, affecting the eye health of children and adolescents [3]. As a result, myopia prevention and control have gained global attention and are now central to health strategies in various countries.

The development of myopia is influenced by both genetic and environmental factors [4], with urbanization, socioeconomic status, excessive near-work, and insufficient outdoor activity identified as key contributors [3]. Efforts to slow myopia progression have focused on environmental, optical, and pharmaceutical interventions. In recent years, to address the increasing global burden, research on myopia control has intensified worldwide [5, 6]. This article reviews current clinically proven and potential interventions from both optical and pharmaceutical perspectives.

Optical intervention scheme

Early optical interventions primarily examined the effects of refractive undercorrection on myopia progression [7]. However, a recent Cochrane review [8] concluded that there is insufficient evidence to support the use of refractive overcorrection, undercorrection, or micro-monocular vision in delaying myopia progression [9]. Similarly, the International Myopia Institute's white paper notes state that the effect of bifocal glasses and single-vision soft contact lenses on myopia control is similar to that of standard single-vision glasses [10].

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Progressive addition lenses (PALs)

PALs are currently one of the most widely researched interventions for myopia control. Their design gradually increases refractive power from the distance zone at the top of the lens to the near zone at the bottom. PALs reduce the need for accommodation or accommodation lag during close-up tasks. Leung [11] first proposed using PALs, instead of bifocals, to slow myopia progression by minimizing accommodation demands. Their results showed that myopia progression in children using +1.50 and +2.00 D PALs was significantly slower than with single-vision lenses (SVL). However, this study lacked full randomization. Subsequent RCTs conducted in the U.S., Hong Kong, and Japan [12-14] found that while PALs can reduce refractive error progression, the difference from SVL was often less than 0.25 D, which is generally considered clinically insignificant for myopia control. A 2022 study by Zhu et al., based on Chinese children with myopia, also showed that PALs did not significantly improve accommodation lag or accommodative heterophoria to slow myopia progression [15]. Additionally, Li et al. [16] found better myopia control in Asian children compared to white and black children, possibly due to more pronounced accommodation lag and greater close-up eye use in Asian children.

Optical interventions like under-refraction, bifocal glasses, and PALs, aimed at reducing accommodation demand and improving accommodative lag, have not shown significant effects on myopia progression. However, studies have found that PALs improve peripheral retinal defocus in myopic children [17-19]. Further research has demonstrated that myopic peripheral defocus reduces axial length growth, while hyperopic defocus promotes axial elongation [20-22]. Consequently, the focus of optical interventions is shifting toward manipulating peripheral retinal defocus, with myopic defocus now considered the primary strategy. A variety of frame glasses designed based on this principle have emerged.

Defocus incorporated multiple segments (DIMS)

The DIMS lens features a central far-corrected optical zone with a 9 mm diameter, surrounded by numerous micro-lenses (approx. 1.03 mm in diameter) that generate myopic defocus with a refractive power of +3.50 D. Lam et al. [23] reported that children wearing DIMS lenses showed a 52% reduction in myopia progression and a 62% reduction in axial growth compared to those wearing SVL. Notably, 21.5% of children wearing DIMS lenses experienced no significant progression over two years, compared to only 7.4% in the SVL group. When the control group switched from SVL to DIMS, myopia progression was significantly reduced, reaching similar levels as the initial DIMS group after one additional year [24]. However, a significant age difference between the two groups could confound the axial length comparison. A retrospective study of 3,639 children wearing DIMS and 6,838 wearing SVL found that after one year, myopia progression in the DIMS and SVL groups was both limited to $\leq$ 0.25 D in 40% and 19% of children, respectively. After two years, 33% and 20% of children in the DIMS and SVL groups, respectively, had a progression of $\leq$ 0.50 D [25]. While the results were somewhat lower than previous RCTs, this large-scale, diverse dataset provides robust evidence supporting DIMS' effectiveness in clinical myopia control.

Slightly/highly aspherical lenslets (SAL/HAL)

SAL and HAL lenses feature peripheral aspherical microlenses that continuously refract light non-linearly, producing myopic defocus (VoMD) in front of the retina. Bao et al. [26, 27] conducted a two-year study on 170 Chinese children with myopia, showing that myopia progression was significantly reduced in those wearing SAL or HAL, with HAL demonstrating superior efficacy. HAL controlled 41% of myopic refractive progression and 64% of axial growth compared to SVL. A 2023 randomized double-blind crossover trial [28] further confirmed HAL's effectiveness in controlling myopia progression, without rebound effects upon switching to SVL. However, the long-term efficacy and safety of HAL still require additional trials and extended follow-up.

Although frame glasses designed around the peripheral retinal defocus theory have been shown to slow myopia progression, their effectiveness varies widely (20% to 80%) across studies [29]. This variation may be linked to peripheral or off-axis gaze, as the distance between the lens and cornea, along with mis-

Table 1. Comparison of the efficacy of optical intervention methods for controlling myopia progression

Type	Design	Effect (slowing down the progression of myopia)	Axial growth reduction	Others
PALs	Progressive multifocal design	Decreased progression of myopia	-	No significant difference compared to SVL
DIMS	Central vision correction	52%	62%	Long-term effects are stable
SAL	Non-spherical lens design	Decreased progression of myopia	-	Safety requires further verification
HAL	Non-spherical lens design	41%	64%	Efficacy superior to SAL, safety requires further verification

PAL: Progressive Addition Spectacle lenses; DIMS: Defocus Incorporated Multiple Segments; SAL: Slightly Aspherical Lenslets; HAL: Highly Aspherical Lenslets.

alignment between the lens optical axis and the visual axis, can be influenced by eye movement, reducing the peripheral myopic defocus and weakening the effect. The need for individualized adaptation and more rigorous studies to confirm the effectiveness of these lenses is clear. In contrast, contact lenses, which fit more closely to the cornea and move synchronously with eye movement, may offer better myopia control than frame glasses.

The efficacy of various optical interventions for myopia progression control is summarized in **Table 1**.

Corneal contact lens

Dual-focus soft contact lenses (DFSCL)

Bifocal soft contact lenses are designed with either concentric or peripheral bifocal patterns. Research indicates that after 24 months of wearing these lenses, myopia progression is slowed by 30-38%, and axial growth is reduced by 31-51%. Concentric bifocal lenses are approximately 30-50% more effective than peripheral bifocal lenses in controlling myopia progression [30, 31]. A study on Misight concentric bifocal lenses confirmed these results. Children wearing these lenses for three years experienced a 59% reduction in refractive error (0.73 D) and a 56% reduction in axial growth (0.32 mm) compared to the control group (SVL) [32]. Furthermore, no significant change in corneal anterior surface aberration or total ocular aberration was observed in the children wearing concentric bifocal lenses. In contrast, these aberrations increased in children wearing SVL as myopia progressed [33].

A one-year study by Aller et al. [34] involving 79 children (aged 8-18) explored personalized treatments to minimize near eso-fixation disparity while ensuring clear vision. Children wearing concentric bifocal lenses showed a 72% reduction in refractive power growth and an 80% reduction in axial growth compared to those wearing single-vision soft contact lenses. This study highlights the clinical potential of concentric bifocal lenses and emphasizes the importance of personalized fitting for myopia control, tailored to individual eye parameters and lifestyle habits.

Multifocal soft contact lenses

Multifocal soft contact lenses feature a progressive increase in refractive power in the peripheral defocus zone outside the central area. A study showed that after one year of wearing multifocal lenses, refractive power increase was reduced by 34% (-0.57 D vs. -0.86 D in the control group), and axial length increase was reduced by 33% 0.27 mm vs. 0.40 mm [35]. Walline et al. [36] found similar results, with multifocal lenses reducing myopia progression by 50% and axial growth by 29% over two years.

The gradual increase in refractive power in the peripheral zone enhances peripheral myopic defocus, significantly inhibiting the growth of refractive power and axial length over the long term. This is particularly beneficial in controlling high myopia [37, 38].

Compared to traditional frame glasses, soft corneal contact lenses offer a more aesthetically appealing option, leading to higher compliance rates among myopic children. Additionally, daily disposable soft corneal contact lenses, in contrast to reusable hard lenses, significantly reduce the risk of corneal infiltration, highlighting their clinical potential for slowing myopia

Table 2. Comparison of the efficacy of contact lenses for controlling myopia progression

Type	Design	Time	Effect (slowing down the progression of myopia)	Axial growth reduction	Others
DFSCL	Concentric bifocal design	24 months	30-38%	31-51%	The anterior surface aberration and total ocular aberration do not increase with the progression of myopia.
	Peripheral bifocal design	24 months			The effect is inferior to concentric bifocal 30-50%.
Multifocal Soft Contact Lenses	Progressive Multifocal Design	24 months	50%	29%	The refractive power in the peripheral region increases, leading to peripheral myopic defocus on the retina.
OK	Hard design	24 months	50%	41-45%	Nighttime wear, with clear vision during the day after removal.

DFSCL: Dual-Focus Soft Contact Lenses; OK: Orthokeratology.

progression in children and adolescents [39-41].

Orthokeratology (OK) lenses

OK lenses are rigid contact lenses worn overnight, providing clear vision during the day after removal. The myopia control effect of OK lenses is attributed to peripheral retinal myopic defocus induced by corneal epithelial cell migration [42].

A two-year prospective study by Cho et al. [43] in 2005, involving 35 myopic children aged 7-12, showed that axial growth in the OK lens group was 0.23 mm, compared to 0.48 mm in the control group, representing a 50% reduction in myopia progression. Subsequent global studies consistently confirmed the effectiveness of OK lenses in controlling myopia compared to SVL [42, 44, 45]. Recent meta-analyses report a 41-45% reduction in myopia progression with OK lenses [46], further validating their efficacy.

Hiraoka et al. [47] showed that OK lenses effectively slow axial growth over five years. During this period, the eye axis increased by 0.99 mm in the OK lens group and 1.41 mm in the control group. The treatment effect was greatest in the first year, with the reduction in axial growth decreasing from 50% in year one to 30% by year five. This suggests that while OK lenses offer long-term benefits, their efficacy may plateau with extended use.

Concerns have been raised about the potential for regression or rebound effects after discontinuing OK lenses. Cho et al. [48] found that after two years of OK lens use followed by six months without lenses, the axial length growth in children was significantly faster than in those who continued wearing them, resembling the growth rate of the control group. Unlike atropine, the discontinuation of OK lenses did not lead to accelerated myopia progression [49].

OK lenses are widely used in clinical practice to slow myopia progression, particularly in children with low to moderate myopia. Recently, their use has expanded to include patients with anisometropia, hyperopia, high astigmatism, or those who have undergone refractive corneal surgery. However, eye development and corneal morphology vary significantly among myopic children. Studies show that older children, those with larger baseline spherical equivalents, and those with larger pupil diameters experience less axial elongation and myopia progression when using OK lenses. Thus, personalized fitting is essential for optimal outcomes [50-52].

Despite their benefits, OK lenses carry risks, such as corneal abrasion and infection, mainly due to fitting difficulties and night-time wear. Given variations in personal hygiene, parental education, and adherence to care instructions, standardized testing, fitting, and monitoring are crucial for ensuring safe and effective use [53]. The efficacy and characteristics of different types of contact lenses for controlling myopia progression are summarized in **Table 2**.

Medications

Atropine

Atropine is a non-selective muscarinic (M) receptor antagonist with high affinity for M1-M5

receptors in the pupillary sphincter and ciliary muscle, causing pupil dilation and ciliary muscle paralysis. Since the 1970s, extensive research has been conducted to explore atropine's effects on myopia progression. Clinical trials have consistently shown that atropine eye drops can effectively slow myopia progression in children, with success rates ranging from 56% to 96% [54]. A study by the American Academy of Ophthalmology found that atropine treatment could reduce myopia progression by approximately 1 D per year [55]. The effect of atropine in controlling myopia is concentration-dependent. Common side effects of high-concentration atropine include photophobia, blurred vision, and reduced accommodation amplitude due to its mydriatic and cycloplegic effects. Long-term side effects may include early presbyopia and potential lens or retinal phototoxicity [56].

The Atropine for the Treatment of Myopia 1 study [57] observed a rebound effect after discontinuing atropine, with significant acceleration in myopia progression following one year of withdrawal from 1% atropine treatment (atropine group: -1.14±0.80 D, placebo group: -0.38±0.39 D). The Atropine for the Treatment of Myopia 1 study [58] further evaluated atropine concentrations of 0.1%, 0.5%, and 0.01% for myopia control. Results indicated that 0.01% atropine effectively controlled myopia with minimal side effects and a small rebound effect after discontinuation [59]. Some studies have suggested that 0.05% atropine, which has similar side effects and rebound characteristics to 0.01%, is more effective in controlling myopia progression [60-62].

While atropine's use in myopia control is promising, further evidence-based research is needed to establish optimal concentration, frequency, duration, and the impact of individual differences on efficacy. Additionally, more studies are required to understand the rebound mechanisms and to optimize treatment strategies for different age groups of myopic children.

Pirenzepine

Pirenzepine is a selective M receptor antagonist, with high affinity for M1 and M4 receptors. Unlike atropine, which is non-selective, pirenzepine does not cause cycloplegia or mydriasis, making it a safer alternative. Animal studies have shown that pirenzepine effectively reduces form deprivation myopia and axial length growth [63]. A 2008 randomized clinical trial on children aged 8-12 years using 2% pirenzepine gel twice daily demonstrated that it effectively reduced refractive error progression, though no significant effect was observed on axial growth. Moreover, pirenzepine solution did not cause systemic side effects in adult volunteers and was found to be safe and well-tolerated [64]. However, as a hydrophilic compound, pirenzepine has very low corneal permeability and ocular bioavailability, limiting its effectiveness in inhibiting myopia [65]. Consequently, pirenzepine eye drops are not currently used as a clinical treatment for myopia.

Apomorphine

In animal experiments, dopamine receptor agonists and acetylcholine receptor antagonists are used to induce axial growth, thereby establishing a myopic model. These findings suggest that both the dopamine and cholinergic systems contribute to the development of myopia. However, acetylcholine receptor antagonists have several adverse reactions [66, 67], limiting their clinical application, whereas dopamine receptor agonists show promise in myopia treatment [68, 69]. Apomorphine, a non-selective dopamine receptor agonist, has been studied in this context. Dong et al. [70] found that apomorphine effectively inhibits the development of form deprivation myopia in animal models, though it does not affect defocus myopia. Despite its potential, there are few studies on apomorphine, and further research is needed to assess its feasibility, safety, and clinical indications for treating myopia.

7-MX

7-MX, a metabolite of caffeine, is a non-selective antagonist of adenosine receptors. Research has shown that oral administration of 7-MX reduces myopia progression in guinea pigs by approximately 50%, eliminating axial growth induced by form deprivation, and preventing scleral changes such as scleral thinning and collagen fiber degradation in the posterior sclera [71]. In primates, 7-MX also reduces axial myopia caused by hyperopic defocus [72]. A clinical trial conducted in Denmark in 2003 [73] found that myopic children treated with

Table 3. Comparison of the efficacy of pharmacological interventions for controlling myopia progression

Medicine	Type	Effect (slowing down the progression of myopia)	Side effect	Others
Atropine	Non-selective M receptor antagonist	56-96%	Photophobia, blurred vision, and decreased accommodative amplitude (with high concentration)	Concentration-dependent, 0.05% shows significant efficacy with minimal side effects
Pirenzepine	Selective M receptor antagonist	Effectively reduces refractive power but does not reduce axial eye growth	No significant side effects	Low corneal permeability, not suitable for clinical treatment
Apomorphine	Non-selective dopamine receptor agonist	Inhibits the development of form-deprivation myopia	Safety requires further verification	Limited research, primarily used in animal studies
7-MX	Non-selective antagonist of adenosine receptors	50%	No significant side effects	Dose-dependent, studies conducted only in Denmark

7-MX: 7-Methylxanthine.

oral 7-MX showed a reduction in axial growth compared to the control group over a 12-month period (0.35±0.15 mm for the experimental group vs. 0.38±0.17 mm for the placebo group), although the difference was not statistically significant (P=0.567). A more recent real-world study [74] analyzed data from 711 Danish myopic children who received oral 7-MX (0-1200 mg per day). The study concluded that oral 7-MX slowed myopia progression and axial growth in a dose-dependent manner, with the highest dose (1200 mg per day) showing the most effective control. However, all current human trials of oral 7-MX have been conducted in Denmark. The efficacy of 7-MX in controlling myopia progression requires further validation through experimental studies from other countries and randomized controlled trials. The efficacy and side effects of different pharmacological interventions for controlling myopia progression are summarized in **Table 3**.

Optical and pharmaceutical intervention programs

Low-level red-light therapy (LLRT)

Since 2021, there have been reports on the effect of low-intensity red light therapy (LLRT) in slowing myopia progression. A retrospective study by Zhou et al. [75] demonstrated that after nine months of LLRT treatment (twice daily for 3 minutes at 0.4 mW power and 635 nm wavelength), the axial length change in the LLRT group (-0.06±0.19 mm) was significantly smaller than in the control group wearing SVL (0.26±0.15 mm). A randomized controlled trial by Jiang et al. [76] confirmed this result, showing a reduction of 0.26 mm in axial growth and 0.59 D in refractive progression in the LLRT group compared to the SVL group, with no serious adverse events. Dong et al. [77] found that 100% power LLRT significantly reduced myopia progression over 6 months when compared to a 10% power pseudo-treatment device. Some studies suggest that LLRT may be safer and more acceptable than orthokeratology [78].

Despite the significant effect of LLRT compared to other optical or pharmaceutical interventions, there are several unexplained phenomena in the reported studies [79]. For instance, most eyes show axial regression in the early stages (within the first month) [80], accompanied by a corresponding refractive shift (hyperopic shift). Additionally, choroidal thickening occurs in the macular region, whereas the choroid thins in the control group. However, the mechanism behind axial regression remains unclear and cannot be fully explained by choroidal thickening alone. The safety of LLRT also remains uncertain, especially regarding potential retinal light damage in the macular region. Moreover, it is unclear whether regression or rebound will occur after treatment cessation. These aspects require further investigation through sensitive objective tests and long-term follow-up studies to confirm the safety and long-term efficacy of LLRT.

Diffusion optics technology (DOT)

Since 2022, DOT lenses have been reported to slow myopia progression by reducing retinal contrast signals [81, 82]. The Cypress study [82] was a 3-year, multi-center RCT involving

Table 4. Comparison of the efficacy of emerging optical and pharmacological interventions

Method	Effect (slowing down the progression of myopia)	Side effect	Others
LLRT	Reduction in axial growth and refractive progression	Safety requires further verification	Early axial regression of the eye and increased thickness of the macular choroid
DOT	Reduction in axial growth and refractive progression	Safe for children aged 6 years and older	Reduction in retinal contrast signals
Vitamin D	Myopia severity decreases as vitamin D levels decrease	Safety requires further verification	Associated with outdoor activities, the relationship with myopia development requires further research

LLRT: Low-Level Red-Light Therapy; DOT: Diffusion optics technology.

256 myopic children aged 6-10 years from 14 clinical centers across North America. After 12 months of wearing DOT lenses, the equivalent spherical lens growth in the treatment group decreased by -0.40 D (74%) and axial growth by 0.15 mm. Participants in the DOT group showed good distance/near vision, with no significant difference from the control group. This study demonstrated that DOT lenses can effectively slow myopia progression and axial elongation, and are safe, effective, and well-tolerated in children aged 6 and older. DOT lenses, which modify both peripheral retinal defocus and retinal contrast, offer a promising new intervention for myopia. They suggest that previous optical interventions may have combined effects, involving both retinal contrast signal reduction and myopic defocus.

Vitamin D

In recent years, the role of vitamin D in the onset and progression of myopia has gained significant attention. A 2020 study by Jung et al. [83] found that for every 1 ng/ml decrease in serum vitamin D, the degree of myopia increased by 0.01 D. In 2023, Wolf et al. [84] reported that the serum vitamin D level in myopic individuals was lower than in those with normal vision. However, current epidemiological studies have not reached a consensus on whether vitamin D directly influences myopia development. Research has shown that the duration of outdoor activity is closely associated with myopia, with vitamin D serving as a covariate rather than an independent factor in myopia control [85-87]. Consequently, further prospective studies and randomized controlled trials are needed to determine whether vitamin D acts as an independent protective factor for myopia or if its role is secondary to outdoor activities. The efficacy, potential advantages, and limitations of emerging optical and pharmacological interventions are summarized in **Table 4**.

Summary

The correction of myopia and the prevention and control of its progression have become a focal point of both clinical practice and societal concern. This article reviews various optical and pharmacological interventions for controlling clinical myopia progression in children, alongside the advancements in myopia prevention and control methods. Although numerous strategies exist for managing myopia in children, practical challenges persist in their application. As our understanding of myopia's underlying mechanisms deepens and new technologies emerge, personalized optical designs are likely to be a key direction. By integrating biometric parameters such as refractive error, axial length, and corneal curvature, more precise and customized correction plans can be developed. This approach promises to enhance intervention efficacy while minimizing adverse effects. The development of novel optical materials, such as lightweight, highly oxygen-permeable, and blue light-blocking lenses, will further optimize comfort and image quality. These innovations can also reduce peripheral hyperopic defocus, potentially offering better inhibition of myopia progression. Long-term safety and efficacy evaluations remain essential research priorities, with large-scale, multi-center randomized controlled trials needed to provide robust evidence on the safety and effectiveness of optical interventions.

In pharmacological intervention, low-concentration atropine (e.g., 0.05%) has emerged as

one of the most effective treatments, significantly slowing myopia progression while minimizing side effects. Future research will likely focus on further lowering doses or exploring new drug delivery methods to enhance the safety and tolerability of atropine. Additionally, personalized treatment protocols for children of different age groups and varying myopia progression rates will be critical for future development. Beyond M receptors and dopamine receptors, future studies will seek to identify additional molecular targets involved in myopia's onset and progression, aiming to develop drugs with higher selectivity and specificity. Research into potential drug targets, such as adenosine receptor antagonists and vitamin D, may provide new avenues for myopia control. Furthermore, advanced therapies like gene and cell therapy hold promise for future applications in myopia prevention and treatment.

The combined use of pharmacological and optical interventions is likely to be a significant trend. For instance, combining low-concentration atropine with orthokeratology lenses or peripheral defocus spectacles may produce more pronounced effects in slowing myopia progression. Combination therapies can also mitigate the limitations of single interventions, reduce adverse reactions, and enhance patient compliance. Ultimately, a comprehensive prevention and control system, incorporating the promotion of outdoor activities, the development of healthy eye usage habits, dietary adjustments, and other non-pharmacological interventions, will be crucial in shaping a multifaceted approach to myopia prevention in the future.

Disclosure of conflict of interest

None.

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References

[1] Chen H, Liu X, Zhou X, Fu J and Wang L. Advancements in myopic macular foveoschisis research. Ophthalmic Res 2024; 67: 424-434.

[2] Arrigo A, Aragona E, Bianco L, Antropoli A, Saladino A, Bandello F and Battaglia Parodi M. The clinical role of the choroidal assessment in high myopia: characteristics and association with neovascular and atrophic complications. Invest Ophthalmol Vis Sci 2023; 64: 16.

[3] Zhu Z, Chen Y, Tan Z, Xiong R, McGuinness MB and Müller A. Interventions recommended for myopia prevention and control among children and adolescents in China: a systematic review. Br J Ophthalmol 2023; 107: 160-166.

[4] Wang YM, Lu SY, Zhang XJ, Chen LJ, Pang CP and Yam JC. Myopia genetics and heredity. Children (Basel) 2022; 9: 382.

[5] Tariq F, Mobeen R, Wang X, Lin X, Bao Q, Liu J and Gao H. Advances in myopia prevention strategies for school-aged children: a comprehensive review. Front Public Health 2023; 11: 1226438.

[6] He X, Wang J, Zhu Z, Xiang K, Zhang X, Zhang B, Chen J, Yang J, Du L, Niu C, Leng M, Huang J, Liu K, Zou H, He M and Xu X. Effect of repeated low-level red light on myopia prevention among children in China with premyopia: a Randomized clinical trial. JAMA Netw Open 2023; 6: e239612.

[7] Logan NS and Bullimore MA. Optical interventions for myopia control. Eye (Lond) 2024; 38: 455-463.

[8] Lawrenson JG, Shah R, Huntjens B, Downie LE, Virgili G, Dhakal R, Verkicharla PK, Li D, Mavi S, Kernohan A, Li T and Walline JJ. Interventions for myopia control in children: a living systematic review and network meta-analysis. Cochrane Database Syst Rev 2023; 2: CD014758.

[9] Logan NS and Wolffsohn JS. Role of un-correction, under-correction and over-correction of myopia as a strategy for slowing myopic progression. Clin Exp Optom 2020; 103: 133-137.

[10] Jonas JB, Ang M, Cho P, Guggenheim JA, He MG, Jong M, Logan NS, Liu M, Morgan I, Ohno-Matsui K, Pärssinen O, Resnikoff S, Sankaridurg P, Saw SM, Smith EL 3rd, Tan DTH, Walline JJ, Wildsoet CF, Wu PC, Zhu X and Wolffsohn JS. IMI prevention of myopia and its progression. Invest Ophthalmol Vis Sci 2021; 62: 6.

[11] Leung JT and Brown B. Progression of myopia in Hong Kong Chinese schoolchildren is slowed by wearing progressive lenses. Optom Vis Sci 1999; 76: 346-354.

[12] Yang Z, Lan W, Ge J, Liu W, Chen X, Chen L and Yu M. The effectiveness of progressive addition lenses on the progression of myopia in Chinese children. Ophthalmic Physiol Opt 2009; 29: 41-48.

[13] Gwiazda J, Hyman L, Hussein M, Everett D, Norton TT, Kurtz D, Leske MC, Manny R, Marsh-Tootle W and Scheiman M. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. Invest Ophthalmol Vis Sci 2003; 44: 1492-1500.

[14] Hasebe S, Ohtsuki H, Nonaka T, Nakatsuka C, Miyata M, Hamasaki I and Kimura S. Effect of progressive addition lenses on myopia progression in Japanese children: a prospective, randomized, double-masked, crossover trial. Invest Ophthalmol Vis Sci 2008; 49: 2781-2789.
[15] Zhu X, Wang D, Li N and Zhao F. Effects of customized progressive addition lenses vs. single vision lenses on myopia progression in children with esophoria: a randomized clinical trial. J Ophthalmol 2022; 2022: 9972761.
[16] Li SM, Ji YZ, Wu SS, Zhan SY, Wang B, Liu LR, Li SY, Wang NL and Wang JJ. Multifocal versus single vision lenses intervention to slow progression of myopia in school-age children: a meta-analysis. Surv Ophthalmol 2011; 56: 451-460.
[17] Varnas SR, Kaphle D, Schmid KL, Suheimat M and Atchison DA. Effect of multifocal spectacle lenses on accommodative errors over time: possible implications for myopia control. J Vis 2023; 23: 3.
[18] Smith SL, Maldonado-Codina C, Morgan PB and Read ML. Gaze and behavioural metrics in the refractive correction of presbyopia. Ophthalmic Physiol Opt 2024; 44: 774-786.
[19] Legras R, Vincent M and Marin G. Does visual acuity predict visual preference in progressive addition lenses? J Optom 2023; 16: 91-99.
[20] Lam CSY, Tang WC, Zhang HY, Lee PH, Tse DYY, Qi H, Vlasak N and To CH. Long-term myopia control effect and safety in children wearing DIMS spectacle lenses for 6 years. Sci Rep 2023; 13: 5475.
[21] Graff B, Lam CSY, Vlasak N and Kaymak H. Age-matched analysis of axial length growth in myopic children wearing defocus incorporated multiple segments spectacle lenses. Br J Ophthalmol 2024; 108: 1060-1066.
[22] Agyekum S, Chan PP, Adjei PE, Zhang Y, Huo Z, Yip BHK, Ip P, Wong ICK, Zhang W, Tham CC, Chen LJ, Zhang XJ, Pang CP and Yam JC. Cost-effectiveness analysis of myopia progression interventions in children. JAMA Netw Open 2023; 6: e2340986.
[23] Lam CSY, Tang WC, Tse DY, Lee RPK, Chun RKM, Hasegawa K, Qi H, Hatanaka T and To CH. Defocus incorporated multiple segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol 2020; 104: 363-368.
[24] Lam CS, Tang WC, Lee PH, Zhang HY, Qi H, Hasegawa K and To CH. Myopia control effect of defocus incorporated multiple segments (DIMS) spectacle lens in Chinese children: results of a 3-year follow-up study. Br J Ophthalmol 2022; 106: 1110-1114.
[25] Liu J, Lu Y, Huang D, Yang J, Fan C, Chen C, Li J, Wang Q, Li S, Jiang B, Jiang H, Li X, Yang Z and Lan W. The efficacy of defocus incorporated multiple segments lenses in slowing myopia progression: results from diverse clinical circumstances. Ophthalmology 2023; 130: 542-550.
[26] Bao J, Huang Y, Li X, Yang A, Zhou F, Wu J, Wang C, Li Y, Lim EW, Spiegel DP, Drobe B and Chen H. Spectacle lenses with aspherical lenslets for myopia control vs single-vision spectacle lenses: a randomized clinical trial. JAMA Ophthalmol 2022; 140: 472-478.
[27] Bao J, Yang A, Huang Y, Li X, Pan Y, Ding C, Lim EW, Zheng J, Spiegel DP, Drobe B, Lu F and Chen H. One-year myopia control efficacy of spectacle lenses with aspherical lenslets. Br J Ophthalmol 2022; 106: 1171-1176.
[28] Sankaridurg P, Weng R, Tran H, Spiegel DP, Drobe B, Ha T, Tran YH and Naduvilath T. Spectacle lenses with highly aspherical lenslets for slowing myopia: a randomized, double-blind, cross-over clinical trial: parts of these data were presented as a poster at the annual research in vision and ophthalmology meeting, 2022. Am J Ophthalmol 2023; 247: 18-24.
[29] Sankaridurg P, Conrad F, Tran H and Zhu J. Controlling progression of myopia: optical and pharmaceutical strategies. Asia Pac J Ophthalmol (Phila) 2018; 7: 405-414.
[30] Sankaridurg P, Bakaraju RC, Naduvilath T, Chen X, Weng R, Tilia D, Xu P, Li W, Conrad F, Smith EL 3rd and Ehrmann K. Myopia control with novel central and peripheral plus contact lenses and extended depth of focus contact lenses: 2 year results from a randomised clinical trial. Ophthalmic Physiol Opt 2019; 39: 294-307.
[31] Li SM, Kang MT, Wu SS, Meng B, Sun YY, Wei SF, Liu L, Peng X, Chen Z, Zhang F and Wang N. Studies using concentric ring bifocal and peripheral add multifocal contact lenses to slow myopia progression in school-aged children: a meta-analysis. Ophthalmic Physiol Opt 2017; 37: 51-59.
[32] Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D and Young G. A 3-year randomized clinical trial of MiSight lenses for myopia control. Optom Vis Sci 2019; 96: 556-567.
[33] Lopes-Ferreira D, Ruiz-Pomeda A, Perez-Sanchez B, Queiros A and Villa-Collar C. Ocular and corneal aberrations changes in controlled randomized clinical trial MiSight(R) assessment study spain (MASS). BMC Ophthalmol 2021; 21: 112.
[34] Aller TA, Liu M and Wildsoet CF. Myopia control with bifocal contact lenses: a randomized clinical trial. Optom Vis Sci 2016; 93: 344-352.

[35] Sankaridurg P, Holden B, Smith E 3rd, Naduvilath T, Chen X, de la Jara PL, Martinez A, Kwan J, Ho A, Frick K and Ge J. Decrease in rate of myopia progression with a contact lens designed to reduce relative peripheral hyperopia: one-year results. Invest Ophthalmol Vis Sci 2011; 52: 9362-9367.
[36] Walline JJ, Greiner KL, McVey ME and Jones-Jordan LA. Multifocal contact lens myopia control. Optom Vis Sci 2013; 90: 1207-1214.
[37] Peng T and Jiang J. Efficiency and related factors of multifocal soft contact lenses in controlling myopia. Eye Contact Lens 2023; 49: 535-541.
[38] Nti AN, Gregory HR, Ritchey ER, Wolffsohn JS and Berntsen DA. Contrast sensitivity with center-distance multifocal soft contact lenses. Optom Vis Sci 2022; 99: 342-349.
[39] Ono T, Kaida T, Higashi S, Mori Y, Nejima R, Iwasaki T, Kagaya F, Miyai T and Miyata K. Corneal endothelial density and morphology in long-term soft contact lens users in Japan: a retrospective cross-sectional study of 17,732 eyes. Cutan Ocul Toxicol 2024; 43: 335-340.
[40] Kim YH, Lin MC, Peng CC and Radke CJ. Prevention of localized corneal hyperosmolarity spikes by soft-contact-lens wear. Cont Lens Anterior Eye 2022; 45: 101722.
[41] Fu L, Jiang Y, Lian H, Lou J, Chen R, Li Z and Zhang Y. The corneal biomechanical differences after wearing orthokeratology lenses and multifocal soft lenses in children: a self-control study. Cont Lens Anterior Eye 2024; 47: 102089.
[42] Hiraoka T. Myopia control with orthokeratology: a review. Eye Contact Lens 2022; 48: 100-104.
[43] Cho P, Cheung SW and Edwards M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopic control. Curr Eye Res 2005; 30: 71-80.
[44] Swarbrick HA, Alharbi A, Watt K, Lum E and Kang P. Myopia control during orthokeratology lens wear in children using a novel study design. Ophthalmology 2015; 122: 620-630.
[45] Nakamura Y, Hieda O, Yokota I, Teramukai S, Sotozono C and Kinoshita S. Comparison of myopia progression between children wearing three types of orthokeratology lenses and children wearing single-vision spectacles. Jpn J Ophthalmol 2021; 65: 632-643.
[46] Si JK, Tang K, Bi HS, Guo DD, Guo JG and Wang XR. Orthokeratology for myopia control: a meta-analysis. Optom Vis Sci 2015; 92: 252-257.
[47] Hiraoka T, Kakita T, Okamoto F, Takahashi H and Oshika T. Long-term effect of overnight orthokeratology on axial length elongation in childhood myopia: a 5-year follow-up study. Invest Ophthalmol Vis Sci 2012; 53: 3913-3919.
[48] Cho P and Cheung SW. Discontinuation of orthokeratology on eyeball elongation (DOEE). Cont Lens Anterior Eye 2017; 40: 82-87.
[49] Bullimore MA and Johnson LA. Overnight orthokeratology. Cont Lens Anterior Eye 2020; 43: 322-332.
[50] Sarkar S, Khuu S and Kang P. A systematic review and meta-analysis of the efficacy of different optical interventions on the control of myopia in children. Acta Ophthalmol 2024; 102: e229-e244.
[51] Qin G, Chao C, Lattery LJ, Lin H, Fu W, Richdale K and Cai C. Tear proteomic analysis of young glasses, orthokeratology, and soft contact lens wearers. J Proteomics 2023; 270: 104738.
[52] Lattery LJ, Chao C, Walline JJ, Bullimore MA, Ritchey ER, Skidmore K and Richdale K. Patient and parent perceptions of myopia modalities. Cont Lens Anterior Eye 2023; 46: 101772.
[53] Wu TY, Yeh LK, Su CY, Huang PH, Lai CC and Fang HW. The effect of polysaccharides on preventing proteins and cholesterol from being adsorbed on the surface of orthokeratology lenses. Polymers (Basel) 2022; 14: 4542.
[54] Kang P. Optical and pharmacological strategies of myopia control. Clin Exp Optom 2018; 101: 321-332.
[55] Pineles SL, Kraker RT, VanderVeen DK, Hutchinson AK, Galvin JA, Wilson LB and Lambert SR. Atropine for the prevention of myopia progression in children: a report by the american academy of ophthalmology. Ophthalmology 2017; 124: 1857-1866.
[56] Song YY, Wang H, Wang BS, Qi H, Rong ZX and Chen HZ. Atropine in ameliorating the progression of myopia in children with mild to moderate myopia: a meta-analysis of controlled clinical trials. J Ocul Pharmacol Ther 2011; 27: 361-368.
[57] Tong L, Huang XL, Koh AL, Zhang X, Tan DT and Chua WH. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. Ophthalmology 2009; 116: 572-579.
[58] Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A and Tan D. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology 2012; 119: 347-54.
[59] Chia A, Chua WH, Wen L, Fong A, Goon YY and Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5. Am J Ophthalmol 2014; 157: 451-457, e451.

[60] Yam JC, Li FF, Zhang X, Tang SM, Yip BHK, Kam KW, Ko ST, Young AL, Tham CC, Chen LJ and Pang CP. Two-year clinical trial of the low-concentration atropine for myopia progression (LAMP) study: phase 2 report. Ophthalmology 2020; 127: 910-919.
[61] Yam JC, Zhang XJ, Zhang Y, Wang YM, Tang SM, Li FF, Kam KW, Ko ST, Yip BHK, Young AL, Tham CC, Chen LJ and Pang CP. Three-year clinical trial of low-concentration atropine for myopia progression (LAMP) study: continued versus washout: phase 3 report. Ophthalmology 2022; 129: 308-321.
[62] Li FF, Kam KW, Zhang Y, Tang SM, Young AL, Chen LJ, Tham CC, Pang CP and Yam JC. Differential effects on ocular biometrics by 0.05%, 0.025%, and 0.01% atropine: low-concentration atropine for myopia progression study. Ophthalmology 2020; 127: 1603-1611.
[63] Cottriall CL and McBrien NA. The M1 muscarinic antagonist pirenzepine reduces myopia and eye enlargement in the tree shrew. Invest Ophthalmol Vis Sci 1996; 37: 1368-79.
[64] Siatkowski RM, Cotter SA, Crockett RS, Miller JM, Novack GD and Zadnik K; U.S. Pirenzepine Study Group. Two-year multicenter, randomized, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. J AAPOS 2008; 12: 332-339.
[65] Li Y, Zhang Y, Li P, Mi G, Tu J, Sun L, Webster TJ and Shen Y. Ion-paired pirenzepine-loaded micelles as an ophthalmic delivery system for the treatment of myopia. Nanomedicine 2017; 13: 2079-2089.
[66] Thomson K, Karouta C, Weber D, Hoffmann N, Morgan I, Kelly T and Ashby R. The role of the serotonergic system in atropine's anti-myopic effects. Biomed Pharmacother 2023; 167: 115542.
[67] Barathi VA, Ho CEH and Tong L. Molecular basis of transglutaminase-2 and muscarinic cholinergic receptors in experimental myopia: a target for myopia treatment. Biomolecules 2023; 13: 1045.
[68] Tapia F, Peñaloza V, Silva-Olivares F, Sotomayor-Zárate R, Schmachtenberg O and Vielma AH. Glucagon increases retinal rod bipolar cell inhibition through a D1 dopamine receptor-dependent pathway that is altered after lens-defocus treatment in mice. Invest Ophthalmol Vis Sci 2024; 65: 46.
[69] Shu Z, Chen K, Wang Q, Wu H, Zhu Y, Tian R, Yan W, Huang Q, Zhang C, Xiong W, Qu J, Zhou X and Huang F. The role of retinal dopamine D1 receptors in ocular growth and myopia development in mice. J Neurosci 2023; 43: 8231-8242.
[70] Dong F, Zhi Z, Pan M, Xie R, Qin X, Lu R, Mao X, Chen JF, Willcox MD, Qu J and Zhou X. Inhibition of experimental myopia by a dopamine agonist: different effectiveness between form deprivation and hyperopic defocus in guinea pigs. Mol Vis 2011; 17: 2824-2834.
[71] Cui D, Trier K, Zeng J, Wu K, Yu M, Hu J, Chen X and Ge J. Effects of 7-methylxanthine on the sclera in form deprivation myopia in guinea pigs. Acta Ophthalmol 2011; 89: 328-334.
[72] Hung LF, Arumugam B, Ostrin L, Patel N, Trier K, Jong M and Smith EL III. The adenosine receptor antagonist, 7-methylxanthine, alters emmetropizing responses in infant macaques. Invest Ophthalmol Vis Sci 2018; 59: 472-486.
[73] Trier K, Munk Ribel-Madsen S, Cui D and Brogger Christensen S. Systemic 7-methylxanthine in retarding axial eye growth and myopia progression: a 36-month pilot study. J Ocul Biol Dis Infor 2008; 1: 85-93.
[74] Trier K, Cui D, Ribel-Madsen S and Guggenheim J. Oral administration of caffeine metabolite 7-methylxanthine is associated with slowed myopia progression in Danish children. Br J Ophthalmol 2023; 107: 1538-1544.
[75] Zhou L, Xing C, Qiang W, Hua C and Tong L. Low-intensity, long-wavelength red light slows the progression of myopia in children: an Eastern China-based cohort. Ophthalmic Physiol Opt 2022; 42: 335-344.
[76] Jiang Y, Zhu Z, Tan X, Kong X, Zhong H, Zhang J, Xiong R, Yuan Y, Zeng J, Morgan IG and He M. Effect of repeated low-level red-light therapy for myopia control in children: a multicenter randomized controlled trial. Ophthalmology 2022; 129: 509-519.
[77] Dong J, Zhu Z, Xu H and He M. Myopia control effect of repeated low-level red-light therapy in chinese children: a randomized, double-blind, controlled clinical trial. Ophthalmology 2023; 130: 198-204.
[78] Xiong F, Mao T, Liao H, Hu X, Shang L, Yu L, Lin N, Huang L, Yi Y, Zhou R, Zhou X and Yi J. Orthokeratology and low-intensity laser therapy for slowing the progression of myopia in children. Biomed Res Int 2021; 2021: 8915867-8915810.
[79] Xiong R, Zhu Z, Jiang Y, Kong X, Zhang J, Wang W, Kiburg K, Yuan Y, Chen Y, Zhang S, Xuan M, Zeng J, Morgan IG and He M. Sustained and rebound effect of repeated low-level red-light therapy on myopia control: a 2-year post-trial follow-up study. Clin Exp Ophthalmol 2022; 50: 1013-1024.
[80] Xiong R, Zhu Z, Jiang Y, Wang W, Zhang J, Chen Y, Bulloch G, Yuan Y, Zhang S, Xuan M, Zeng J and He M. Longitudinal changes and predictive value of choroidal thickness for myopia

control after repeated low-level red-light therapy. Ophthalmology 2023; 130: 286-296.
[81] Neitz M, Wagner-Schuman M, Rowlan JS, Kuchenbecker JA and Neitz J. Insight from OPN1LW gene haplotypes into the cause and prevention of myopia. Genes (Basel) 2022; 13: 942.
[82] Rappon J, Chung C, Young G, Hunt C, Neitz J, Neitz M and Chalberg T. Control of myopia using diffusion optics spectacle lenses: 12-month results of a randomised controlled, efficacy and safety study (CYPRESS). Br J Ophthalmol 2023; 107: 1709-1715.
[83] Jung BJ and Jee D. Association between serum 25-hydroxyvitamin D levels and myopia in general Korean adults. Indian J Ophthalmol 2020; 68: 15-22.
[84] Wolf AT, Klawe J, Liu B and Ahmad S. Association between serum vitamin D levels and myopia in the national health and nutrition examination survey (2001-2006). Ophthalmic Epidemiol 2024; 31: 229-239.
[85] Zhang D, Sun B, Wu M, Liu H, Zhou L and Guo L. Prevalence and associated factors of myopia among school students in Shenyang, China: a cross-sectional study. Front Public Health 2023; 11: 1239158.
[86] Liu T, Tan W, Fu Y, Cheng B, Tian H, Liu C, Wang Z, Zhang Y, Guan S and Liu Z. Association of outdoor artificial light at night with myopia among Chinese adolescents: a representative cross-sectional study. Front Med (Lausanne) 2024; 11: 1469422.
[87] Liao S, Li X, Bai N, Wu D, Yang W, Wang F and Ji HZ. An empirical study on the effect of outdoor illumination and exercise intervention on Children's vision. Front Public Health 2023; 11: 1270826.