Myopia: A Review and Summary

Part 3: Therapies for myopia

Introduction

In parts 1 and 2 of this series, we looked at both the epidemiology and pathophysiology of myopia and its secondary complications.

This article will explore the many theories behind therapeutic interventions for myopia management (MM) and current and future products available to patients.

Where possible, we shall also look at long-term studies exploring the varied efficacies of various MM therapies.

A New Landscape

The W.C.O. (World Council of Optometry) has recently made its stance on myopia very clear. In 2021, the W.C.O. President stated, ***'Establishing a standard of care that regularly and consistently applies these interventions, particularly at an early age, may prevent or delay the onset of myopia, or halt or slow its progression'.***

The W.C.O. established three 'pillars' on which practitioners should base their approach to myopia management. These were ***Mitigation, Measurement and Management.***

Whereas applying methods to reduce myopia progression should be, but is not, the current standard of care amongst many optometrists;

Whereas the lack of an established standard of care in myopia management is a disservice to the optometric profession, patients, and public health; and

Whereas simply correcting the refractive error is no longer sufficient, and myopia management should not be optional, and rather be an obligation of optometrists;

Now, therefore, be it resolved, that the World Council of Optometry, on behalf of its members:

1. Defines the evidence-based standard of care as comprising of three main components:

- Mitigation — optometrists educating and counseling parents and children, during early and regular eye exams, on lifestyle/dietary/other factors to prevent/ delay onset of myopia
- Measurement — optometrists evaluating the status of a patient during regular comprehensive vision and eye health exams, (e.g. refractive error and axial length whenever possible)
- Management — optometrists addressing patients' needs of today by correcting myopia, while also providing evidence-based interventions (e.g., contact lenses, spectacles, pharmaceuticals) that slow the progression of myopia, for improved quality of life and better eye health today and into the future; and

2. Advises optometrists to incorporate the standard of care for myopia management within their practice that shifts from not only correcting vision but includes public education and early and frequent discussions with parents that explains:

- what myopia is
- lifestyle factors that may impact myopia
- the increased risks to long-term ocular health that myopia brings
- the available approaches that can be used to manage myopia and slow its progression.

In the U.K., how do we, therefore, alter our clinical routines to ensure that we always look at myopia as worthy of further investigation?
It's clear that MM should become part of the standard eye examination for all children. But surely, we must charge extra for it.
The only G.O.S. provision at present is a six-monthly G.O.S. sight test for children from 0-7 who have a B.V. anomaly / refractive error (myopia?) and 7-16 B.V. anomaly or rapidly progressing myopia (how rapid?).
Early retest codes include: 3.1 Patient is at risk of frequent prescription changes for reasons not requiring medical referral or for reasons already known to a medical practitioner.
3.2 mentions pathology 'likely to worsen' – one imagines this could certainly now include progressive myopia according to the W.C.O.
Ultimately, the fees simply don't cut, and the frequency of tests needs to be increased to be effective.

More recently, the College of Optometrists has released its guidance on Myopia and Myopia Management (MM). There are a few key points to take away from this recent guidance:

1. Optometrists must inform patients/parents about myopia, its causes, its progressive nature, its potential effects, and the possibility of slowing its progression.
2. Optometrists must ensure they prepare themselves with the necessary study and ensure they are experienced and confident before undertaking MM.
3. Patients and parents must sign a disclaimer should they not wish to engage in MM, and optometrists must offer alternative clinical assistance should they not want to provide MM to their patients.
4. Cycloplegic refraction is important, but cycloplegic auto-refraction is acceptable. Axial length measurements (likely by optical biometry) are perhaps more reliable and valid in terms of MM, certainly where Ortho-K is being offered to the patient, as the refraction can no longer be measured in such circumstances.

So, considering all this, let's look at the therapies available.

Recap

As we saw in the first and second parts of this series, there are several theories behind myopisation, including the following:

- Hyperopic defocus blur
- Accommodative lag, prolonged Accommodation
- Light deprivation and/or limited outdoor time
- Binocular vision anomalies
- Genetic and family history

Most currently accepted therapies primarily provide solutions based on the hyperopic defocus blur theory of Myopisation. However, an increasing number of experimental treatments rely on other methods of slowing globe elongation.

When we talk about myopia management, it is, perhaps, more appropriate to think about **axial length management.** Controlling the habitual long-term 'final' myopic prescription is all well and good, but it's clear the axial length increase (globe elongation) leads to numerous secondary complications in myopia. The fact that the surfaces of the optical media and the refractive indices may produce an unreliable prediction for axial length, optical biometry is considered the **measurement of primary importance** in myopia management (MM).

MM aims to help reduce the amount of axial elongation of the eyes and reduce the inherent risks of conditions like glaucoma, MMD (myopia macular degeneration), retinal detachment, cataract, and others.

Therapeutic Modalities

Ultimately, there are several ways in which myopia management therapies can be delivered. These could be categorised in the following way:

1. Optical / light related
2. Pharmaceutical
3. Behavioural
4. Combination

Optical / Light related MM Therapies

Optical forms of myopia management can be broken down into Spectacle and Contact Lens options. These can then be further subdivided into more sub-categories.

Spectacles:

- Under corrected single-vision spectacles or standard fully corrected single-vision spectacles – controversial at best
- Bifocal or multifocal spectacles
- Myopic defocus blur spectacles
- Contrast altering lenses

Contact Lenses:

- Dual-focus soft contact lenses
- E.D.O.F. soft contact lenses and multi-focus variants
- Orthokeratology (Ortho-K) G.P. hard lenses

Others:

- Kubota Glass Technology
- Repeated low-level Red-Light Therapy (R.L.R.L.)
- Tsubota Lab Violet Lens

Pharmaceutical MM Therapies

Eye Drops (proven in human trials):

- 0.01% Atropine
- Pirenzepine
- 7-Methylxanthine (7MX – a derivative of caffeine)

Eye Drops (experimental):

- Ketorolac tromethamine
- Oral Riboflavin
- BHVI2

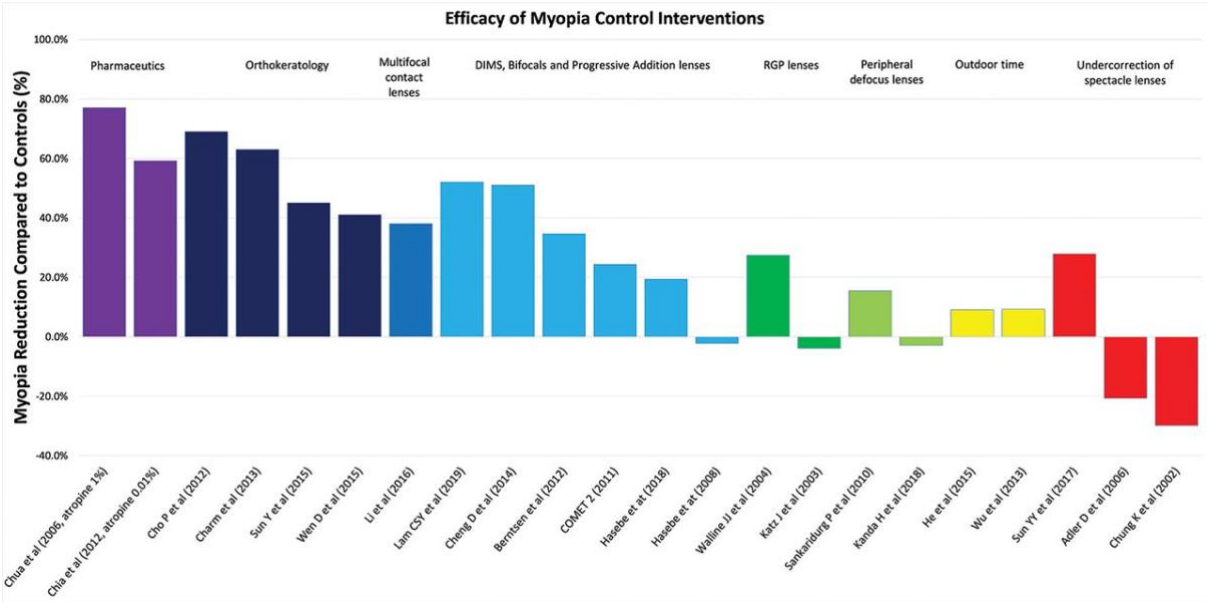
Behavioural MM Therapies

- **Measure the daily tasks – Vivior (A.I. assistance)**

Combination MM Therapies

- Atropine 0.01% and Ortho-K
- Soft contact lenses and MM spectacles
- Behavioural with other interventions

Gene Therapy
Anisometropic Amblyopia Therapies
Scleral buckle for high myopia



Ang M, Flanagan JL, Wong CW, et al. Br J Ophthalmol 2020;104:1482–1487.

As you can see from the graph above, there is considerable variance in the efficacy of these multiple myopia management therapeutic options. Nevertheless, we'll now consider each option individually.

Myopia Management Spectacles

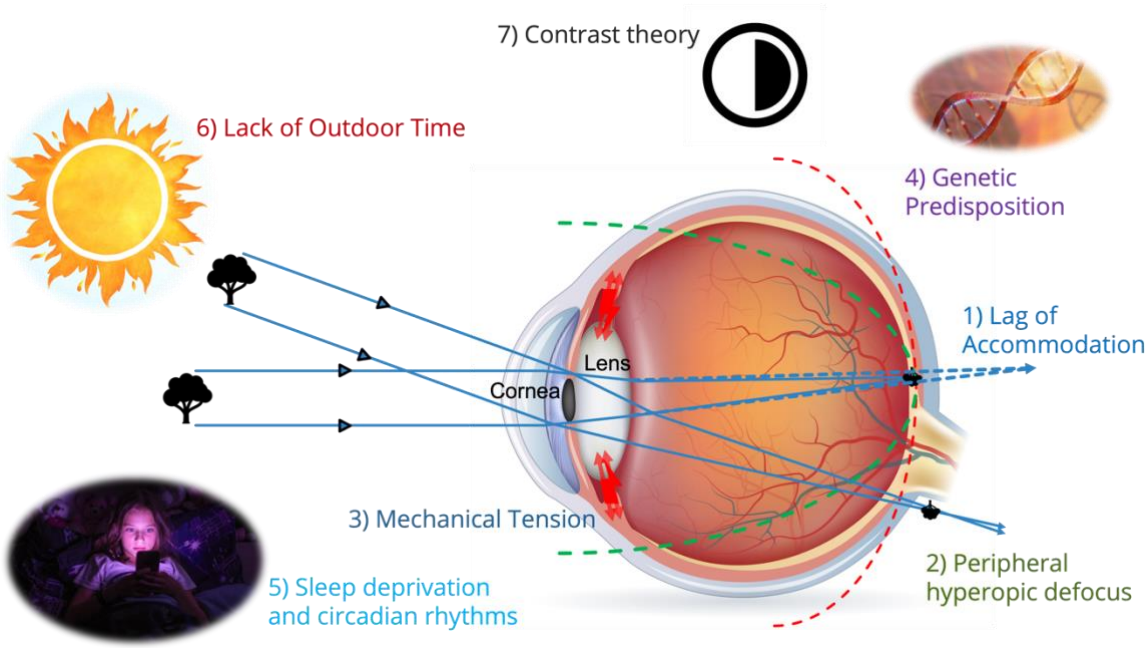
Under correction of myopia was considered a valid approach to reducing the developmental extent of a patient's myopic prescription. However, studies, including the COMET study, showed that this under-correction could exacerbate the speed and amount of myopia progression. Therefore, under correction of the myopic refractive error is no longer considered a valid or appropriate treatment modality.

When correcting myopia, clinicians aim to maximise the patient's visual acuity and prescribe the full myopic refraction. However, it is important to understand the potential for accommodative tonus, particularly in younger children. Therefore, cycloplegic refraction is always recommended when initially considering the level of refractive error to be corrected. Furthermore, the effect of the spectacles at assisting with accommodative convergence issues and near esophoria must be considered.

However, according to many studies, simply correcting the full cycloplegic refractive error is ineffective in slowing globe elongation (myopic progression).

In terms of using spectacles to help to reduce axial growth, those that shift the image shell to a more peripherally myopic shape tend to be more effective than standard single-vision lenses or standard bifocal/multifocal lenses.

Theories of Myopia Development



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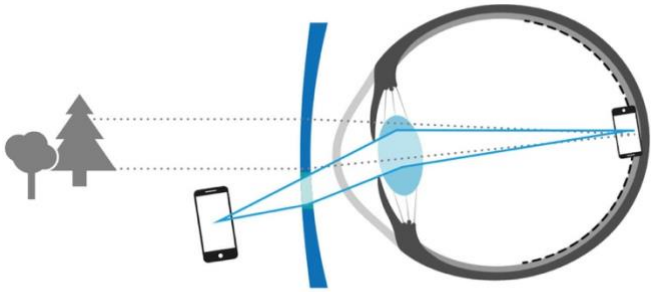
Where standard bifocals or P.A.L.s are provided for myopia management, a reduction in accommodative lag and mechanical tension are the main reasons this is effective. However, the overall results of using bifocals and P.A.L.s seem to only be truly effective where issues with accommodative lag and esophoria exist. In these cases, the effects can be quite dramatic.

In general, however, where no such binocular vision problems are evident, bifocals and P.A.L.s' efficacy is limited compared to standard single-vision lenses.

One of the more effective 'multifocal' myopia management lenses is the Zeiss MyoKids® lens range. These have a hybrid multifocal design, where the upper part of the lens is a standard single-vision correction for the full cycloplegic refraction. There is a bottom zone for near vision, reducing Accommodation for near work and helping to reduce hyperopic defocus for near work.



Picture from the Zeiss website.

The lens has a freeform design where the centre of rotation of the eye is considered, along with BVD, when ordering the specific design of the lower P.A.L. portion.

These lenses are effective where esophoria and accommodative lag are present.

Peripheral Myopic Defocus Spectacles

Peripheral hyperopic defocus blur is one of the most significant causes of myopia progression (Article 1). A range of lenses use similar technologies to bring about myopic peripheral defocus. Many studies with these lenses have shown significant benefits in slowing axial elongation in a substantial proportion of subjects. Those subjects with notable binocular vision abnormalities sometimes don't appear to benefit as much from these lenses.

There are several ways in which the peripheral myopic defocus can be delivered.

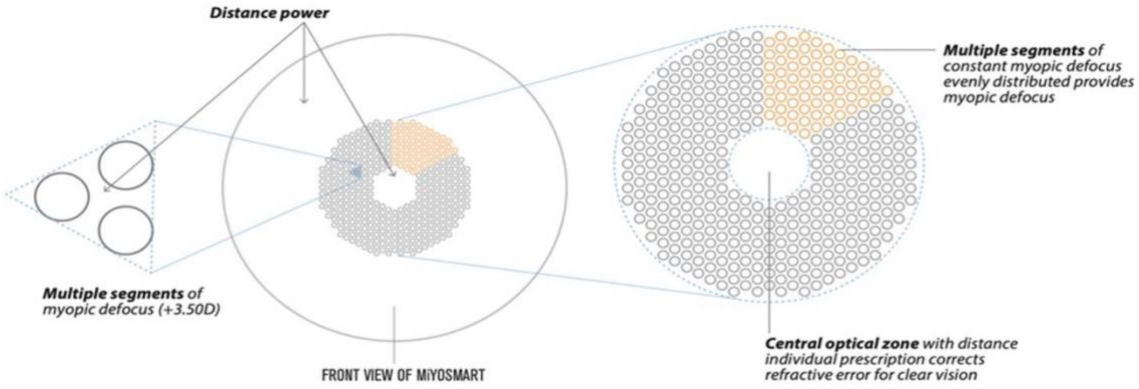
- D.I.M.S. (Defocus Incorporated Multiple Segments)
- H.A.L.T. (Highly Aspheric Lenslet Target)
- Peripheral Aspheric Design

D.I.M.S

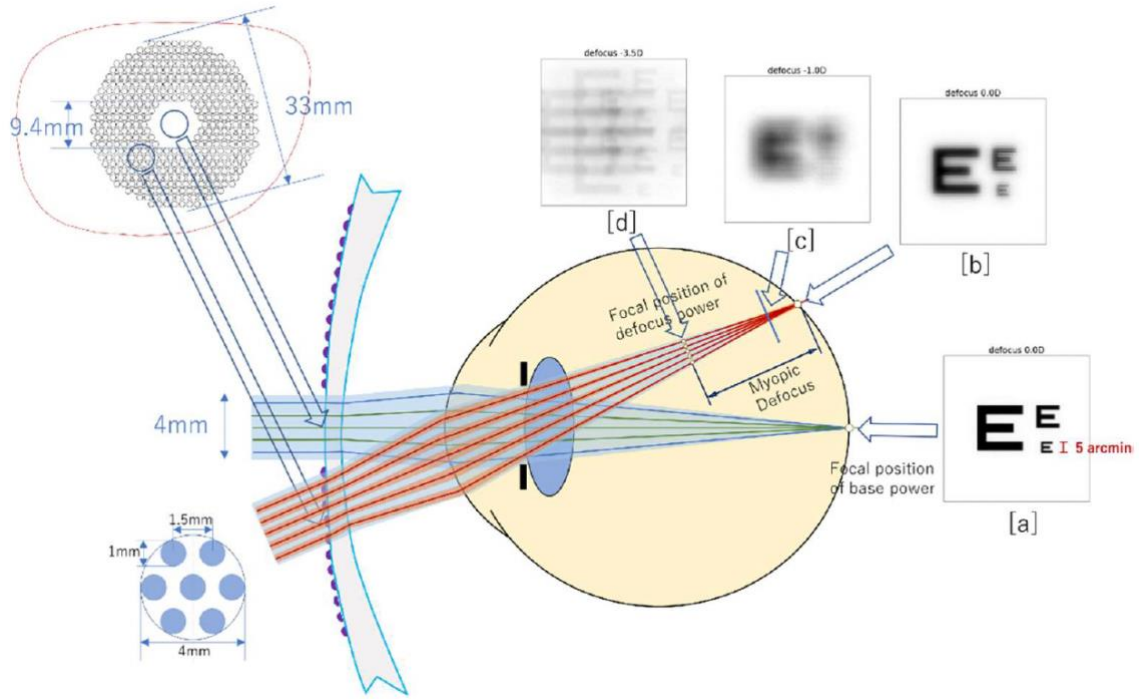
Currently known as MiyoSmart, made by Hoya, these lenses consist of micro lenslets arranged in a circular pattern around a clear central focussed zone

containing the distance prescription. The lenslets provide +3.50DS of additional focusing power, rendering a myopic' blur shell' at the user's peripheral retina. This myopic defocus has been clinically proven to reduce globe elongation.

Outside this ring of lenslets, the lens has the same spectacle prescription as the central zone.



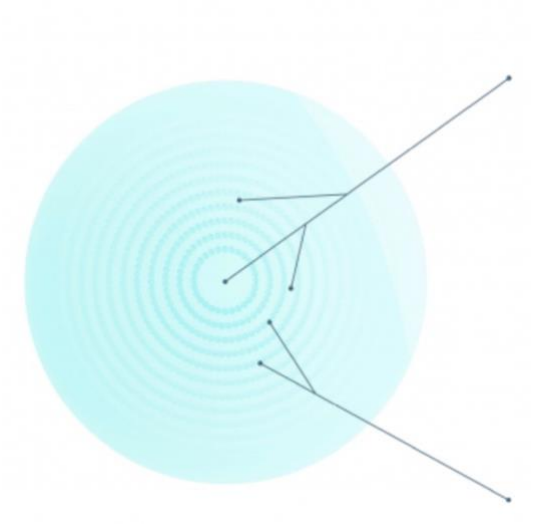
Images from: Carlà, M.M.; Boselli, F.; Giannuzzi, F.; Gambini, G.; Caporossi, T.; De Vico, U.; Savastano, A.; Baldascino, A.; Rizzo, C.; Kilian, R.; et al. Overview on Defocus Incorporated Multiple Segments Lenses: A Novel Perspective in Myopia Progression Management. Vision 2022, 6, 20.



As can be seen, central vision is preserved clearly, but hyperopic defocus is eliminated by the front surface lenslets (the lens back surface provides the toroidal cross curves to complete the full distance correction).

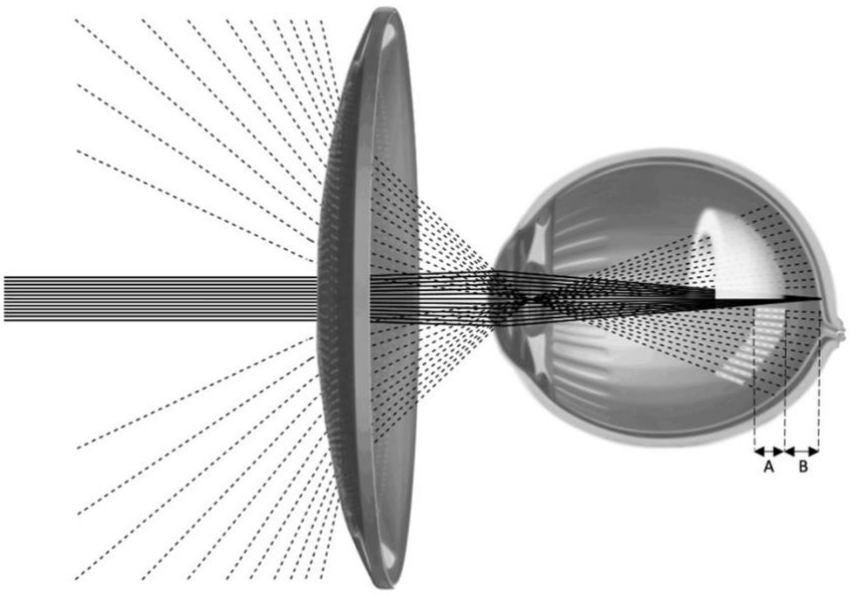
H.A.L.T

Highly aspheric target lenses, known as Stellest, made by Essilor, are like the MiyoSmart, but use a different array of small lenslets. These lenses use an array of rings, which provide normal distance annular zones along with peripheral myopic defocus zones consecutively, increasing in asphericity from the centre to the edge.



Standard single-vision distance zones

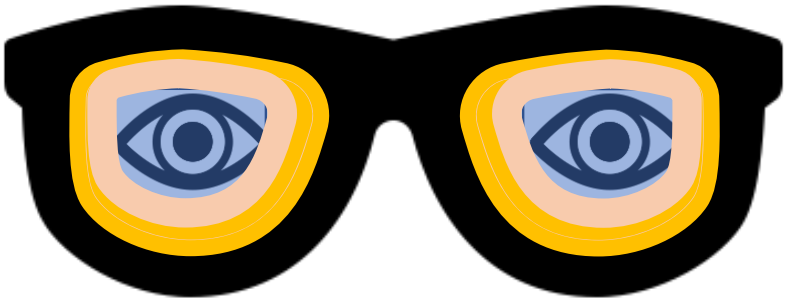
Aspheric mini lenses create zones of peripheral myopic defocus.



The result is a central focussed zone of viewing and a myopic peripheral image shell which reduces retinal impetus to increase axial length.

Peripheral Aspheric Design

Zeiss produce the MyoVision Pro lenses, which use a central standard optical zone (blue in the image below), and then peripheral zones of increasing myopic defocus asphericity.



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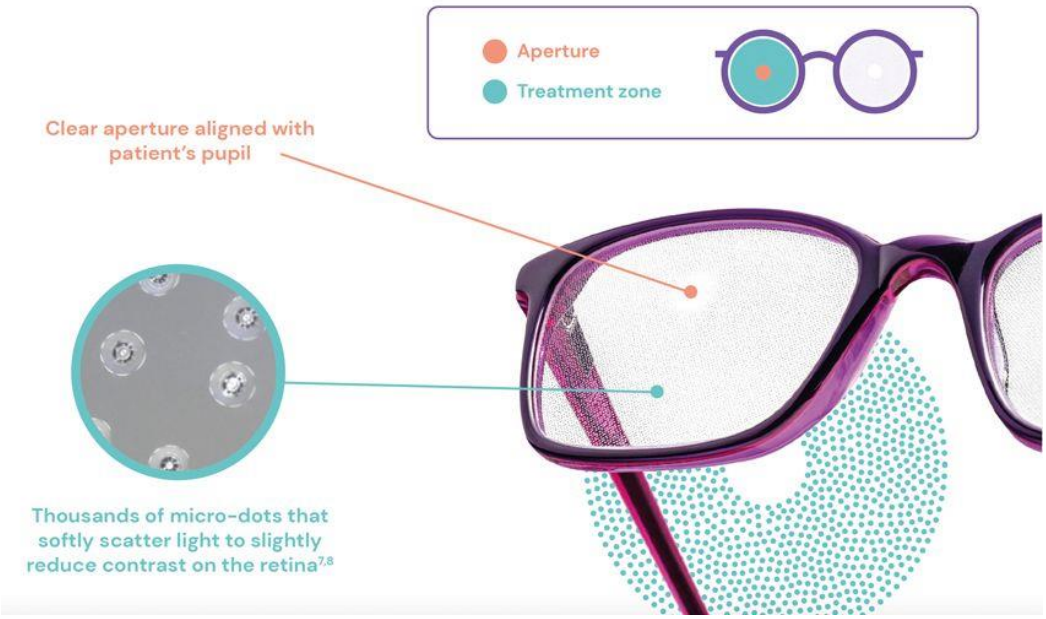
These lenses have also been shown to reduce axial elongation and may produce a lower effect on vision in terms of glare and noticing lenslet reflections.

Contrast altering lenses: D.O.T.

These are a new design of lenses currently being developed and trialled by SightGlass vision. D.O.T. stands for Diffusion Optics Technology. These lenses rely on the Contrast Theory of Myopisation. Emmetropisation works because the young hyperopic child can see distant objects clearly and in high contrast, promoting axial growth. When the eye grows towards emmetropia, the distant image becomes less clear and has lower contrast. This lower contrast signals the retina to slow and stop globe elongation.
Modern lifestyles now provide too much high contrast near work, and it is proposed that this 'fools' the eye into continued axial elongation.

What the D.O.T. lens does is to reduce the high-contrast elements of the image at all distances.

Image from CooperVision website



The D.O.T. lenses comprise a central clear zone which should be centred on the pupil. Beyond this zone, the lens is covered with thousands of tiny light-scattering micro-dots, which reduce retinal contrast for all distances viewed. Initial results of

studies show a high degree of efficacy, with up to 59% reduction in myopia over a three-year study (CYPRESS).

Summary of Spectacle Lens Options

Thanks to Professor Padmaja Sankaridurg and Insight magazine

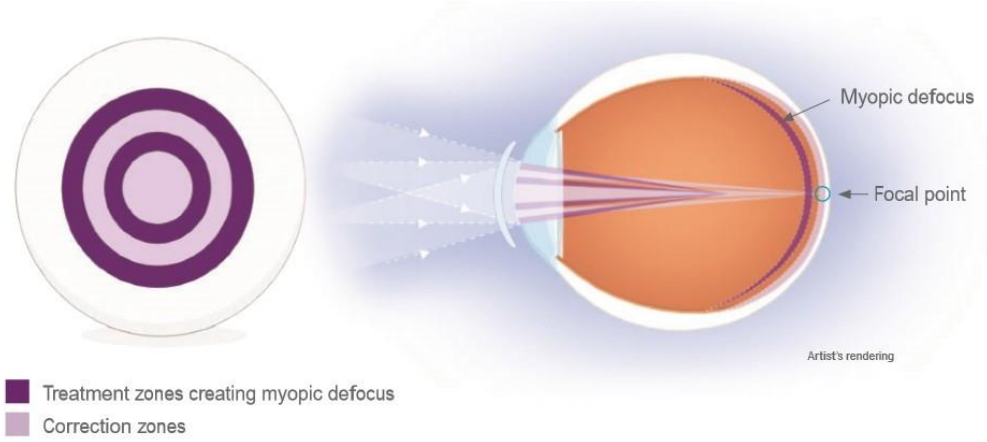
	Bifocal/Progressive Addition lenses	Peripheral Defocus spectacles	Defocus incorporated multiple segments	Highly aspherical lenslet technology	Diffusion Technology
Rationale	Reduce accommodative lag.[11,12]	Reduce peripheral retinal defocus.[13,14]	Simultaneous myopic defocus.[7]	Induce a volume of myopic defocus at the retina.[8]	High contrast differential between neighbouring cones drives growth; reduce retinal contrast with diffusive dots.[15]
Lens design	Upper segment for distance viewing; near segment that is relatively positive compared to distance segment.	Clear asymmetric central zone designed to accommodate near viewing: surrounding peripheral zone is relatively positive. The positive power increases towards periphery.	Clear central zone: multiple discrete segments of +3.50D in mid peripheral zone.	Clear central zone: highly aspherical lenslets in a concentric ring formation; rings[11] separated by clear distance zone. Power of lenslets in each ring is similar but varies between rings.	Clear central zone: peripheral zone with diffuse dots that are non-refractive.
Schematic					

Myopia Management Contact Lenses

Dual Focus Soft Contact Lenses

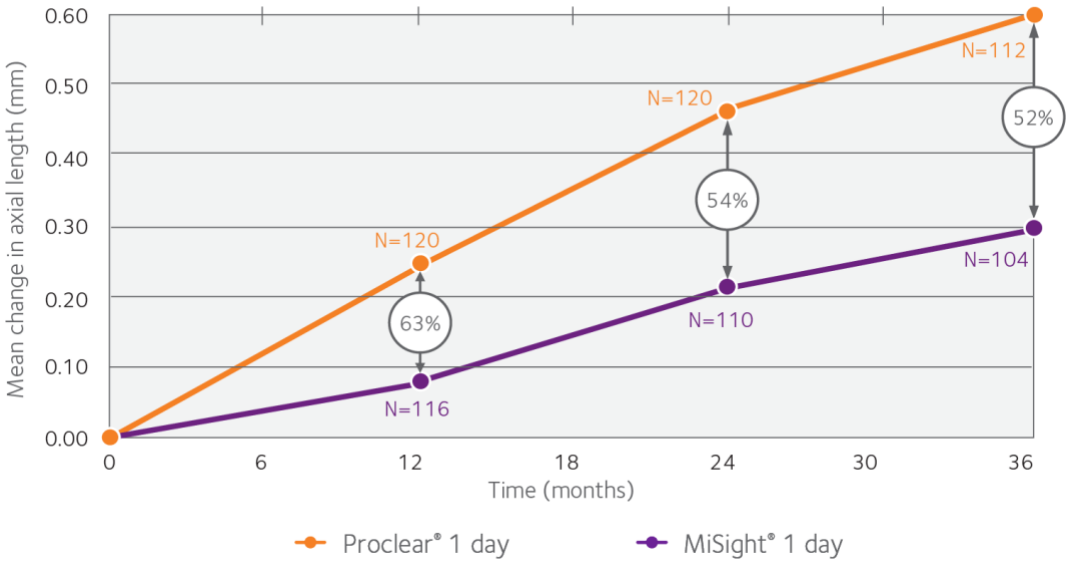
The first classic dual-focus soft contact lens for myopia management was the CooperVision Misight lens.

This lens has a central distance zone and multiple concentric alternating zones of distance and myopic peripheral defocus, as shown in the image below.

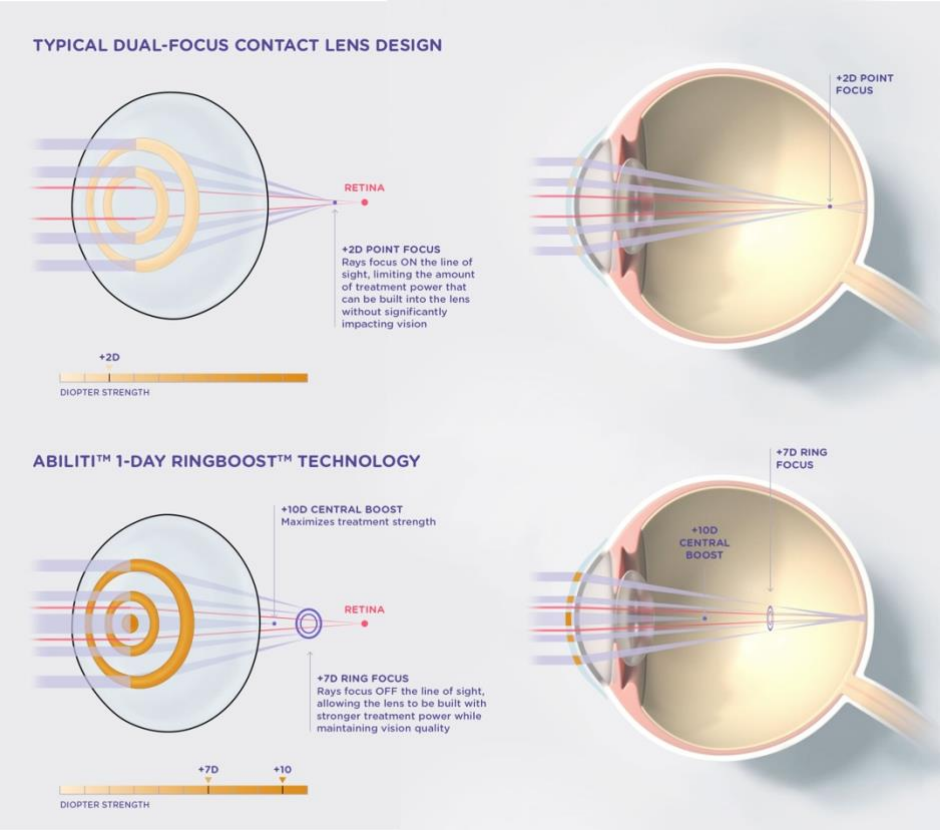


This lens ensures that a full myopic correction occurs for the distance refraction whilst also providing a myopic peripheral defocus image shell to help to reduce the drivers for globe elongation.

There have been many studies showing the efficacy of these lenses, and the results have been very encouraging. Below is an image comparing the MiSight lenses to standard soft contact lenses. The reduction in axial growth over the three years averaged 56.3%.



Another new lens came to the market recently, from Johnson & Johnson, the Acuvue Abiliti lens. This is a slightly enhanced dual focus lens, using what they call RingBoost® technology.



Johnson & Johnson claim that this adjusted dual focus design removes the myopic defocus rays from the line of sight, allowing for stronger myopia paraxial powers and less impact on the patient's vision.

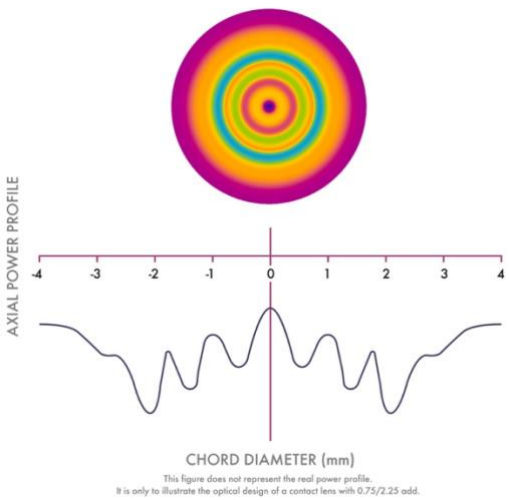
E.D.O.F. soft contact lenses and multi-focus variants

Several options are available within this soft contact lens design category for myopia management. The B.H.V.I. (Brien Holden Vision Institute) designed an E.D.O.F. (extended depth of focus) soft contact lens to correct presbyopia. However, different designs are effective at reducing axial length progression in children.

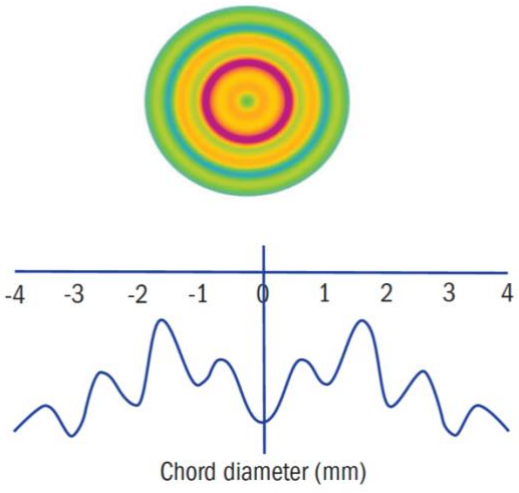
The effect of the E.D.O.F. lens was to create zones of peripheral myopic defocus but using a more blended difference between the zones so that there isn't a dual focus effect, more of a blended distance, intermediate and near multi-focus effect.

According to one study, these lenses showed a reduction in axial elongation by 22 to 32%. It's clear that such lens designs are effective; ultimately, different designs of E.D.O.F. and multifocal lenses could prove effective. It's also evident that the effectiveness of such lenses will vary from patient to patient and lifestyle differences between patients will also play a role in the efficacy of lenses in such trials.

Standard E.D.O.F. for Presbyopia



Myopia Management E.D.O.F.



The table below highlights the various lenses available and the technology they use.

Manufacturer	**Mark Ennovy**	**Menicon**	**VTi**	**Johnson and Johnson**	**CooperVision**
Product Name	M.Y.L.O.	Bloom Day	Natural View	Acuvue Abiliti	MiSight

Product Design	B.H.V.I. Myopic E.D.O.F. design	Centre distance EDOF lens VTi design	Centre distance EDOF lens VTi design	RingBoost Dual Focus	Dual Focus

Some manufacturers refer to their soft lenses as 'Day' lenses as they are used during the day for correcting ametropia and reducing myopic progression, as opposed to Ortho-K lenses (below).

Orthokeratology (Ortho-K) G.P. hard lenses

Orthokeratology (Ortho-K) has been used to correct myopia for several decades. It is a non-permanent method of reshaping the cornea through overnight wear of hard gas-permeable contact lenses during sleep. The lenses are removed upon waking, and the reshaped cornea provides clear distance vision for many wearers. There are limitations to the refractive power that can be corrected.

More recently, it became clear that during the process of reshaping the cornea during sleep, there was also an effect on the spherical aberration of the cornea, which led, in many cases, to induced peripheral myopic defocus. It became clear that this effect significantly reduced the rate and amount of axial elongation in many wearers. Latterly, new lens designs have come about that aim to maximise these corneal reshaping effects leading to very high levels of reported efficacy.

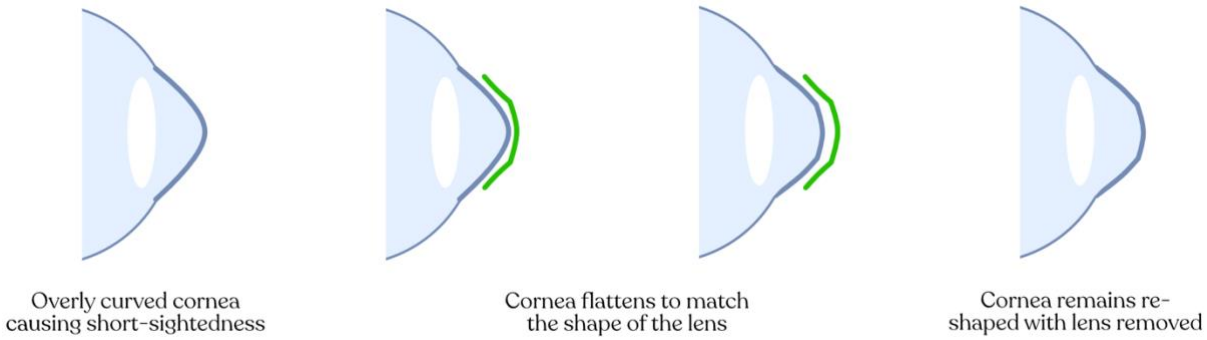
One major advantage of Ortho-K is the added confidence such therapy can give to children. The author has seen cases where children lacked confidence at school or socially, particularly in sports before Ortho-K. This was primarily because of the difficulty with spectacles or contact lenses falling off or out during many sports or issues with the cosmetic appearance of glasses socially.

Removing the need for contact lenses and spectacles during the day has a profound positive effect on children's confidence, ability, and willingness to partake in sports. This has a knock-on effect of increasing their time spent outdoors and improving their mental and physical health because of increased exercise and social participation.

Many manufacturers refer to their Ortho-K lenses as 'Night' lenses as this is a more parent/patient-friendly description of the lenses and when they are worn. It's important to remember that often; we will be asking much younger patients to wear these lenses than perhaps we have been previously used to. Removing jargon makes it easier to persuade parents and children to try such lenses.

Without going into too much detail, Ortho-K or night lenses require detailed anterior corneal mapping (topography) to design so-called 'reverse geometry' hard G.P. lenses.
The design of the lens back surface creates pressure points that alter the corneal shape considerably during sleep. Once the lens is removed in the morning, the cornea retains that shape for the rest of the day.

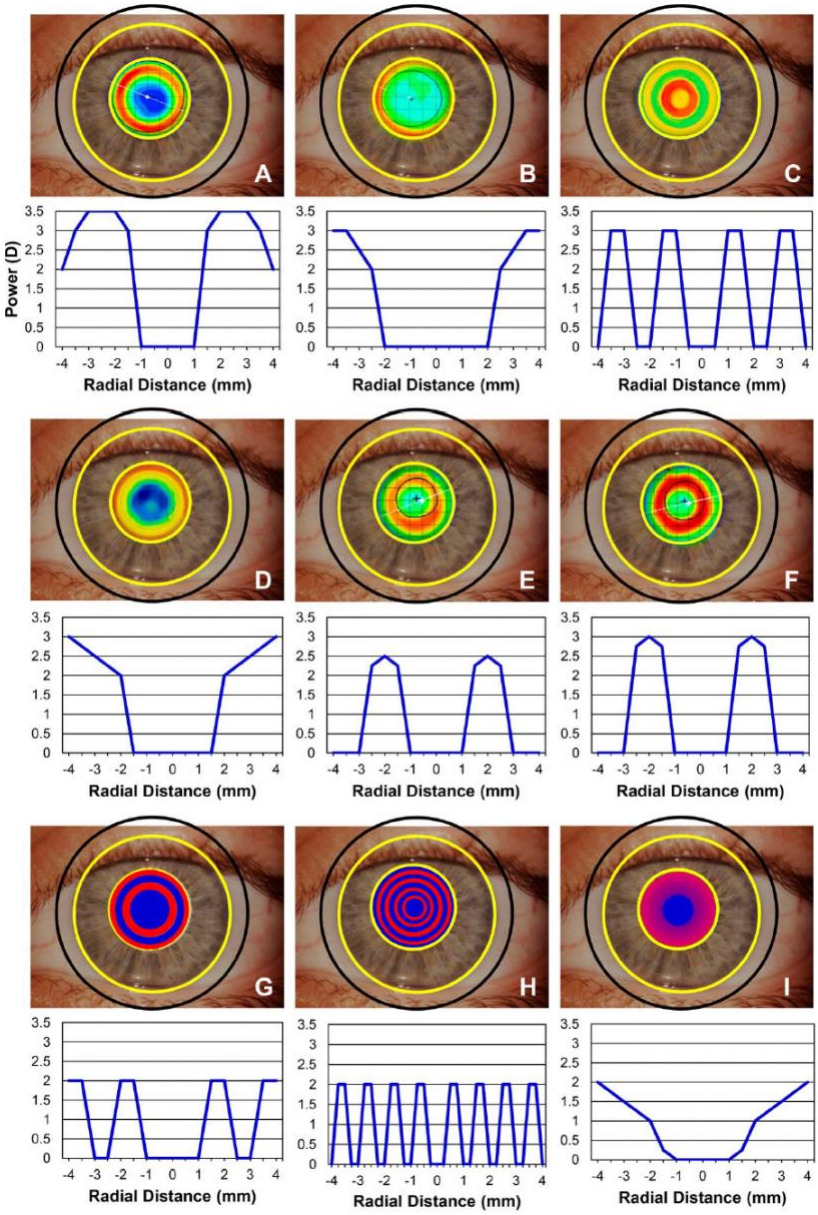
Diagram explaining how Ortho-K reshapes the cornea during sleep



There are subtle variations in modern lens designs. Still, the results are similar – central clear distance optical zone and peripheral rings of myopic peripheral defocus, reducing the impetus for axial elongation.
Some of the major manufacturers and lens types are listed in the table below.

Manufacturer	Lens Name	Details
Menicon	Bloom Night	Toric also available. Up to -4.00DS currently
J&J Acuvue	Abiliti Overnight	Just received F.D.A. to -6.00DS with toric too
No.7	EyeDream	
Scotlens	Nightlens	Up to -7.00 with toric option

A well-fitting Ortho-K lens. Image taken from the Innovative Eye Care website.



Representation of the optical design of different contact lenses with potential to retain myopia progression over the 6 mm of the pupil and graphs representing the approximate power profile over the central 8 mm: (A) corneal refractive therapy for an axial myopia of 23.5 D; (B) corneal refractive therapy for axial myopia of +1.5 D; (C) bifocal annular design; (D) power profile of a multifocal centre-distance soft contact lens as measured in vitro; (E) and (F) power profile of a multifocal centre-distance soft contact lens on-eye with +3.00 and +4.00 D of addition for near, respectively, as measured with a corneal topographer; (G) dual-focus as described by Anstice and Phillips; (H) defocus incorporated special contact lens (DISC); and (I) peripheral gradient design as described by Sankaridurg et al.

González-Méijome JM, Peixoto-de-Matos SC, Faria-Ribeiro M, Lopes-Ferreira DP, Jorge J, Legerton J, Queiros A. Strategies to Regulate Myopia Progression with Contact Lenses: A Review. Eye Contact Lens. 2016 Jan;42(1):24-34.

One of the most important things to note when considering Ortho-K lenses as a myopia management option is that you will need a biometer, preferably optical. You will no longer be able to measure the myopic Rx once regular Ortho-K use has commenced. You will need to monitor the treatment's effect, which will require you to assess the rate of change in axial length compared to the predicted rate of change and/or the previously measured rate of change before starting Ortho-K.
This ultimately speaks to the cause of damage in progressive myopia. It's not the Rx that counts; it's the axial length (A.L.). The increasing A.L. is what leads to all the damage in myopia. Refractive myopes with normal axial lengths are at no more risk of secondary comorbidities than emmetropes and hyperopes. It's the axial myopes we are concerned about. The Rx and K readings do not always give us a truly reliable and repeatable measure of the real A.L. This is why the preferred gold standard measure in MM is axial length, preferably by optical biometry.

Ultrasound biometry is an option, but indentation will lead to less repeatable and accurate measurements and the procedure will require more drops, an increased risk of infection/abrasion and is less sustainable.

Kubota Glass Technology

Kubota report that their device uses nanotechnology to actively project peripheral myopia-defocused virtual images using micro-LEDs. This works to actively stimulate the arrest of the axial growth impetus.
The results so far appear exciting, but the data is all from Kubota, so until there are multiple long-term comparison and validity studies, it's impossible to say how effective the treatment is.

Myopia Therapy Competitive Landscape: Comparison of Key Features

	Kubota Glass™ Avg: 13.6 yrs	HOYA MiyoSmart™ Avg: 10.4 yrs	Essilor Stellest™ Avg: 10.7 yrs	CooperVision MiSight® Avg: 10.1 yrs	SightGlass DOT Lens Avg: 8.1 yrs	Tsubota Lab Violet Lens: Avg: 9.4 yrs	RLRL Red Light Device Avg: 9.4 yrs	0.05% Atropine Avg: 8.5 yrs	Ortho-keratology Avg: 9.2 yrs
Mechanism of Action	Active Stimulation: Illuminated peripheral myopic defocus	Passive Stimulation: Peripheral myopic defocus	Passive Stimulation: Peripheral myopic defocus	Passive Stimulation: Peripheral myopic defocus	Passive Stimulation: Peripheral contrast reduction	Passive Stimulation: Transmittance of violet light	Active Stimulation: Exposure to bright red light; possibly heat	Unknown	Passive Stimulation: Peripheral myopic defocus
Form	Spectacle Lens	Spectacle Lens	Spectacle Lens	Soft contact Lens	Spectacle Lens	Spectacle Lens	Tabletop device	Topical medication	Rigid contact lens
Central Clear Zone	9.0mm	9.4mm	9.0mm	3.36mm (Corneal plane)	Approx 9.0mm reported by competitors	N/A	N/A	N/A	Varies
Magnitude of Defocus	+5.00D	+3.50D	+3.50D (axial; tangential may be up to +20.00D in HAL design)	+2.00D	N/A	N/A	N/A	N/A	Varies
Wear Time	2 hours/day 6 days/week	15+ hours/day 7 days per week	12+ hours/day 7 days/week	12-13 hours/day 6 days/week	>12 hours/day 7 days/week	"Full time wear"	3 minutes, twice daily, 5 days/week	N/A	Overnight

Myopia Therapy Competitive Landscape: 1-Year Efficacy Comparison (mean)*

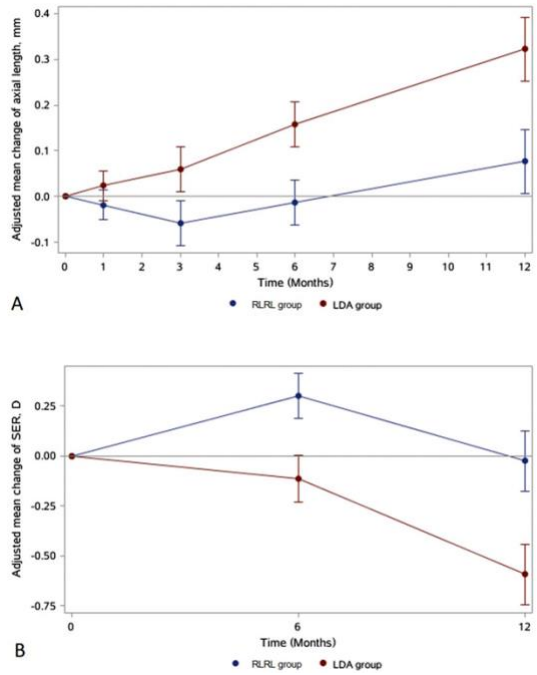
Measure	Kubota Glass™	HOYA MiyoSmart ™	Essilor Stellest™	Cooper-Vision MiSight®	SightGlass DOT Lens	Tsubota Lab Violet Lens	RLRL Red Light Device	0.05% Atropine	Ortho-keratology
SER Progression (Controls, D)	-0.31	-0.55	-0.81	-0.58	-0.54	-0.97	-0.79	-0.81	N/A
SER Progression (Test, D)	0.15	-0.17	-0.28	-0.18	-0.14	-0.75	-0.20	-0.27	N/A
SER Reduction (Test vs Control, D)	0.46	0.38	0.53	0.40	0.40	0.22	0.59	0.54	N/A
SER Reduction (Test vs Control, %)	148%	69%	65%	69%	74%	27%	75%	67%	N/A
AL Progression (Controls, mm)	0.22	0.32	0.36	0.24	0.30	0.50	0.38	0.41	0.37
AL Progression (Test, mm)	0.02	0.11	0.13	0.09	0.15	0.43	0.13	0.20	0.20
AL Reduction (Test vs Control, mm)	0.20	0.21	0.23	0.15	0.15	0.07	0.26	0.21	0.17
AL Reduction (Test vs Control, %)	91%	66%	64%	63%	50%	14%	66%	51%	45%

**Kubota Glass effectiveness data extrapolated from 6-month results of children's Longitudinal Wearable Prototype Study (n=11). Control group data derived from published natural history studies.*

Repeated low-level Red-Light Therapy (R.L.R.L.)

Many studies show red light therapy is effective at slowing axial elongation in myopia management. Red light therapy has been used as a potential treatment for amblyopia but was repurposed for MM. The mechanism at play is not well understood. Still, there appears to be thickening of the choroid, which could help mediate axial growth, or at least provide greater resistance to the mechanical tension of prolonged Accommodation.

One interesting study showed that R.L.R.L. was more effective than low-dose Atropine (LDA). The findings are shown below:



Chen Y, Xiong R, Chen X, Zhang J, Bulloch G, Lin X, Wu X, Li J. Efficacy comparison of repeated low-level red light and low-dose Atropine for myopia control: a randomised controlled trial. Transl Vis Sci Technol. 2022;11(10):33,

The Myproclear RLRL device

There is a commercially available product called The Myproclear, which shows efficacy in reducing axial elongation, it is designed to be used at home.

Interestingly, red light therapy appears to be increasingly effective in treating other eye conditions, including AMD, D.E.D., etc.

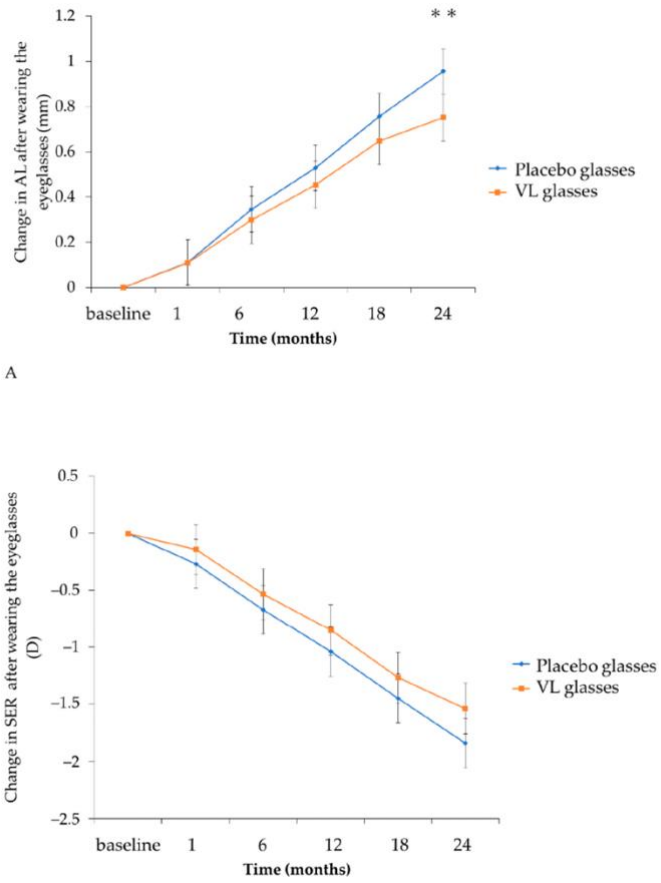
Tsubota Lab Violet Lens

There is widespread evidence that outdoor time is effective at preventing the onset of myopia in very young children. Some more recent studies have cast doubt on the effectiveness of outdoor time in slowing myopia progression once it has begun. However, those studies also concluded that the other benefits of outdoor time could not be overemphasised, so advice on getting kids outdoors needs to remain.

The reason outdoor time appears effective at preventing the onset of myopia is not fully understood, but many theories revolve around exposure to violet light (360-400nm). Ultimately, this is essentially UVA light (UVA (315-400 nm) UVB (280-315 nm) U.V.C. (100-280 nm)).

It is not possible normally to get exposure to this light indoors. Several studies have shown that wearing specific filters in spectacles or contact lenses can help to reduce axial elongation. However, the relative efficacy of the available products seems low compared to other therapies, but perhaps incorporating a filter to enhance violet light exposure into other therapies might show promise. There is, of course, a controversy around blue light exposure risk, so it's this type of therapy may remain controversial.

Mori, K.; Torii, H.; Hara, Y.; Hara, M.; Yotsukura, E.; Hanyuda, A.; Negishi, K.; Kurihara, T.; Tsubota, K. Effect of Violet Light-Transmitting Eyeglasses on Axial Elongation in Myopic Children: A Randomized Controlled Trial. J. Clin. Med. 2021, 10, 5462.



Pharmaceutical MM (Myopia Management) Therapies

There is much evidence to support the effectiveness of pharmacotherapies in myopia management. Low-dose Atropine (LDA) drops have shown considerable promise, but other pharmaceuticals are also being trialled for MM.

Low Dose Atropine

Most studies have shown using low-dose Atropine (LDA) drops in a daily or twice-daily regimen has a substantial effect in reducing myopia progression. Some studies even suggest a dose/response relationship, with higher doses reducing progression rates further.
Studies of the effects of very long-term use of Atropine are yet to be concluded, but increasingly it is considered safe. There was an issue in Australia where pharmacists made up Atropine for optometrists with incorrect doses, including 0.1% and even 1% in one case. Commercially produced solutions will avoid this issue.

The reason for LDA's effectiveness is unclear, as accommodation control does not seem to work in myopia management. Instead, some effect on scleral and retinal muscarinic receptors leads to a reduction in scleral matrix production, thus halting the growth of the globe.

One significant issue is the risk of 'rebound', which is the marked increase in axial elongation once therapy has ceased. Therefore, it is suggested that LDA be tailed off

gradually and should perhaps be continued into the patient's early twenties in some cases.

Dosages generally range from 0.01% to 0.05%, though some suggest higher doses. Side effects such as blurring, mild photophobia, headaches, ocular surface irritation, and even feeling faint are more common in higher doses.

Many of the key studies (LAMP, ATOM1 and 2) were performed on Asian children, so some clinicians are concerned about the relative efficacy of LDA on children with different ethnicity. However, considering the higher predisposition to myopia in Asian children, it may well be that LDA is more effective in children from other ethnicities.

Numerous ongoing studies have recently shown the efficacy of several commercial preparations of LDA in various doses. Studies like CHAMP, MOSAIC and others have shown the effectiveness of several brands of LDA, including SYD-001 from Sydnexis (0.01 and 0.03%), NVK-002 from Nevakar and others which will soon be commercially available in Europe. Currently, there is no clarity on who can prescribe these commercially available drops if and when they are available in the U.K.

Pirenzepine

Pirenzepine is an antimuscarinic agent normally used in treating peptic ulcers, but it has effects on Accommodation and pupil size in a similar way to Atropine in low doses.
Pirenzepine effectively prevented the axial elongation associated with experimental myopia in a dose-dependent manner and via a functional, nontoxic mechanism. Pirenzepine also produced less effect on the pupil. Further studies continue to show that 2% Pirenzepine is safe and effective for myopia management. Pirenzepine is an orally delivered pharmacotherapy.

7-Methylxanthine (7MX – a derivative of caffeine)

7-Methylxanthine (7-MX), also known as hetero-xanthine, is an active metabolite of caffeine (1,3,7-trimethyl xanthine) and theobromine (3,7-dimethylxanthine). It is a non-selective antagonist of the adenosine receptors.

It has been postulated that 7MX could also be effective at reducing axial growth.

Several studies have shown efficacy using this medication. Animal experiments have shown an increase in the thickness and density of the sclera, creating a more rigid eye less capable of axial elongation.
Again, studies continue, but safety tests have shown no toxicity.

Experimental Eye Drops/therapies

- Ketorolac tromethamine
- Oral Riboflavin
- BHVI2
- Dopamine

- Nitric Oxide
- GABA
- Scleral collagen cross-linking (using Riboflavin)

Other drugs, such as those listed, are being trialled in numerous studies, some of which are oral medication rather than eye drops.

Behavioural MM Therapies

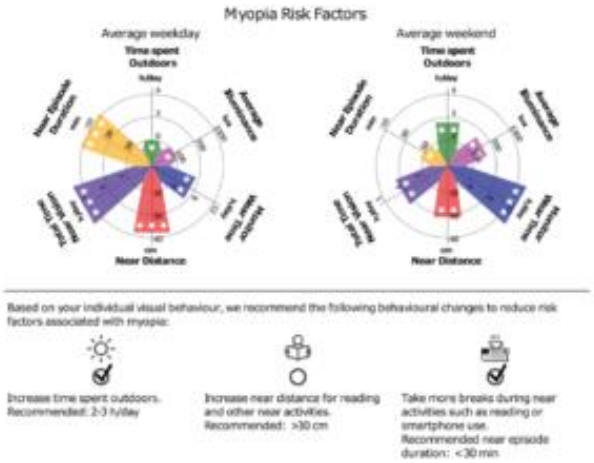
- Increase time spent outdoors (avoiding near work whilst outside too).
- Take visual breaks (20-20-2 rule, for example – spend 20 minutes doing close work then have a 20-minute break looking into the distance and ensure you spend at least 2 hours outside daily).
- Increase working distance for smartphones, tablets, computers, homework, etc.
- Better 'sleep hygiene', earlier to bed, dark rooms with no night lights or artificial light, longer time asleep.
- Less blue light activity before going to bed.
- Improved lighting – including 'redder' lighting before sleep.
- Healthier diet, more exercise, and reduce obesity.
- Improved ventilation.
- Optometrist led improvement Accommodation and vergence / improved binocular fusion.

Measure the daily tasks – Vivior (A.I. assistance)

This fascinating device is often used in refractive and premium IOL cataract surgery. It is a camera fitted to the patient's spectacles, and, over a few days, it monitors the range of customary viewing distances and the general proportion of different viewing distances.

This allows surgeons to help choose the patient's most effective lens or treatment type.

Vivior has since considered the application of this device for children to better understand their viewing habits, and, with the analysis of lighting levels, it can also help practitioners build a more realistic picture of the child's lifestyle. It could make the difference in choosing between certain different therapies.



The reports generated by using the spectacle camera can help provide more evidence-based advice for the patient and the parents.

Combination MM Therapies

- Atropine 0.01% and Ortho-K
- Soft contact lenses and MM spectacles
- Behavioural with other interventions

There is significant evidence to support the use of combination therapies. Two of the most successful therapies, LDA (low dose Atropine) and Ortho-K, can easily be used together to enhance the overall effect of minimising globe elongation (increasing axial length).
This combination therapy, particularly with 0.01% Atropine, helps the child to play sports and get outside more whilst not affecting pupil size and blur too much.

When a child has soft contact lenses, such as dual focus, it's imperative that they also have spectacles to wear when not wearing the contact lenses or if a lens falls out, for example. The spectacles should, of course, also be for myopia management, so ultimately, this is a combination therapy.

Finally, with all interventions for myopia management, it's important to remember that behavioural and lifestyle recommendations should be combined with the other prescribed therapies. So, for example, it could be that a child is asked to do the following:

- Wear dual-focus soft contact lenses during the week at school.
- Wear HALT, DIMS, or D.O.T.-type spectacles when not wearing contact lenses.
- Play more sports and get outdoors more with soft contact lenses (for example – easier with Ortho-K, perhaps).
- Hold near work and smartphones further away and take more regular breaks with increased distance viewing (20,20,2 rule).
- Improve sleep habits and reduce the use of blue light near bedtime.
- Perform the binocular function exercise set by the optometrist.

Such an example shows that MM is really a combination therapy approach.

Gene Therapy

Ultimately, it would be possible to write volumes on Gene Therapy just for myopia. As previously discussed, numerous genes have been identified that are associated with myopia and its progression. Likewise, numerous genes are being identified, which may help to inhibit globe elongation.

There is much ongoing research into what genes and systemic compounds are at play in promoting or inhibiting myopic progression. Some examples of current studies include:

- Is the absence of the protein megalin responsible for high myopia? Dr Tina Storm, U.C.L. Ophthalmology.
- Identifying genetic risk factors for myopia and retinal detachment. University of Edinburgh, Dr Veronique Vitart.
- Understanding the chemical messages between sclera and choroid linked to myopia progression. Prof. Maryse Bailly, U.C.L. Ophthalmology.

Anisometropic Amblyopia Therapies

It's important to remember that in some cases, particularly where there is considerable anisometropia, some children will have a degree of amblyopia. Furthermore, there will be many myopic (and hyperopic) adults who have a degree of anisometropic amblyopia.

It is now possible to improve the B.C.V.A. in anisometropic amblyopic eyes considerably, often by 3-4 lines on the chart. This is made possible by new 'gamified' therapies, usually conducted on a computer (often remotely online), where temporary occlusion of the non-amblyopic eye takes place whilst complex visual tasks are completed by the patient.

Success in such therapies is no longer considered exclusively viable before what we used to call the 'plastic period'. In fact, it appears that these therapies remain effective into old age.

There are a plethora of new companies now offering these specialised, complex vision therapies. Some examples of those in the market include:

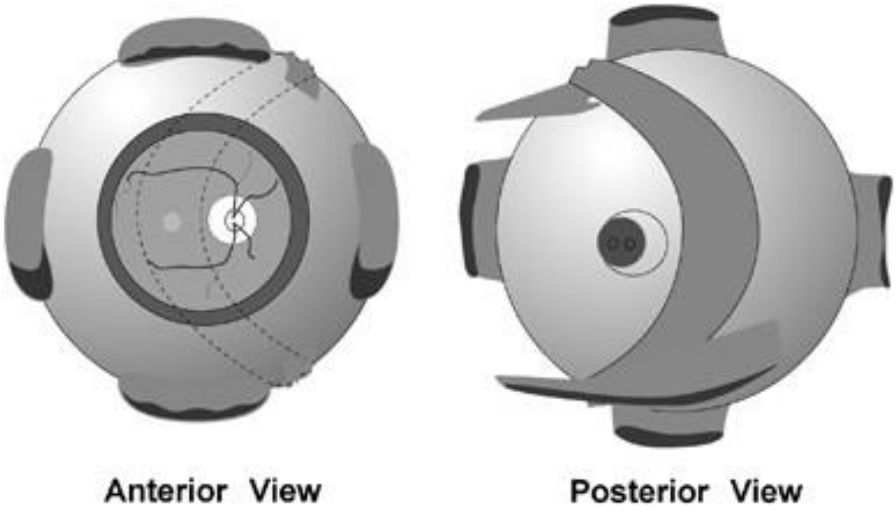
- Revitalvision
- Bynocs
- Amblyoplay

Scleral buckle for high myopia

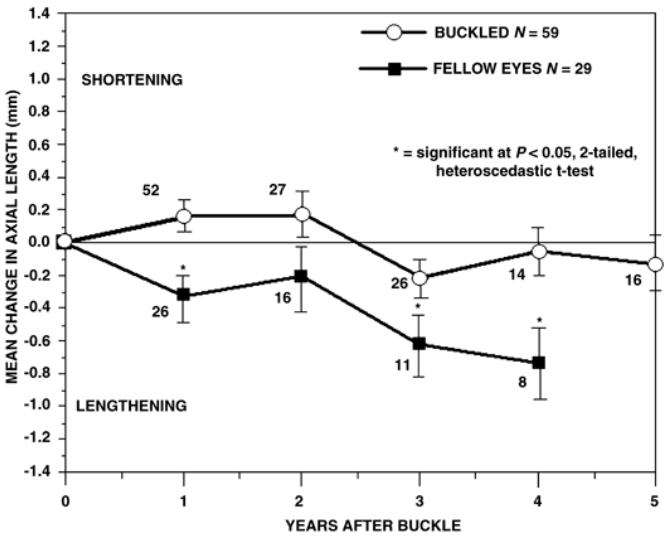
First considered as a treatment option for very high pathological myopes some fifty years ago, scleral buckling is increasingly considered as a potential therapy for slowing continually progressive myopia in adults and as a way to reduce the damage caused by this condition.

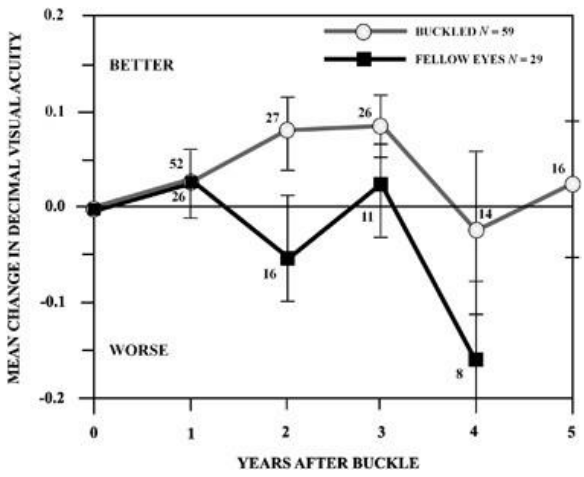
Normally, this relates to very high myopia - the pathologic axial myopes, who make up about 0.3% of myopes overall. However, as techniques improve and as more people become moderately myopic, it is feasible that this technique may become more widespread.

A study published in Nature (*Eye* **23**, 2169–2174 (2009)) showed improved patient outcomes where buckling was performed compared to untreated eyes.



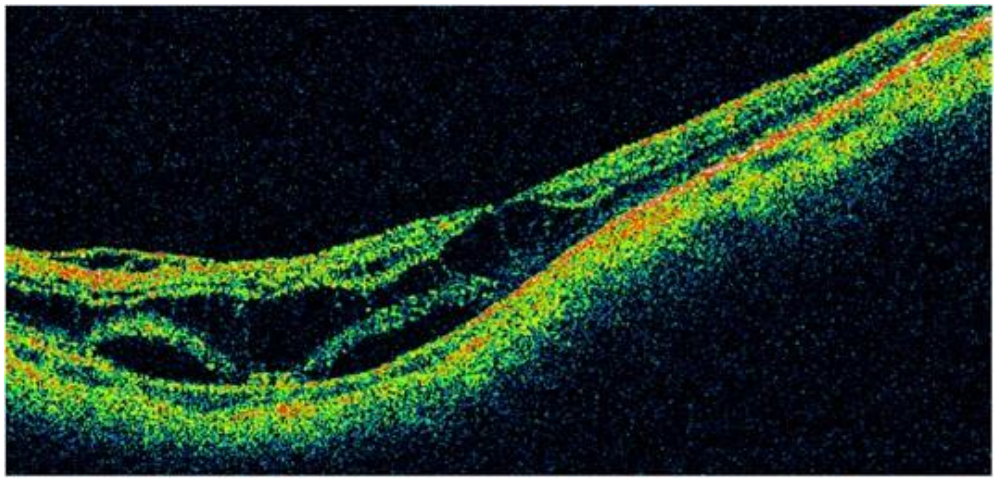
A tight buckle is placed around the posterior pole to prevent the sclera from continuing to move posteriorly.



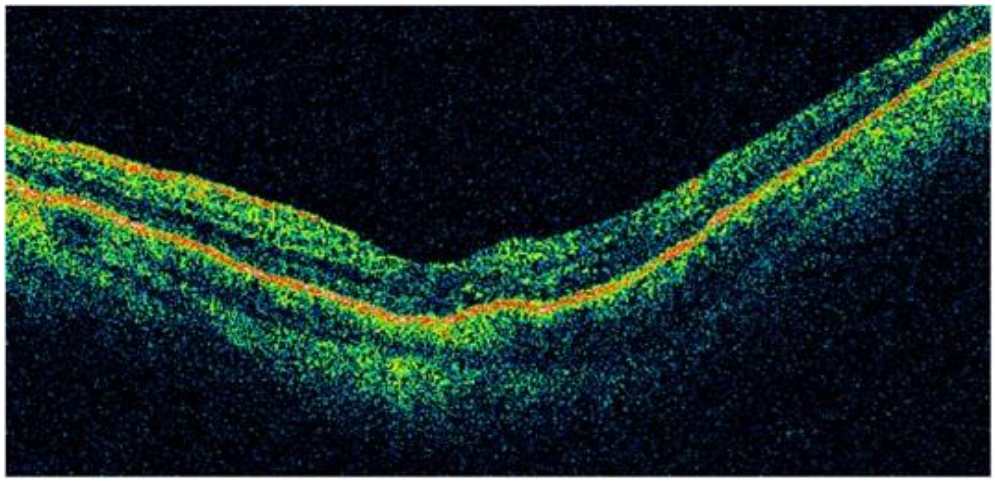


A five-year follow-up study showed that patients found that the scleral buckle had improved their vision, and it was clear that axial elongation was slowed in comparison to the untreated eyes.

Most interestingly, the retinoschisis, which was present in one patient's eyes, resolved after the buckle was inserted. The risk of retinal detachment and sight-threatening complications was reduced significantly in this patient. The OCT images on the next page show the positive effect described.



The upper image shows pre-buckle retinoschisis, and the lower image shows a much more 'settled' retina. This improves the long-term visual prognosis for this patient.



Summary

It's evident that there are numerous treatment options for children facing progressive myopia. However, as just discussed in the last few pages, we must not forget that myopia management is a 'cradle to grave' undertaking for clinicians.

Once a patient develops myopia, they, of course, will require a refractive correction for that condition. Eventually, we must remember that this might include refractive surgery of some form. However, this does not mean they are now 'cured', and, of course, the issue, long axial length, remains.

All our long A.L. patients will require lifelong screening for the secondary complications caused by this axial elongation. Beyond doing all we can to reduce the eventual degree of axial elongation, we must also ensure we check specifically for the comorbidities that such patients face. Just as we would screen for glaucoma in those at higher risk, such as siblings of existing glaucoma patients, we must also ensure that we do all we can to have all members of a myopes family screened for the condition and, if they are older existing myopes, the secondary conditions they may be at higher risk of.

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