

Position Paper

Myopia management: a comprehensive approach

September 2022

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1. Executive Summary

This position paper follows on from an earlier recommendation promoted by the European Council of Optometry and Optics –ECOO- in collaboration with the European Academy of Optometry and Optics -EAOO- (ECOO 2020, available at: <u>https://www.ecoo.info/2021/05/position-paper-on-myopia-in-the-21st-century-its-management-by-ecps/</u>).

This document considers the World Council of Optometry 2021 resolution on myopia management standard of care, considering three main components (WCO 2021 available at https://www.iapb.org/news/world-council-of-optometry-passes-resolution-calling-for-a-standard-of-care-for-myopia-management/):

- <u>Measurement</u>: "optometrists evaluating the status of a patient during regular comprehensive vision and eye health exams, such as measuring refractive error and axial length whenever possible". This is covered in sections 3 and 4.
- <u>Management</u>: "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". This is covered in sections 5 and 6.
- <u>Mitigation</u>: "optometrists educating and counseling parents and children, during early and regular eye exams, on lifestyle, dietary, and other factors to prevent or delay the onset of myopia". The role of stakeholders (see section 7) to promote this domain should not be dismissed.

A comprehensive examination of the myopic patient should include the following aspects:

- a) <u>History taking</u> to understand the <u>risk factors</u> for myopia onset and/or fast progression. This includes family history, age, current refractive status, prescription changes or time spent in indoor and outdoor activities.
- b) <u>Evaluate the presenting visual condition</u>, including refractive, accommodative, binocular vision and ocular health status in consideration for eventual treatment requirements and future follow-up.
- c) <u>Decide</u> which <u>preventive</u>, <u>corrective</u> or <u>management</u> <u>methods</u> can be applied to prevent myopia onset or retard myopia progression.</u>
- d) <u>Monitor the evolution</u> of the ocular condition to promote the early diagnosis, treatment and referral if necessary.

When faced with premyopic or myopic patients, the main goals for an eye care professional (ECP) shall be to:

a) Early detection of children at risk of developing myopia;

- Advise on <u>preventive measures</u>, <u>prescribe treatments</u> and keep them updated; and
- c) Establish a <u>follow-up program</u> according to age, level of myopia and clinical signs.
- d) <u>Prescribe</u> myopia management strategies.
- e) <u>Through-life</u> follow-up to early detect signs of pathology.

A summary of recommendations is provided:

- 1. Encourage <u>early and frequent vision evaluation</u> of all children by the age of 6, particularly those showing risk factors for myopia onset.
- 2. <u>Work with stakeholders at the local level</u> to ensure early visual evaluation of all children in order to have the opportunity to provide them with the most effective methods to manage progressing myopia.
- 3. Provide all premyopic or myopic children and their parents or guardians with <u>updated information on methods of myopia management</u>, from good habits for myopia prevention to active treatments for progressing myopia.
- 4. <u>Outdoor activities</u> might be effective to delay or avoid the onset of myopia, but such activities have not demonstrated efficacy to decrease progression rate on those already myopic. <u>Ergonomic advice</u> on indoor lighting, increasing distance for near work is worth providing but its efficacy on delaying myopia onset or reducing myopia progression rate is still to be confirmed.
- 5. The minimum standard of care for a myopic patient is <u>full prescription of the</u> <u>refractive error for continuous use irrespective of the degree of myopia and the</u> <u>progression rate</u>.
- 6. When deciding which myopia management methods to prescribe, consider the limitations that might exist and <u>provide the methods that can be more accessible, effective and that are likely to promote compliance</u> (care and wear time) by the myopic subject.
- 7. <u>Under-correction</u> and <u>single vision correction</u> with spectacles or contact lenses, <u>including conventional rigid gas permeable contact lenses</u> are not effective methods to reduce axial elongation and myopia progression.
- Follow-up closely the premyopic and progressing myopic children to monitor the progression of the condition and <u>do not stop myopia management treatments</u> <u>until they reach adulthood</u> or when an indication of stable refractive status can be verified.
- 9. Care of the <u>myopia patient is a through-life matter</u> starting at childhood through adulthood and into old age.
- 10. <u>Intra-profession and inter-profession referrals</u> should be considered whenever necessary.

2. Introduction

Myopia and the need for intervention to slow-down its progression is a subject tof concern for a specific clinical and scientific community (Rubin and Midler, 1976; Flitcroft, 1998; Schaeffel, 2016). While the high prevalence of myopia is becoming epidemic in some Asian countries (Dolgin et al, 2015), the European population has seen an increased prevalence of myopia by over 3-fold in just 2 generations (Williams et al, 2015) from less than 15% in older cohorts (+70 years old) to over 45% in younger people (up to 25 years old). The accompanying increase in ocular size and associated co-morbidities allow us to anticipate a public health crisis in the medium-term as the number of myopes and high myopes increase.

This position paper follows an earlier recommendation promoted by the European Council of Optometry and Optics – ECOO- in collaboration with the European Academy of Optometry and Optics -EAOO-(ECOO 2020, available at: https://www.ecoo.info/2021/05/position-paper-on-myopia-in-the-21st-century-itsmanagement-by-ecps/). The concept of myopia management in this document reflects all aspects related to the examination, prescription, compensation, intervention in myopia progression and follow-up to the myopic patient. It is therefore a wide concept that does not necessarily include active interventions to interfere with excessive eye elongation. Interventions aimed to interfere with the growth of the myopic eye should be referred to as myopia control or myopia progression management. While it might not be the preferred term by some eye care practitioners or stakeholders, myopia control will be also used as it is still the concept predicated by the International Myopia Institute (IMI) and widely used across the scientific and clinical literature.

Myopia is an increasingly common eye condition that impairs distance vision. It is anticipated that by 2050 half of the world population will be myopic and 10% of the population might be highly myopic (Holden *et al*, 2016). In Europe, there are indications that myopia prevalence has increased by a 2-fold factor for the last three generations (Williams *et al*, 2015). It is noticed by the subject, enabling early diagnosis by eye care practitioners. After diagnosis, the patient will require refractive correction by means of spectacles or contact lenses. Over a period of time, the refractive correction will need to be updated. After stabilization, other therapeutic approaches can be considered including surgical corneal reshaping or intraocular lens implantation.

Despite its appropriate refractive or surgical management, an eye which is myopic to any degree carries an increased risk of moderate-to-severe vision loss and this risk is higher for higher refractive errors (Flitcroft, 2012). After the age of 50 years the risk of having moderate to severe irreversible vision loss increases exponentially for longer eyes (Tideman *et al*, 2016). By the age of 75 it is estimated that 25%, 50% and 90% of eyes with axial length over 26 mm, 28 mm and 30 mm will present uncorrectable visual

impairment. In ageing western societies, this is clearly a public health concern for the coming years. Considering the simultaneous increase in life expectancy, vision loss associated with myopia might be expected to have a great impact over a number of years for many elderly people in the near future.

The increased body of knowledge on myopia and its comorbidities, as well as the evidence of increasing incidence and prevalence boosted a change in the clinical approach to myopia management: from its refractive compensation and refractive update, towards a holistic approach starting before myopia can be clinically diagnosed in a young person and until its potential consequences decades' after the diagnosis in the elderly population. This changing paradigm means that eye care professionals (ECPs) need to be trained and continuously updated on the best practices.

This position paper considers the World Council of Optometry 2021 resolution on myopia management standard of care considering three main components (WCO 2021 *available at <u>https://www.iapb.org/news/world-council-of-optometry-passes-</u>resolution-calling-for-a-standard-of-care-for-myopia-management/):*

- <u>Mitigation</u>: "optometrists educating and counseling parents and children, during early and regular eye exams, on lifestyle, dietary, and other factors to prevent or delay the onset of myopia". The role of stakeholders (see section 7) to promote this domain should not be dismissed.
- <u>Measurement</u>: "optometrists evaluating the status of a patient during regular comprehensive vision and eye health exams, such as measuring refractive error and axial length whenever possible". This is covered in sections 3 and 4.
- <u>Management</u>: "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". This is covered in sections 5 and 6.

A summary of recommendations is provided in section 8.

The goal of this position paper is to contribute to a change in the clinical approach towards myopia, shifting from viewing it purely as a refractive condition into a comprehensive evaluation of risk factors before myopia onset, early diagnosis, consideration of myopia management treatments and follow-up of the myopic person throughout their life to decrease the risk of uncorrectable vision impairment, including moderate-to-severe vision loss. It is not the goal of this position paper to provide detailed information on specific treatments or the details of the clinical trials or body of evidence behind each option.

3. Definition and Classification

According to the International Myopia Institute White paper published in 2019 and updated in 2021 (Wolffsohn *et al.*, 2019a; Jong *et al.*, 2021), myopia is defined as "A refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed. This usually results from the eyeball being too long from front to back but can be caused by an overly curved cornea or a lens with increased optical power, or both. It is also called near sightedness.". Besides "myopia", three other qualitative definitions are made: "axial myopia", "refractive myopia" and "secondary myopia". Four other quantitative definitions are provided: "Premyopia", "Myopia", "Low Myopia" and "High myopia".

Due to the potential value of adequately identifying premyopic subjects its definition is also very relevant in this context "refractive state of an eye of \leq +0.75 D and > -0.50 D in children where a combination of baseline refraction, age, and other quantifiable risk factors provide a sufficient likelihood of the future development of myopia to merit preventative interventions."

4. Risk factors

Early screening and evaluation of children is key to detect those at risk of developing myopia (premyopic), those who have already developed myopia recently, and/or those whose myopia is progressing fast (over 0.50D/year or higher) for appropriate diagnosis, advice and treatment. There are also risk factors that raise awareness at an early stage for the need for closer follow-up because they suggest a greater statistical likelihood for someone to develop myopia in the short term.

<u>Family history</u>: children with one or both biological parents with myopia have an increased risk of developing and achieve higher degrees of myopia (Kurtz *et al.,* 2007).

<u>Presenting Rx</u>: children with low hyperopia or emetropia before the age of 8 have a higher likelihood of becoming myopic (Jones-Jordan *et al.*, 2010).

<u>Outdoor time</u>: children who spend less time on outdoor activities are more likely to develop myopia (Rose *et al.,* 2008).

<u>Ethnicity</u>: East Asian ethnicity has been associated to higher degrees of myopia and faster progression (Dolgin *et al.*, 2015; Mutti *et al.*, 2007). There are geographical, cultural and educational factors interacting with this factor. In fact, some studies have demonstrated that Asian and Caucasian people raised in the same geographical location present similar progression rates (French *et al.*, 2013).

<u>Other risk factors</u>: many other different risk factors have been identified in different studies including indoor lighting, distance for near vision work/activities, use of digital devices, educational level achieved, etc. However, the conclusions on these factors are still somewhat controversial between different studies. Despite this, ergonomic advice should be provided.

Though many of these risk factors might interact with each other, those children presenting one or more of the aforementioned factors should be considered at higher risk and followed closely for early myopia onset detection and appropriate management (Mutti et al, 2002; Verhoeven et la, 2013).

5. Examination of the myopic patient

The current approach to myopia management requires a comprehensive analysis of the patient. This should include refractive history, visual acuity, refractive error, binocular vision and accommodation as well as ocular health examination (Gifford *et al.*, 2019). Whenever possible, axial length should be a relevant part of the examination. However, not having a biometer should not be a definitive barrier for myopia control. Cycloplegic refraction might be required in some young subjects to accurately determine their initial refractive error and its progression. However, cycloplegic refraction should not be necessary in most cases where accommodative control can be secured by objective and subjective refractive methods that allow the ECP to reach an accurate conclusion.

Other exams might be necessary in order to prescribe some treatments, such as corneal topography which is an essential part of the orthokeratology treatment.

A comprehensive examination of the myopic patient should include the following aspects:

- a) <u>History taking</u> to understand the <u>risk factors</u> for myopia onset and/or fast progression. This includes family history, age, current refractive status, prescription changes or time spent in-indoors and outdoor activities.
- b) <u>Evaluate the presenting visual condition</u>, including refractive, accommodative, binocular vision and ocular health status in consideration for eventual treatment requirements and future follow-up.
- c) <u>Decide</u> which <u>preventive</u>, <u>corrective</u> or <u>management</u> <u>methods</u> can be applied to prevent myopia onset or retard myopia progression.</u>
- d) <u>Monitor the evolution</u> of the ocular condition to promote the early diagnosis, treatment and referral if necessary.

Regular follow-up visits should be prescribed to ensure that the refractive error is constantly updated and whenever possible check for potential axial length changes.

Initial follow-up visits can be set at a higher frequency (i.e. 3 months intervals) to check for potentially rapid changes in refractive error and axial length. Further, in fast progressors (>0.50D/year), follow-up should be done every 3 months, while slow progressors (≤0.50D/year) can be done every 6 months. Some treatments with potential side effects (contact lenses, orthokeratology, atropine) can require more frequent visits.

6. Current approach to myopia management

When faced with premyopic or myopic patients, the main goals for an ECP shall be:

a) Early detection of children at risk of developing myopia;

b) Advise on preventive measures, prescribe treatments and keep them updated; and

c) Establish a <u>follow-up program</u> according to age, level of myopia and clinical signs.

d) Prescribe myopia management strategies.

e) <u>Through-life</u> follow-up to early detect signs of pathology.

The science and clinical paradigm on myopia and myopia management is continuously evolving and these perspectives might change as knowledge advances. While the interventions for visual acuity, accommodation and binocular vision restoration and optimization are part of the conventional approach to myopia management (<u>myopia compensation</u>), the following sections of this paper are focused on interventions intended to interfere with the natural elongation of the myopic eye and increase of the myopic prescription (<u>myopia control or myopia progression management</u>). Below is a presentation of the treatments depending on their efficacy to interfere with the natural course of growth and refractive deterioration of the myopia eye.

<u>Non-effective interventions</u>: ECPs should be aware of those treatments with no efficacy in myopia control. This is particularly relevant as some have been used and promoted for several decades.

<u>Single vision spectacles or contact lenses, including rigid gas permeable contact</u> <u>lenses</u> (Walline *et al.*, 2004) does not reduce axial elongation or rate of myopia progression.

<u>Conventional Bifocal or progressive addition lenses (PAL)</u> primarily used for presbyopia correction have shown very limited efficacy in reducing the rate of axial elongation and myopia progression (COMET group 2011; 2013).

<u>Visual therapy</u> to improve accommodation response in myopes did not show consistent efficacy to reduce axial elongation or myopia progression (Allen *et al*,

OPO 2013). While some myopic patients might benefit from visual therapy interventions to improve their binocular vision and/or accommodative function, current evidence does not support its use as treatments to decrease myopia progression.

<u>Special short-wavelength filters, i.e. blueblockers</u>, have gained popularity during the last decade and are often marketed as "premium" products in terms of ocular and general health. These lenses have however shown no beneficial effect in terms of slowing myopia progression.

<u>Passive interventions</u>: includes approaches where no treatment is provided. Instead, more outdoor activities are recommended to reduce the risk of myopia onset (Xiong *et al*, 2017) or ergonomic advice is provided for near vision activities (distance, illumination, posture, breaks).

<u>Active interventions</u>: there are currently interventions with proved efficacy in reducing the likelihood of developing myopia and mainly to reduce the progression of myopia in those who have already developed it. Due to their relevance in everyday clinical practice, these are detailed in the next section.

Whenever an active intervention is to be applied, the use of an Informed Consent Form is advised. The ECP should inform the patient and her/his parents or guardians in writing about the purpose, method used, intended effect, benefits and risks associated with the treatment. Additionally, the ECP might incorporate the schedule for follow-up. This document should be adapted to the treatment prescribed, professional context and national legislation. Consent has to be given by parents or guardians, and it is desirable that children also provide their agreement.

6.1 Myopia management scope of practice across Europe

The availability of these treatments for patients might be limited depending on scope of practice of ECPs country-to-country (ECOO Blue Book, 2022). **Table 1** below describes the level of myopia management intervention and the coverage of such treatments by public and private health insurance systems.

Table 1. Scope of practice connected with myopia management across Europe with focus on potential restrictions to examination, prescription, management and treatment or referrals. Source: ECOO 2020 Blue book.

Country	Exam	Optical Rx	Myopia	Treatment	Referral
	Restriction	Restriction	Management	Restriction	Opht/Hos
Austria	None	None	Authorised	Atr	Authorised
Belgium	<12	None	Practised	Atr	Authorised
Bulgaria	<12	None	Practised	Atr	Opth/Hos
Croatia	None	None	Authorised	Atr	Practised
Cyprus	None	None	Authorised	Atr	Practised
Czech Republ.	<12	None	Authorised	Atr	Opth/Hos
Denmark	None	None	Authorised	Atr	Opth/Hos
Estonia	None	None	Authorised	Atr	Authorised
Finland	<6	None	Authorised	Atr	Opth/Hos
France	<12	CL/SP	Authorised	Atr	Authorised
Germany	None	None	Authorised	Atr	Authorised
Greece	None	None	Authorised	Atr	Opth/Hos
Hungary	<6	CL/SP	Prohibited	Atr	Authorised
Ireland	None	None	Authorised	Atr	Authorised
Italy	None	None	Authorised	Atr	Authorised
Latvia	<12	None	Authorised	Atr	Authorised
Lithuania	<12	None	Prohibited	Atr	Authorised
Luxembourg	None	None	Authorised	Atr	Opth/Hos
N. Macedonia	<12	CL	Authorised	Atr	n.a
Malta	None	None	Authorised	Atr	Authorised
Netherlands	None	None	Authorised	Atr	Authorised
Norway	None	None	Authorised	Atr	Authorised
Poland	None	None	Authorised	Atr	Opth/Hos
Portugal	None	None	Authorised	Atr	Practised
Romania	None	None	Authorised	Atr	Opth/Hos
Serbia	None	None	Authorised	Atr	Prohibited
Slovenia	None	None	Authorised	Atr	Practised
Spain	None	None	Authorised	Atr	Practised
Sweden	<6	None	Authorised	Atr	Authorised
Switzerland	None	None	Practised	Atr	Authorised
Turkey	<12	None	Authorised	Atr/Cls	Practised
United Kingdom	None	None	Prohibited	None	Authorised

Eye care practitioners (ECP): OPM: optometrists; OPC: optician Treatments (Tx): Atr: atropine; Cls: contact lens; Spec: spectacles Referrals: Oph: ophthalmologist; Hos: eye hospital Others: Rx: prescription; n.a: information not available

7. Interventions

Interventions available to ECP can vary country to country across Europe due to country-specific scope of practice or due to industry options. Currently, the options for an ECP go from advising premyope patients on behaviours that can reduce the likelihood to become myope (*Outdoor time*), to myopia correction (*Single vision Spectacles and Single vision Contact Lenses*), to actively preventing myopia progression with optical interventions (*Orthokeratology*, *Multifocal Contact Lenses*, *Contact lenses and Spectacle lenses designed for myopia control*) and pharmaceutical interventions (*Low or medium dose atropine*).

ECPs making clinical decisions should be guided as much as possible by the outcomes of randomized clinical trials (RCT), multicentric whenever possible, or meta-analysis of RCT. The treatments to manage myopia control should be stated during the rapid growth period following myopia onset (Thorn et la, 2005; Mutti et al., 2007). Delaying the start of treatment might result in lower overall effectiveness of the treatment in the longer term (Bullimore and Brennan, 2019).

However, ECPs should be cautious when communicating expectations to patients and parents/guardians. Most studies provide treatment effects from clinical trials conducted over 2 to 3 years. Only a few studies have followed patients for longer periods (see for example Hiraoka *et al*, 2012 or Chamberlain *et al*, 2022). However, as the treatment effect tends to be maximal for the first year of treatment, the shorter the follow-up period, the higher the average effect size will be, but this should not be extrapolated over a longer period of time (Kaphle et al, 2020).

ECPs should also bear in mind that in most cases, if the devices are not used, the therapeutic effect is expected to decrease (Lam et al, 2014). Therefore, the results reported in the literature should be observed in those specific conditions of application, and not extrapolated to other cases (i.e. similar but not the same optical designs, dosages, wearing schedule, frequency of application, sample characteristics, etc).

Sub-sections below provide more detail on each type of treatment approach depending on the clinical option agreed between the eye care practitioner and the parents and patients. The standard examination presented in section 4 will be applied to each of the following treatments, while other specific exams required or recommended will be mentioned accordingly. For further detail consult IMI report on interventions (Wildsoet et al., 2019) as well as published reports on randomized controlled clinical trials, systematic reviews and/or meta-analysis.

Most mechanisms of action shown below are tentative explanations as the actual fundamental physical, biological and biochemical mechanisms are presently unknown.

7.1 Outdoor time

<u>Outdoor time</u> should be advised to premyopes as a measure to reduce the likelihood of developing myopia. Previous research has confirmed that additional outdoor time can delay the onset of myopia in children.

<u>Indication</u>: all children, particularly those at risk of developing myopia (premyopes).

<u>Mechanism of action</u>: exposure to high levels of light with more short wavelength spectral composition might be involved.

<u>Advantages</u>: non-invasive, does not require any prescription, might limit the time in other myopiogenic and self-isolation indoor habits.

<u>Limitations/challenges</u>: requires the child to change her/his habits which is usually difficult.

<u>Restrictions</u>: might be more difficult to reconcile with higher educational demands as children grow-up or are in highly demanding educational context.

Specific exams: does not require any specific exam.

<u>Prescription</u>: recommended to increase as much as possible the exposure to outdoor activities. The need for protection against damage from radiation (UV) should be emphasized.

<u>Efficacy</u>: every 2 additional hours of weekly exposure to outdoor activities reduces by 2% the chances of becoming myopic. No known efficacy on myopia progression.

<u>Side effects</u>: no visual side effects besides episodes of photophobia, glare, etc. Possibility of sunburn if not properly protected (skin and eye).

7.2 Single vision spectacle lenses and contact lenses

<u>Single vision CL and spectacle lenses</u> are the minimum standard of care. When myopia is detected, the very minimum that should be done is to correct myopia and advise the use of the optical correction for all activities, including near work. Single vision prescription might be usual as a first step while assessing progression.

<u>Indication</u>: all myopic children should at least receive a full myopic prescription as soon as they are diagnosed.

<u>Mechanism of action</u>: single vision correction provides a sharp image on the retina to reduce the chances of faster progression due to deprivation-driven axial elongation.

<u>Advantages</u>: good quality of vision. Widely available in all practices. Contact lenses provide benefits over spectacles in terms of self-perception of young children (Walline et al, 2007).

<u>Limitations/challenges</u>: does not interfere with myopia progression in the way other available treatments do. Requires compliance to keep the retinal image in focus all time. Compliance might be lower in spectacle lens wearers that dislike to use them. Contact lens wearers might skip some days of wearing their lenses. Compliance might be lower in low-to-moderate young myopes who do not rely on their prescription to have a minimally functional vision for their daily activities.

<u>Restrictions</u>: limitation in access to prescription foro economic reasons.

Specific exams: does not require any specific exam.

<u>Prescription</u>: full prescription, for constant use (distance and near work), update as required.

<u>Efficacy</u>: though it reduces the myopia progression compared to under correction or no correction, it does not provide additional efficacy in terms of myopia control.

<u>Side effects</u>: no visual side effects. Contact lenses might increase the risk of adverse events compared to spectacles.

7.3 Orthokeratology

<u>Orthokeratology</u> has become increasingly used for myopia control since 2005. Cohort studies and controlled clinical trials, including some randomized trials, have shown consistently that orthokeratology reduces the rate of axial elongation and myopia progression in children aged 8 to 12 years of age (Sun et al., 2015; Huang *et al*, 2016).

<u>Indication</u>: any progressing myope who can be fitted with orthokeratology lenses.

<u>Mechanism of action</u>: stigmatic defocus induced for off-axis refracting light changes the focalization and contrast in the retinal image, presumably driven signals for slower axial growth.

<u>Advantages</u>: once the treatment is stabilized, provides constant therapeutic effect, maximizing compliance. The lenses are used only under home/parental supervision and are not used outside.

<u>Limitations/challenges</u>: treatment might not be applicable in some patients whose corneal topography and/or refractive error falls off the range of application of the corneal reshaping lens. Some patients and their families might be more reluctant to choose this treatment as lenses are less comfortable in the

short term, requires the child to sleep in lenses, and the high costs of this specialty treatment.

<u>Restrictions</u>: available only at specialized practices. Might not be applicable in patients with epithelial fragility showing recurring corneal erosion, lens binding, etc, that cannot be solved by refitting.

<u>Specific exams</u>: besides a comprehensive ophthalmic examination, requires close evaluation and follow-up of corneal topography.

<u>Prescription</u>: lenses should fully correct the refractive error and keep good visual acuity throughout the day.

<u>Efficacy</u>: different studies conducted with different lens designs in different countries/ethnic groups showed similar efficacy ranging from 30 to 60% (Cho and Cheung, 2012; Santodomingo-Rubido et al, 2012; Hiraoka et al, 2012).

<u>Side effects</u>: recurrent corneal erosion, decrease in retinal image quality and contrast sensitivity, glare and haloes, decreased visual acuity in the end of the day. Adverse events might be more frequent with orthokeratology when compared with spectacles or other modalities of daily contact lens wear.

7.4 Bifocal and multifocal contact lenses

<u>Bifocal and multifocal contact lenses</u> can be an option for an ECP without access to specially devised treatments. These are usually contact lenses primarily designed for presbyopia correction. Mostly they are two-zone or multiple concentric-zone bifocal contact lenses or center-distance multifocal contact lenses (Li *et al.*, 2017).

<u>Indication</u>: any progressing myope who cannot be fitted with another more specific and dedicated method for myopia control.

<u>Mechanism of action</u>: astigmatic defocus induced for off-axis refracting light changes the focalization and contrast in the retinal image, presumably driven signals for slower axial growth.

<u>Advantages</u>: widely available in regular practices fitting bifocal/multifocal contact lenses. Same parameters are suitable for myopic children.

<u>Limitations/challenges</u>: treatment might not be applicable for some patients whose refractive error falls off the range of application. Some patients and their families might be more reluctant to choose the fitting of contact lenses in young children.

<u>Restrictions</u>: in myopes with astigmatism, only a limited number of multifocal/bifocal lenses might provide simultaneous astigmatic prescription.

<u>Specific exams</u>: besides a comprehensive ophthalmic examination, suitability for contact lens wear and fitting process should be established.

<u>Prescription</u>: lenses should fully correct the refractive error and keep good and comfortable distance and near visual acuity throughout the day.

<u>Efficacy</u>: different studies conducted with different lens designs showed efficacy ranging from 20 to 50%.

<u>Side effects</u>: decrease in retinal image quality and contrast sensitivity, glare and haloes, decreased visual acuity in the end of the day. Adverse events might be more frequent with contact lenses when compared with spectacles. Young age does not present additional risk of adverse events compared to young adults.

7.5 Specially designed contact lenses

There are several contact lens designs specifically developed for myopic children. They can be categorized into <u>dual focus</u> contact lenses incorporating three or more concentric zones alternating between distance and treatment power, or peripheral gradient contact lenses that incorporate a positive power in a peripheral area around a central distance zone dedicated to the distance prescription. The main purpose of these optical designs is to induce myopic astigmatic defocus for light entering the eye at increasing angles from the line of sight, with the aim to provide visual signals that inhibit eye elongation.

<u>Indication</u>: children and adolescents who can be fitted with contact lenses and are able to wear, handle and care for contact lenses, with good hygiene habits and are able to attend follow-up visits to check prescription and ocular surface health status. Current contact lens wearers or those where contact lenses are used for other reasons such as sports.

<u>Mechanism of action</u>: change the retinal image quality by providing a dual/bifocal, multifocal or increased depth of focus effect and peripheral myopic astigmatism defocus.

<u>Advantages</u>: contact lenses promote compliance with the treatment and can be handled in the family environment, when frequently replaced or daily disposed it allows for quick update of prescription, are more convenient to practice sports and well accepted by children or adolescents who dislike wearing glasses.

<u>Limitations/challenges</u>: might be available only in specialized practices. Might not be available in some countries. Some devices might be limited to compensation of spherical refractive errors, leaving astigmatism uncorrected, might require slightly longer chair time compared to spectacle prescription.

<u>Restrictions</u>: should not be prescribed to children that do not meet the criteria to wear contact lenses, or do not demonstrate autonomy for their insertion, removal and care after first weeks of wear.

<u>Specific exams</u>: besides a comprehensive optometric examination, keratometry or corneal topography should be required to assess potential molding effects on the cornea.

<u>Prescription</u>: most lenses provide a single set of diameter and base curve, so check for proper fitting; besides distance refractive error correction, treatment power use to be constant for each device, so check for satisfactory visual outcomes at distance and near vision before prescription.

Efficacy: Specially designed contact lenses have been marketed by several manufacturers in the last decade. Their efficacy has been shown in randomized controlled clinical trials, including some double-blind trials. These include dual-focus lenses, extended depth of focus or peripheral gradient lenses designed for children with myopia, taking advantage of their larger pupils to provide larger areas dedicated to distance vision (Chamberlain et al., 2019; Sankaridurg et al., 2019). To date, availability of these devices is limited in some regions. In a study conducted in Spain (Ruiz-Pomeda et al., 2018), daily use of dual focus lenses (MiSight, Coopervision) resulted in 0.22 mm shorter eye elongation compared to spectacle lens wearers over a period of two years in 8-12 years-old children with baseline myopia of -0.75 to -4.00D. Another study, again in Spain (Paune et al., 2015), evaluated the efficacy of a peripheral gradient contact lens compared to orthokeratology and single vision spectacles over two years resulting in 0.14mm/0.42 D less elongation/myopia progression in the peripheral gradient contact lens group compared to the single vision spectacle control group. Limitations to this study included its non-randomized nature and eye length being measured with ultrasound biometry. A multicentric randomized, controlled double-blind clinical trial with the MiSight contact lens involved 4 sites including 1 site in the United Kingdom and 1 site in Portugal. The results of this trial showed that over three years of lens wear eyes wearing the test lens were 0.32mm/0.65D lower elongation/myopia progression compared to the single vision contact lens wearers in the control group over three years follow-up (Chamberlain et al., 2019). Further information on the long-term results of this trial have been recently published showing that the device is effective in the long term up to six years of treatment, is effective for those children treated later after three years in the control group (Chamberlain *et al.*, 2022).

<u>Side effects</u>: visual complaints in the short-term in the form of haloes, handling issues, non-compliance (wear regime, replacement schedule, follow-up visits), contact lens related adverse events have been described in some trials. Contact lenses carry an increased risk of cornea and ocular surface adverse events. No clinical trial reported contact lens related serious adverse events that impaired visual acuity showing that the treatments can be considered safe.

7.6 Specially designed spectacle lenses

<u>Specially designed spectacle lenses</u> have been marketed by several manufacturers. Their efficacy has been shown in randomized controlled clinical trials, including some doubleblind trials. These include executive bifocal lenses with or without prismatic prescription, peripheral defocus spectacles, multisegment defocus spectacle lenses, among others (Cheng et al, 2012; Cheng *et al.*, 2014; Lam *et al.*, 2017; Bao *et al.*, 2022), while other designs showed much lower efficacy (Kanda *et al.*, 2018).

Indication: any progressing myope.

<u>Mechanism of action</u>: astigmatic defocus induced for on-axis and off-axis refracting light changes the focalization and contrast in the retinal image, presumably driven signals for slower axial growth.

<u>Advantages</u>: only requires the prescription of spectacle lenses which is a wellaccepted regular practice for children by every ECP.

<u>Limitations/challenges</u>: might be available only in specialized practices. Might not be available in some countries. Treatment might not be applicable in some patients whose corneal topography and/or refractive error falls off the range of application of the corneal reshaping lens. Some patients and their families might be more reluctant to choose this treatment as lenses are less comfortable in the short term, requires the child to sleep in lenses and the high costs of this specialty treatment.

<u>Restrictions</u>: compliance might be at risk, particularly in children who do not like to wear spectacles. Spectacles might not be adequate for some leisure and sports limiting the kids to be involved in such activities.

Specific exams: does not require any specific exams.

<u>Prescription</u>: lenses should fully correct the refractive error and keep good and comfortable distance and near visual acuity.

<u>Efficacy</u>: different studies conducted with different lens designs in different countries/ethnic groups showed similar efficacy ranging from 30 to 60%.

Side effects: no known side effects.

7.7 Low dose atropine

<u>Low dose atropine</u> (typically 0.01%) has become a mainstream treatment (Chia *et al*, 2014; 2016). More recent meta-analysis of randomized clinical trials involving eight different concentrations of atropine (1%, 0.5%, 0.25%, 0.1%, 0.05%, 0.025%, 0.02%, and 0.01%.) showed that 0.05% concentration was similarly effective to higher concentration, while keeping the adverse events at a low rate (Ha *et al.*, 2022). These treatments are commonly available in commercial or laboratory-made preparations.

The use of atropine in many European countries is not available for optometrists. Therefore, referrals might be necessary for whenever use of atropine alone or combined with other optical treatments is advised.

Indication: any progressing myope who is not allergic to atropine.

<u>Mechanism of action</u>: atropine might act directly at the retinal, choroidal level or scleral level by interfering with biochemical cascades that signal directly or indirectly the reinforcement of the scleral tissue and reducing axial elongation.

<u>Advantages</u>: requires only the application of eyedrops.

<u>Limitations/challenges</u>: usually require parental application to ensure administration and appropriate delivery to the ocular surface. Application might generate short-term ocular discomfort.

<u>Restrictions</u>: in some countries only ophthalmologists can prescribe atropine. Compliance might be limited if not applied by parents/guardians.

Specific exams: does not require any specific exams.

<u>Prescription</u>: 0.01% and more recently 0.05% might be the prescription of choice for single or twice-a-day application.

Efficacy: different studies showed efficacy ranging from 50 to 60%.

<u>Side effects</u>: with low-dose atropine minimal pupil dilatation and 2-3 diopters of accommodation amplitude should be expected. Some patients might report photophobia

7.8 Combined treatments

Combination of optical and pharmaceutical treatments have proved to improve the efficacy over the use of either one alone, although the effects cannot be expected to be linearly additive. Some clinical trials have demonstrated that the association of atropine with other treatments, such as orthokeratology, have a synergistic effect, providing higher efficacy, reducing axial elongation and myopia progression.

<u>Indication</u>: progressing myopes showing faster progression or poor response to habitual treatments.

<u>Mechanism of action</u>: the joint application of different treatments might synergistically interact to increase the therapeutic effect through the same or different physical and/or biological paths.

<u>Advantages</u>: requires only adding the application of eyedrops to current treatment.

<u>Limitations/challenges</u>: simultaneous application of different treatments requires more compliance from the patient and parents/guardians and will have increased costs associated.

<u>Restrictions</u>: the same applied to each treatment individually.

<u>Specific exams</u>: those of the specific treatment(s) involved.

<u>Prescription</u>: as required for each individual treatment and trying not to interact negatively with each other.

<u>Efficacy</u>: the effects cannot be expected to be linearly additive from those shown for individual treatments. A meta-analysis study showed that the application of low dose atropine ($\leq 0.05\%$) increases the size effect of by additional 0.12 mm of reduction in axial elongation compared to orthokeratology treatment alone (Zheng and Tan, 2022).

<u>Side effects</u>: with low-dose atropine minimal pupil dilatation (1-2 mm) and 2-3 diopters of accommodation amplitude should be expected.

7.9 Emerging treatments

New treatment approaches are being developed, which are currently at different stages of maturity and which will eventually reach the market, including patents, preclinical experiments (Amorim-de-Sousa *et al.*, 2020; Schilling *et al*, 2022), recruiting and finished clinical trials (Jiang *et al.*, 2022). Some of these treatments explore the exposure to spectrally selective sources of light to interfere with the mechanism of eye growth. In the case of blue light stimulation with 450 nm source selectively directed to the optic nerve head, it is intended to stimulate the implicit photosensitive retinal ganglion cells at that location to increase the production of dopamine in the inner plexiform layer of the retina (Amorim-de-Sousa *et al.*, 2020). In the case of low-level red-light therapy, it is intended to increase the blood flow to the choroid and by that mechanism reduce the axial elongation of the eye (Jiang *et al.*, 2022).

ECPs should be aware that most of these treatments are not yet available and others are still under efficacy and safety evaluation in clinical trials.

8. Stakeholders

Relevant stakeholders in myopia management include those that might facilitate the early evaluation of premyopes and early myopes (*parents, schools*, etc), entities able to implement global plans to screen the population (*local and national governments*, etc), those involved in providing treatments (*industry*), those connected with the

development of guidelines to evaluate and follow-up the premyope and the myope subject (*professional associations*), as well as institutions and associations devoted to supporting people with diseases related with myopia (*patient associations, careqiving institutions, fundraising initiatives*, etc). Additionally, entities with the capability to reach the target population - namely young children at risk of or already developing myopia, as well as adults with moderate and high myopia at risk of developing visual impairment and vision loss - should be also considered (*mass media, social media*, etc).

Action at the aforementioned levels can have a positive impact in the early diagnosis and early intervention in myopia, reducing the incidence and limiting the progression rate, with the goal to ultimately decrease the risks of vision impairment and vision loss association with higher degrees of axial elongation and high myopia.

<u>Parents and schools</u> are key to incentivise younger children with no obvious vision problems to follow early (before myopia onset if possible) and frequent (yearly) examinations to identify risk factors or already existing non-diagnosed myopia.

<u>Local and national governments</u> have the ability to dictate and implement screening programmes for early detection of premyopes and early myopic patients. National governments are also key to promoting awareness that the scope of practice of an ECP encompasses the advances in the scientific knowledge and clinically available treatments, in collaboration with professional associations.

<u>Professional associations</u> are responsible for promoting continuing education and establishing clinical practice guidelines to raise the standard of care in a changing paradigm care for the myopic subject.

<u>Scientists</u> and scientific work have the potential to continuously improve the knowledge on myopia and its management, reinforcing the acceptability of new approaches and providing ground information to explain to patients and parents the rationale of the treatments.

<u>Industry</u> is key to providing safe and effective interventions that allow any ECP to provide their patients safe and effective methods to decrease the rate of axial elongation and myopia progression. This should take into account the limitations that certain ECPs might have at the national level, promoting the availability of treatments that they can provide to their patients, promoting the likelihood that every myopic patient can have an adequate standard of care.

<u>Patient associations and other institutions</u> can provide complementary support to patients and lobbying with local, national and international associations to raise awareness on the role of prevention, early treatment and early diagnosis of myopia and related pathological conditions.

<u>Mass media and social media</u> are key to approach the target population by simultaneously raising awareness of parents and their young children at risk of developing or already developing myopia, as well as the older population at risk of developing pathologies related with myopia.

9. Recommendations

- 1. Encourage <u>early and frequent vision evaluation</u> of all children by the age of 6, particularly those whose family history, outdoor habits and personal history suggests that they might be at risk of developing myopia or rapidly progressing myopia.
- 2. <u>Work with stakeholders at the local level</u> to ensure early visual evaluation of all children in order to have the opportunity to provide them with the most effective methods to manage progressing myopia. Whenever possible facilitate visual health promotion educational sessions for kids, parents and educators.
- Provide all premyopic or myopic children and their parents or guardians with <u>updated information on methods of myopia management</u>, from good habits for myopia prevention to active treatments for progressing myopia. This should include perspectives on the risks associated with myopia progression in adulthood and elderly.
- 4. <u>Outdoor activities</u> might be effective to delay or avoid the onset of myopia, but such activities have not demonstrated efficacy to decrease progression rate on those already myopic. <u>Ergonomic advice</u> on indoor lighting, increasing distance for near work is worth providing but its efficacy on delaying myopia onset or reducing myopia progression rate is still to be confirmed.
- 5. The minimum standard of care for a myopic patient is full prescription of the refractive error for continuous use irrespective of the degree of myopia and the progression rate. For those showing faster progression, myopia management strategies should be advised.
- 6. When deciding which myopia management methods to prescribe, consider the limitations that might exist and <u>provide the methods that can be more accessible, effective and that are likely to promote compliance</u> (care and wear time) by the myopic subject.
- <u>Undercorrection</u> and <u>single vision correction</u> with spectacles or contact lenses, <u>including conventional rigid gas permeable contact lenses</u> are not effective methods to reduce axial elongation and myopia progression.
- 8. <u>Follow-up closely</u> the premyopic and progressing myopic children to monitor the progression of the condition, ensure that the refractive correction is updated when necessary, the treatment option is being used on a daily basis and all

compliance indications are met. Unless otherwise indicated, <u>do not stop myopia</u> <u>management treatments until they adulthood</u> or when an indication of stable refractive status can be verified.

- 9. Care of the <u>myopia patient is a through-life matter</u> starting at childhood where myopia should be detected, fully corrected and if appropriate, managed using appropriate treatment options, through adulthood and into old age, where the risks of eye disease, moderate to severe visual impairment and blindness associated with the condition increases exponentially with age and degree of axial length and refractive error increase.
- 10. <u>Intra-profession and inter-profession referrals</u> should be considered whenever necessary for the young patients requiring treatments not provided by the ECP or to any patient at risk of developing secondary eye conditions related with moderate and high myopia condition.

10. References

Allen PM, Radhakrishnan H, Price H, Rae S, Theagarayan B, Calver RI, Sailoganathan A, Latham K, O'Leary D Sankaridurg J. A randomised clinical trial to assess the effect of a dual treatment on

Amorim-de-Sousa A, Schilling T, Fernandes P, Seshadri Y, Bahmani H, González-Méijome JM. Blue light blind-spot stimulation upregulates b-wave and pattern ERG activity in myopes. Sci Rep. 2021;11(1):9273.

Bao J, Huang Y, Li X, et al. Spectacle Lenses With Aspherical Lenslets for Myopia Control vs Single-Vision Spectacle Lenses: A Randomized Clinical Trial. JAMA Ophthalmol. 2022;140(5):472-478

Bullimore MA, Brennan NA. Myopia Control: Why Each Diopter Matters. Optom Vis Sci. 2019;96:463-465.

Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year Randomized Clinical Trial of MiSight Lenses for Myopia Control. Optom Vis Sci. 2019;96:556-567.

Chamberlain P, Bradley A, Arumugam B, et al. Long-term Effect of Dual-focus Contact Lenses on Myopia Progression in Children: A 6-year Multicenter Clinical Trial. Optom Vis Sci. 2022;99(3):204-212.

Cheng D, Schmid KL, Woo GC, Drobe B. Randomized trial of effect of bifocal and prismatic bifocal spectacles on myopic progression: two-year results. Arch Ophthalmol. 2010;128(1):12-19.

Cheng D, Woo GC, Drobe B, Schmid KL. Effect of bifocal and prismatic bifocal spectacles on myopia progression in children: three-year results of a randomized clinical trial. JAMA Ophthalmol. 2014;132:258-64.

Chia A, Chua WH, Cheung YB, *et al*. 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(2):347-354.

Chia A, Chua WH, Wen L, Fong A, Goon YY, 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

Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eyedrops. Ophthalmology. 2016;123:391-399.

Cho P, Cheung SW. Retardation of myopia in Orthokeratology (ROMIO) study: A 2-year randomized clinical trial. Invest Ophthalmol Vis Sci 2012;53:7077–7085

Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group. Progressive-addition lenses versus single-vision lenses for slowing progression of myopia in children with high accommodative lag and near esophoria. Invest Ophthalmol Vis Sci. 2011;52(5):2749-2757.

COMET Group. Myopia stabilization and associated factors among participants in the Correction of Myopia Evaluation Trial (COMET). Invest Ophthalmol Vis Sci. 2013;54:7871-84.

Dolgin E. The myopia boom. Nature. 2015;519:276-8.

ECOO. Blue Book 2021. Available at: https://ecoo.info/wp-content/uploads/2022/02/ECOO_BlueBook_2021_7-1.pdf Accessed on March 28th, 2022.

Flitcroft DI. Ophthalmologists should consider the causes of myopia and not simply treat its consequences. Br J Ophthalmol. 1998;82:210-211.

Flitcroft DI. The complex interactions of retinal, optical and environmental factors in myopia aetiology. Prog Retin Eye Res. 2012;31(6):622-660.

French AN, Morgan IG, Burlutsky G, Mitchell P, Rose KA. Prevalence and 5- to 6-year incidence and progression of myopia and hyperopia in Australian schoolchildren. Ophthalmology. 2013;120(7):1482-1491

Gifford KL, Richdale K, Kang P, Aller TA, Lam CS, Liu YM, Michaud L, Mulder J, Orr JB, Rose KA, Saunders KJ, Seidel D, Tideman JWL, Sankaridurg P. IMI - Clinical Management Guidelines Report. Invest Ophthalmol Vis Sci. 2019;60:M184-M203.

Ha A, Kim SJ, Shim SR, Kim YK, Jung JH. Efficacy and Safety of 8 Atropine Concentrations for Myopia Control in Children: A Network Meta-Analysis. Ophthalmology. 2022;129(3):322-333.

Hasebe S, Jun J, Varnas SR. Myopia control with positively aspherized progressive addition lenses: a 2-year, multicenter, randomized, controlled trial. Invest Ophthalmol Vis Sci. 2014;55:7177-88.

Hiraoka T, Kakita T, Okamoto F, Takahashi H, 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;53:3913-9.

Holden BA y cols. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-42.

Huang J, Wen D, Wang Q, McAlinden C, Flitcroft I, Chen H, Saw SM, Chen H, Bao F, Zhao Y, Hu L, Li X, Gao R, Lu W, Du Y, Jinag Z, Yu A, Lian H, Jiang Q, Yu Y, Qu J. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology. 2016;123:697-708.

Jiang Y, Zhu Z, Tan X, et al. Effect of Repeated Low-Level Red-Light Therapy for Myopia Control in Children: A Multicenter Randomized Controlled Trial. Ophthalmology. 2022;129(5):509-519.

Jones-Jordan LA, Sinnott LT, Manny RE, Cotter SA, Kleinstein RN, Mutti DO, Twelker JD, Zadnik K; Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study Group. Early childhood refractive error and parental history of myopia as predictors of myopia. Invest Ophthalmol Vis Sci. 2010;51:115-21.

Jong M, Jonas JB, Wolffsohn JS, et al. IMI 2021 Yearly Digest. Invest Ophthalmol Vis Sci. 2021;62(5):7.

Kanda H, Oshika T, Hiraoka T, Hasebe S, Ohno-Matsui K, Ishiko S, Hieda O, Torii H, Varnas SR, Fujikado T. Effect of spectacle lenses designed to reduce relative peripheral hyperopia on myopia progression in Japanese children: a 2-year multicenter randomized controlled trial. Jpn J Ophthalmol. 2018;62:537-543.

Kaphle D, Atchison DA, Schmid KL. Multifocal spectacles in childhood myopia: Are treatment effects maintained? A systematic review and meta-analysis. Surv Ophthalmol. 2020;65:239-249.

Kurtz D, Hyman L, Gwiazda JE, Manny R, Dong LM, Wang Y, Scheiman M; COMET Group. Role of parental myopia in the progression of myopia and its interaction with treatment in COMET children. Invest Ophthalmol Vis Sci. 2007;48:562-70.

Lam CS, Tang WC, Tse DY, Tang YY, To CH. Defocus Incorporated Soft Contact (DISC) lens slows myopia progression in Hong Kong Chinese schoolchildren: a 2-year randomised clinical trial. Br J Ophthalmol 2014;98:40-45.

Lam CSY, Tang WC, Tse DY, Lee RPK, Chun RKM, Hasegawa K, Qi H, Hatanaka T, 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.

Li SM, Kang MT, Wu SS, y cols. 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.

Mutti DO, Mitchell GL, Moeschberger ML, Jones LA, Zadnik K. Parental myopia, near work, school achievement, and children's refractive error. Invest Ophthalmol Vis Sci. 2002;43:3633–40.

Mutti DO, Hayes JR, Mitchell GL, et al. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. Invest Ophthalmol Vis Sci. 2007;48(6):2510-2519.

Pauné J, Morales H, Armengol J, Quevedo L, Faria-Ribeiro M, González-Méijome JM. Myopia Control with a Novel Peripheral Gradient Soft Lens and Orthokeratology: A 2-Year Clinical Trial. Biomed Res Int. 2015;2015:507572.

Rose KA, Morgan IG, Ip J, *et al*. Outdoor activity reduces the prevalence of myopia in children. Ophthalmology. 2008;115(8):1279-1285.

Rubin ML, Milder B. Myopia--a treatable "disease"? Surv Ophthalmol. 1976;21:65-9.

Ruiz-Pomeda A, Pérez-Sánchez B, Valls I, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C. MiSight Assessment Study Spain (MASS). A 2-year randomized clinical trial. Graefes Arch Clin Exp Ophthalmol. 2018;256:1011-1021

Sankaridurg P, Bakaraju RC, Naduvilath T, *et al*. 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(4):294-307.

Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, y cols. Myopia control with orthokeratology contact lenses in Spain: Refractive and biometric changes. Invest Ophthalmol Vis Sci 2012;53:5060–5065.

Schaeffel F. Myopia-What is Old and What is New?. Optom Vis Sci. 2016;93:1022-1030.

Schilling T, Amorim-de-Sousa A, A Wong N, Bahmani H, González-Méijome JM, Fernandes P. Increase in b-wave amplitude after light stimulation of the blind spot is positively correlated with the axial length of myopic individuals. Sci Rep. 2022;12(1):4785.

Sun Y, Xu F, Zhang T, Liu M, Wang D, Chen Y, Liu Q. Orthokeratology to control myopia progression: a metaanalysis. PLoS One. 2015;10:e0124535. Erratum in: PLoS One. 2015;10(6):e0130646.

Thorn F, Gwiazda J, Held R. Myopia progression is specified by a double *et al*tial growth function. Optom Vis Sci. 2005;82:286-97.

Tideman JW, Snabel MC, Tedja MS, van Rijn GA, Wong KT, Kuijpers RW, Vingerling JR, Hofman A, Buitendijk GH, Keunen JE, Boon CJ, Geerards AJ, Luyten GP, Verhoeven VJ, Klaver CC. Association of Axial Length With Risk of Uncorrectable Visual Impairment for Europeans With Myopia. JAMA Ophthalmol. 2016;134:1355-1363.

Verhoeven VJ, Buitendijk GH; Consortium for Refractive Error and Myopia (CREAM), Rivadeneira F, Uitterlinden AG, Vingerling JR, Hofman A, Klaver CC. Education influences the role of genetics in myopia. Eur J Epidemiol. 2013;28:973-80.

Walline JJ, Jones LA, Mutti DO, Zadnik K. A randomized trial of the effects of rigid contact lenses on myopia progression. Arch Ophthalmol. 2004;122(12):1760-1766.

Walline JJ, Gaume A, Jones LA, Rah MJ, Manny RE, Berntsen DA, Chitkara M, Kim A, Quinn N. Benefits of contact lens wear for children and teens. Eye Contact Lens. 2007;33:317-21.

Walline JJ, Greiner KL, McVey ME, Jones-Jordan LA. Multifocal contact lens myopia control. Optom Vis Sci. 2013;90:1207-14.

Walline JJ, Jones LA, Sinnott LT. Corneal reshaping and myopia progression. Br J Ophthalmol 2009;93:1181–1185.

Walline JJ, Walker MK, Mutti DO, Jones-Jordan LA, Sinnott LT, Giannoni AG, Bickle KM, Schulle KL, Nixon A, Pierce GE, Berntsen DA; BLINK Study Group. Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial. JAMA. 2020;324:571-580.

WCO 2021 resolution on myopia management standard of care. Available at <u>https://www.iapb.org/news/world-</u> <u>council-of-optometry-passes-resolution-calling-for-a-standard-of-care-for-myopia-management/</u> Accessed on March 28th, 2022

Wildsoet CF, Chia A, Cho P, Guggenheim JA, Polling JR, Read S, Sankaridurg P, Saw SM, Trier K, Walline JJ, Wu PC, Wolffsohn JS. IMI - Interventions Myopia Institute: Interventions for Controlling Myopia Onset and Progression Report. Invest Ophthalmol Vis Sci. 2019;60:M106-M131.

Williams KM, Verhoeven VJ, Cumberland P, Bertelsen G, Wolfram C, Buitendijk GH, Hofman A, van Duijn CM, Vingerling JR, Kuijpers RW, Höhn R, Mirshahi A, Khawaja AP, Luben RN, Erke MG, von Hanno T, Mahroo O, Hogg R, Gieger C, Cougnard-Grégoire A, Anastasopoulos E, Bron A, Dartigues JF, Korobelnik JF, Creuzot-Garcher C, Topouzis F, Delcourt C, Rahi J, Meitinger T, Fletcher A, Foster PJ, Pfeiffer N, Klaver CC, Hammond CJ. Prevalence of refractive error in Europe: the European Eye Epidemiology (E(3)) Consortium. Eur J Epidemiol. 2015;30:305-15.

Williams KM, Bentham GC, Young IS, McGinty A, McKay GJ, Hogg R, Hammond CJ, Chakravarthy U, Rahu M, Seland J, Soubrane G, Tomazzoli L, Topouzis F, Fletcher AE. Association Between Myopia, Ultraviolet B Radiation Exposure, Serum Vitamin D Concentrations, and Genetic Polymorphisms in Vitamin D Metabolic Pathways in a Multicountry European Study. JAMA Ophthalmol. 2017;135:47-53.

Wolffsohn JS, Flitcroft DI, Gifford KL, Jong M, Jones L, Klaver CCW, Logan NS, Naidoo K, Resnikoff S, Sankaridurg P, Smith EL 3rd, Troilo D, Wildsoet CF. IMI - Myopia Control Reports Overview and Introduction. Invest Ophthalmol Vis Sci. 2019a;60:M1-M19.

Xiong S, Sankaridurg P, Naduvilath T, Zang J, Zou H, Zhu J, Lv M, He X, Xu X. Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. Acta Ophthalmol. 2017;95:551-566.

Zheng NN, Tan KW. The synergistic efficacy and safety of combined low-concentration atropine and orthokeratology for slowing the progression of myopia: A meta-analysis [published online ahead of print, 2022 Aug 2]. Ophthalmic Physiol Opt. 2022;10.1111/opo.13029. doi:10.1111/opo.13029