



Christopher Wolfe, OD, FAAO, Dipl. ABO

Myopia Defined

As we know myopia occurs when light from **infinity converges to a point in front of the retina**. This can occur from 2 main situations:

- The refractive power of the cornea/lens combination is too convergent (too much plus in power)
- The axial length of the eye too long for the refractive elements of the eye

Myopia Classified

Understanding the different classifications of myopia can allow us to consider treatments that can correct the condition and possibly slow or even prevent it. In this section, we will discuss the classification systems that have been proposed to understand myopia [1].

Rate of Progression

One classification system that has been proposed is based on the time and rate of progression of myopia, these categories include [2]:

- **Stationary myopia** occurs when there are typically low (-1.50 to -2.00 D) amounts of myopia and usually occurs prior to the age of 18 and is stable during adulthood
- **Temporarily progressive myopia** typically begins during puberty and will progress until the late 20's at which point it tends to remain stable
- **Permanently progressive myopia** occurs at a relative rapid rate until around 30 years old, then continues to advance in "jumps" throughout life

Anatomical Causes of Myopia

Another way to think about the classification of myopia is to look at the anatomical causes of the condition. In terms of treatment or optical effects of that treatment, it can be useful

Myopia Amount

Myopia has been classified by severity [2] [51]:

Common: < -6.00
Mild: -1.00 to -2.99 D
Mod: -3.00 to -5.99 D
High/Severe: ≥ -6.00

Refractive Myopia

A **cataract** would be a classic cause of **index myopia**.

Keratoconus would be a classic cause of **curvature myopia**
Ciliary effusion secondary to topiramate would be a classic cause of **anterior chamber myopia**

to understand the underlying anatomical issues that lead to myopia. These include [3]:

- **Axial myopia** occurs when the eye is too long for its focal length
- **Refractive myopia** occurs when the refractive elements create a focal length that is too short for the length of the eye.
 - Index of refraction – causing myopia when there is a difference from physiological normal leading to a refractive change
 - Curvature – causing myopia when there is an increase in curvature (or shortening of radius) leading to a refractive change
 - Anterior chamber depth – causes myopia when there is a shortening of the anterior chamber depth that leads to myopia

Theory of Development

The etiology of myopia has been proposed (and have withstood scrutiny) as a way to classify myopia, current thinking includes some overlap of each theory. These theories include:

- **Environmental** – Many studies have found that an increased prevalence of myopia associated with populations who performed significant amounts of near activities [4] [5] [6]
- **Emmetropization** – In an effort to stabilize distance vision a feedback loop that leads to axial elongation to eliminate retinal defocus (possibly hyperopic defocus) during development [7]. Additionally, this theory has been expanded to include both central and (possibly more importantly) peripheral hyperopic defocus [8] [9].

Night Myopia

Night myopia occurs in situations where there is dim illumination. The main theory is that low light levels cause stimulation of accommodation because distant objects cannot be viewed to cause relaxed accommodation. This causes the accommodative system to be suspended at a distance that is not infinite. This phenomenon occurs secondary to:

1. Increased accommodative response (~0.75 D) is thought to account for the majority of the response [10] [11]
2. Increased chromatic aberration [1]
3. Purkinje Shift [1]

Pseudomyopia

Pseudomyopia is not a true refractive error but can cause a temporary myopic shift due to a ciliary muscle spasm.

Manifest refraction will typically be more minus (usually 1 D or more) than retinoscopy. Cycloplegia will reduce accommodation and eliminate the response [1].

Purkinje Shift

As the eye changes sensitivity from photopic to scotopic conditions, the visual systems peak sensitivity shifts to shorter wavelengths (510nm). Shorter wavelengths fall more anteriorly (myopic) to the retina, which explains a small part of night myopia [1].

Myopia Prevalence and Incidence

While there is a multitude of studies on the prevalence of myopia these studies are not consistent with the amount of myopia they are including as being significant enough to include in the study. For most of these studies myopia is defined as a spherical equivalent refractive error of -0.50 D but some studies will use smaller or larger amounts to define myopia [12].

Prevalence and Incidence

Children

What is the prevalence of American children between the ages of 6 months and 6 years old [13] [14]?

1. 1.2% in non-Hispanic whites
2. 3.7% in Hispanics
3. 3.98% in Asians
4. 6.6% in African Americans

What is the prevalence of myopia in Australian school-aged children of East Asian and European Caucasian ethnicity [15]?

1. East Asian
 - 12-year-olds: 42.7%
 - 17-year-olds: 59.1%
2. Caucasian
 - 12-year-olds: 8.3%
 - 17-year-olds: 17.7%

What is the annual incidence of myopia in Australian school-aged children of East Asian and European Caucasian ethnicity [15]?

1. East Asian
 - 12-year-olds: 6.9%
 - 17-year-olds: 7.3%
2. Caucasian
 - 12-year-olds: 1.3%
 - 17-year-olds: 2.9%

Is there a difference in myopia prevalence between rural and urban areas?

1. Children between the ages of 5-15 in **rural northern China** showed a prevalence of **16.2%** [16].
2. Children between the ages of 5-15 in **rural Nepal** showed a prevalence of **1.2%** [17]
3. Children between the ages of 5-15 in **large urban Chinese cities** showed a prevalence of **38.1%** (Guangzhou) [18] and **36.7%** (Hong Kong) [19].

Adults

How does the prevalence of myopia change in adult populations [20]?

1. Adults aged 43–54: 42.9%

Pediatric Trends

Prevalence in myopia tends to increase dramatically in children once they are old enough to start reading. Rural vs urban areas also appear to have an impact on myopia prevalence, one could speculate about the causes of this including; near work and outdoor time.

2. Adults aged 55–64: 25.1%
3. Adults aged 65–74: 14.8%
4. Adults aged 75+: 14.4%

Myopia Risk Factors

While we still do not fully understand the underlying mechanism of the development or progression of myopia, most of the evidence suggests that myopia results from a combination of genetic and environmental factors. These risk factors will be discussed below.

Family History

What is the impact of parental refractive error on the risk of myopia development in children [21] [22]?

1. If **both parents** are **emmetropic** the myopia prevalence for their offspring is **6.3-7.6%**
2. If **one parent** is **myopic** the myopia prevalence for their offspring is **14.9-18.2%**
3. If **both parents** are **myopic** the myopia prevalence for their offspring is **32.9-43.6%**

Family Trends

Prevalence in myopia tends to increase in children as the number of parents with myopia increases.

Is myopia progression secondary to near work (environmental risk factor) an inherited trait [21]?

1. Researchers **did not find** that children with myopic parents can inherit a susceptibility to myopia progression due to near work

Socioeconomic Status

What socioeconomic factors increase the prevalence of myopia [23] [24] [25]?

1. Higher levels of education
2. Better housing
3. Higher income
4. Occupations associated with near work

Near Work

What impact do near activities (reading, writing, device use) have on the prevalence of myopia?

1. In one study, children who **read more than 2 books per week were 3X more likely to develop myopia (-3.00 D or more)** [26].
2. This same study also found that children who read for more than 2 hours per day were no more likely to develop myopia than children who read less [26].
3. Another study found that the association between parental myopia and near work were not significant. This indicates that there is no increased risk associated with near work with an increase in number of parents with myopia. To say this another way, in this study while there was an increased risk of myopia with increasing number of parents with myopia, increasing near work did not increase the risk of myopia [21].

Near Trends

Prevalence of myopia increases with increasing near work. This may be secondary to an increase in axial length during near work or a peripheral hyperopic defocus.

4. The Sydney Adolescent Vascular and Eye Study (SAVES) found that children who became myopic performed 2 more hours of near work per week (19.4 vs. 17.6 hours; $P=0.02$) than patients who did not become myopic. This effect is less strong the older the patient is [15].

What is the potential mechanism that leads to the relationship between near activities and myopia?

1. In early onset and progressing myopes there is a greater temporary increase in axial length while doing near work than in emmetropic patients [27].
2. Patients with a high lag of accommodation during near work will have a hyperopic retinal defocus and that may lead to myopia progression [28].

Outdoor Activity

What impact do outdoor activities have on the prevalence of myopia?

1. More hyperopic refractions and lower myopia prevalence was found in 12-year-olds with higher levels of outdoor activity (sports or leisure) [28].
 - Children with high levels of near work AND low levels of outdoor activity had the least hyperopic mean refraction
 - Children with low levels of near work AND high levels of outdoor activity had the most hyperopic mean refraction
 - The odds of developing myopia were the lowest in children reporting the highest levels of outdoor activity
 - No difference between males and females
2. In younger (6-year-old) patients there was no association between refraction and outdoor activity [28].
3. Another study to evaluate outdoor activity in 7-12 year old children risk of myopia progression and onset found [30]:
 - **Design**
 - i. 571 students: 333 interventional, 238 control
 - ii. Recess time: 80 minutes/day
 - iii. Outdoor P.E.: 2 hours/wk
 - iv. Patients on atropine therapy prior to and throughout the study:
 1. 29% of intervention
 2. 20% of control
 - **Results:**
 - i. Myopia Onset After 1 year:
 1. 8.41% - Interventional
 2. 17.61% – Control
 3. NNT - 10
 - ii. Myopia Progression After 1 year:
 1. -0.25D/year – Interventional

Outdoor Trends

Prevalence of myopia decreases with increasing outdoor activities. The “light-dopamine” theory was proposed as a possible mechanism for this effect.

2. -0.38D/year – Control

How much time should children spend outdoors to make an impact on myopia?

1. A meta-analysis of 7 studies found that the odds of developing myopia is reduced by 2% per additional hour of time spent outdoors per week [29].

What is the potential mechanism that leads to the inverse relationship between outdoor activities and myopia?

1. One theory is that the increased light intensity during outdoor activities leads to an **increase in dopamine release**. It is hypothesized that **dopamine reduces axial elongation** leading to lower prevalence of myopia [28][30].

Treatment and Management of Myopia Progression

Undercorrection

During development, the process of emmetropization must occur. During this process, retinal blur or image defocus ought to provide a feedback mechanism that guides the growth of the eye to eliminate refractive error [32]. In order for emmetropization to work perfectly, this feedback mechanism must be able to discern between the blur associated with myopia and blur associated with hyperopia.

One possible theory on why emmetropization occurs is that the visual system interprets retinal defocus as either myopic or hyperopic, thus undercorrecting myopia should halt or slow the progression of the condition.

Does undercorrecting myopia help slow the progression of myopia [33]?

1. 94 myopic (-0.50 or greater with less than -2.00 cyl) children between the ages of 9 and 14 were divided into 2 groups and followed for 2 years:
 - a. Fully corrected
 - b. Undercorrected to 20/40 (~ +0.75 D added to BSCVA)
2. After 2 years of monitoring every 6 months the study found:
 - a. Myopia progression
 - i. Fully corrected: -0.77 D
 - ii. Undercorrected: -1.00 D (statistically significant)
 - b. Axial length increase
 - i. Fully corrected: 0.68 mm
 - ii. Undercorrected: 0.60 mm (statistically significant)

Bifocal and Progressive Addition Lenses (PALs)

Utilizing a bifocal or PAL in slowing myopia progression may work by eliminating or reducing the accommodative demand or lag associated with near tasks [34] [35].

How do bifocal glasses impact myopia progression in patients with near esophoria [36]?

1. In a single masked randomized trial, 82 myopic children with **near esophoria** were randomized into 2 groups (**single-vision lenses** or **bifocals with a +1.50 add**) and followed for 2.5 years.
2. After 30 months of treatment the study found the following average myopia progression:
 - a. Single-vision: -1.24 D
 - b. Bifocals +1.50 add: -0.99 D (statistically significant)

Myopia

Determination

Most studies use refraction measured by autorefraction after cycloplegia to determine myopia amount.

How does the addition of BI prism with executive bifocals impact myopia progression [37]?

1. 135 children (age 8-13 years) with **progressive myopia** (-0.50 D in the preceding year) were randomized into 3 groups (**single-vision lenses, +1.50-D executive bifocals** or **+1.50-D executive bifocals with 3-Δ base-in prism in the near segment of each lens**)
2. After 36 months of treatment the study found the following:
 - a. Myopia progression:
 - i. Single-vision: -2.06 D
 - ii. Executive bifocals: -1.25 D
 - iii. Executive bifocals and BI prism: -1.01 D
 - c. Average axial length increase:
 - i. Single-vision: 0.82 mm
 - ii. Executive bifocals: 0.57 mm
 - iii. Executive bifocals and BI prism: 0.54 mm

Significance

The executive bifocal group had statistically significantly less progression than the SV group, but there was not SS difference between BF groups.

How do PALs impact myopia progression in patients with near esophoria and high accommodative lag [38]?

1. In a double-masked multicenter randomized trial, 118 myopic (spherical equivalent of -0.75 to -2.50) children with **near esophoria** (≥ 2 PD) and a **high accommodative lag** (accommodative response less than 2.50 D for a 3.00-D demand) were randomized into 2 groups either **single-vision lenses** or **PALs with a +2.00 add** and followed every 6 months for 3 years.
2. After 36 months of treatment the study found the following average myopia progression:
 - a. Single-vision: -1.15 D
 - b. PALs +2.00-D add: -0.87 D (statistically significant)

- c. Additionally, patients with large fusional vergence ranges had a greater treatment effect.

Soft Multifocal Contact Lenses

Clinically we typically utilize soft bifocal contact lenses for presbyopic patients as an alternative to monovision to help reduce the need for reading glasses. Center distance soft multifocal lenses also create peripheral myopic defocus which may slow myopic progression by reducing the stimulus (peripheral hyperopic defocus) for axial elongation [39].

What effect do center distance soft multifocal contact lenses have on myopia progression and axial elongation [40]?

1. 40 myopic (-1.00 D to -6.00 D spherical component and less than 1.00 D cyl) children (8-11 years old) fitted with soft multifocal contact lenses with a **+2.00 D add (Proclear Multifocal "D"**; CooperVision). These patients were then age- and gender-matched to control participants from a previous study who were fitted with **single-vision contact lenses** (1 Day Acuvue; Vistakon). They were monitored annually for 2 years.
2. After 24 months of treatment the study found the following:
 - a. Average SE myopia progression:
 - i. Single-vision: -1.03 D
 - ii. Multifocal: -0.51 D (statistically significant)
 - b. Average axial elongation:
 - i. Single-vision: 0.41 mm
 - ii. Multifocal: 0.29 mm (statistically significant)

What effect do center distance soft multifocal contact lenses have on myopia progression and axial elongation in patients with an eso fixation disparity at near [41]?

1. In a prospective, randomized, clinical trial, 86 children (8 to 18 years) with progressive myopia (-0.50 D or more since previous examination) and an eso fixation disparity at near were randomized to wear **single-vision soft contact lenses** (Acuvue 2) or **bifocal soft contact lenses** (Acuvue Bifocal) with enough add power to neutralize the associated phoria and followed for at 6 months and 1 year.
2. After 12 months of treatment the study found:
 - a. Average SE myopia progression:
 - i. Single-vision: -0.79 ± 0.43 D
 - ii. Bifocals: -0.22 ± 0.34 D (statistically significant)
 - b. Average axial elongation:
 - i. Single-vision: 0.24 ± 0.17 mm
 - ii. Bifocals: 0.05 ± 0.14 mm (statistically significant)

Orthokeratology

Orthokeratology (ortho-k) is utilized to temporarily reduce the need for daytime vision correction by flattening the central cornea. Similar to multifocal soft contact lenses, it is thought that the underlying mechanism for slowing myopia progression is by creating peripheral myopic defocus

which may slow myopic progression by reducing the stimulus (peripheral hyperopic defocus) for axial elongation [42].

What effect does orthokeratology have on axial elongation [43]?

1. In a single-masked randomized clinical trial 102 myopic (between 0.50 and 4.00 diopters (D) and astigmatism not more than 1.25D) children (6 to 10 years) were randomized to **ortho-k lenses** or **single-vision glasses** and monitored every 6 months for 2 years.
2. After 24 months of treatment the study found:
 - a. Average axial elongation:
 - i. Single-vision spectacles: 0.63 ± 0.26 mm
 - ii. Ortho-K: 0.36 ± 0.24 mm (statistically significant)

Topical Pharmaceutical Agents

Anti-muscarinic topical pharmaceutical medications used to dilate the pupil or paralyze accommodation have also been used in an attempt to control myopia progression. The theory of how these medications slow the progression of myopia is unclear. It has been hypothesized that the mechanisms may include a reduction in accommodation or through inhibition of the muscarinic receptors in the ciliary body and iris but the evidence for both of these hypothesis are conflicting.

The medications that have been evaluated for myopia control include atropine and pirenzepine. One advantage of pirenzepine over higher doses of atropine is that pirenzepine has action only on M1 anti-muscarinic receptors, which are not as prevalent in the iris or ciliary body, so pirenzepine does not dilate the pupil or reduce accommodation as much as atropine. For the purposes of this course we will focus on atropine because it is a medication that has a long track record utilization in eye care and lower doses reduce the side effect profile as well.

What effect does atropine have on myopia progression [45]?

1. In ATOM1 a parallel-group, placebo-controlled, randomized, double-masked study of 400 myopic (SE -1.00 to -6.00 (D) and -1.50 DC or less) children (6-12 years) and were randomized to receive either 1% atropine or saline drops 1 time per day in one eye and followed for 2 years.
2. After 24 months of treatment the study found myopia progression of:
 - a. Placebo: -1.20 ± 0.69 D
 - b. 1% atropine: -0.28 ± 0.92 D (statistically significant)

After stopping atropine is there a rebound of myopia progression [46]?

1. Utilizing the same cohort as above, this study followed them for an additional year after stopping 1% atropine to determine the extent, if any, rebound myopic progression occurred.
2. 12 months after stopping 1% atropine treatment this study found:
 - a. Average myopia progression in final 12 months:
 - i. Placebo: -0.38 ± 0.39 D
 - ii. 1% atropine: -1.14 ± 0.80 D
 - b. Average myopia progression in total 36 months (24 months of treatment, 12 months without treatment):

- i. Placebo: -5.22+/-1.38 D
- ii. 1% atropine: -4.29+/-1.67 D

Can we minimize side effects and still reduce myopia progression with lower doses of atropine [47]?

3. In the ATOM2 study patients were randomized to receive either 0.5%, 0.1% or 0.01% atropine since there was already proven benefit of atropine the control arm was utilized from ATOM1 since it would not be ethical to prevent patients from receiving treatment that was shown to be effective in the prior study. Medication was administered 1 time per day in each eye and patients were followed for 2 years.
4. After 24 months of treatment the study found myopia progression of:
 - a. 0.5% atropine: -0.30 D
 - b. 0.1% atropine: -0.38 D
 - c. 0.01% atropine: -0.49 D
5. During the study, photochromic glasses with a reading add were prescribed if patients complained of glare or difficulty reading. The side effect profile was less with lower doses of atropine and while the 0.01% atropine group had the greatest rate of myopia progression, accommodative amplitudes, visual acuities and pupil sizes were all less impacted than those in the other treatment groups. Further, the study found that the number of children complaining of near blur and requiring a near add was:
 - a. 0.5% atropine: 70%
 - b. 0.1% atropine: 61%
 - c. 0.01% atropine: 6%

EyeCode Clinical Pearls

1. Studies suggest that **the visual system of myopes have an abnormal mechanism for detecting the direction of retinal image blur leading to axial elongation and myopia progression in the presence of myopic retinal defocus.**
2. Undercorrection of myopia **should not be utilized** as a strategy for slowing myopia progression.
3. While myopia progression is slowed with bifocals spectacles and progressive addition lenses in a statistically significant way, I would argue that reducing myopia by 0.25 D over 2.5 years (for FT) and 0.28 D over 3 years **is not clinically significant.**
4. **Executive bifocal spectacles** can slow myopia progression in children by approximately **40% over 3 years.** It is unclear whether the benefit seen in this study is due to an executive BF (compared to studies using a FT) or if the reason there was a more significant slowing of myopia progression because the study used patients who were already progressing in their myopia as an inclusion factor.
5. There may be some additional benefit of utilizing **BI prism at near to slow myopia progression more** than executive BFs alone in **patients with low accommodative lags** (less than 1.01 D).
6. Center distance soft multifocal contact lenses can **reduce both myopia progression (by 50%) and axial elongation (by 29%)** over 2-years.

7. **Center distance bifocal contacts showed approximately a 70% reduction in myopia progression and an 80% reduction in axial elongation in children with an eso fixation disparity at near after 1 year of treatment.** While rarely done in clinical practice, **factoring in near fixation disparities and prescribing add powers to neutralize the associated phoria** may slow myopia progression more than utilizing a generalized add power.
8. Ortho-K contact lenses can **reduce axial elongation (by 43%)** over 2-years.
9. The rate of microbial keratitis with overnight ortho-k lenses is similar to that of overnight soft contact lens wear [47], so it is prudent to ensure the benefits outweigh the risks prior to initiating overnight wear with any contact lenses. Clinically, **it may be wise to ensure that patients can safely and responsibly wear daytime contact lenses prior to initiating overnight wear options.**
10. When using 1% atropine for myopia control **expect a more rapid progression in myopia after stopping treatment.**
11. There is a significant benefit of reducing myopia progression with 1% atropine even though the effect is not as great once atropine is stopped.
12. To minimize side effects, consider **utilizing 0.01% atropine for myopia control.**

Bibliography

- [1] B. W, Borish's Clinical Refraction, Philadelphia: W.B. Saunders Company, 1998.
- [2] D. FC, On the Anomalies of Accommodation and Refraction of the Eye, London, 1864.
- [3] B. IM, Clinical Refraction, Chicago: Professional Press, 1970.
- [4] C. H, Hygiene of the Eye in Schools, London: Simpkin, Marshall and Co., 1886.
- [5] M. N. Adams DW, "Prevalence of myopia and myopic progression in a population of clinical microscopists," *Optom Vis Sci*, vol. 69, pp. 467-473, 1992.
- [6] S. S. R. K. M. I. K. J. W. J. M. P. Ip JE, "Role of Near Work in Myopia: Findings in a Sample of Australian School Children," *Investigative Ophthalmology & Visual Science*, vol. 49, pp. 2903-2910, 2008.
- [7] H. HW, "Emmetropization - biological process or mathematical artifact?," *Am J Optom Arch Am Acad Optom*, vol. 46, pp. 447-450, 1969.
- [8] M. A. C. X. L. L. S. P. H. B. G. J. Lin Z, "Peripheral defocus with single-vision spectacle lenses in myopic children," *Optom Vis Sci*, vol. 87, no. 1, pp. 4-9, 2010.
- [9] B. C. M. D. Z. K. Berntsen DA, "Peripheral Defocus and Myopia Progression in Myopic Children Randomly Assigned to Wear Single Vision and Progressive Addition Lenses," *Invest Ophthalmol Vis Sci*, vol. 54, no. 8, p. 5761-5770, 2013.
- [10] C. H. G. G. B. Rosenfield M, "Tonic accommodation: A review. I. Basic aspects.," *Ophthal Physiol Opt*, vol. 13, pp. 266-284, 1993.
- [11] C. C. M.-A. A. Schwarz C, "Night Myopia Studied with an Adaptive Optics Visual Analyzer," *Public Library of Science (PLOS) One*, no. <https://doi.org/10.1371/journal.pone.0040239>, 2012.
- [12] J. Y. Foster PJ, "Epidemiology of myopia," *Eye*, vol. 28, no. 2, p. 202-208, 2014.
- [13] T.-H. K. M.-C. R. C. S. B. M. L. J. K. J. V. R. M.-E. P. E. D. S. G. Wen G, "Prevalence of myopia, hyperopia, and astigmatism in non-Hispanic white and Asian children: multi-ethnic pediatric eye disease study.," *Ophthalmology*, vol. 120, no. 10, pp. 2109-16, 2013.
- [14] M.-E. P. E. D. S. Group., "Prevalence of myopia and hyperopia in 6- to 72-month-old african american and Hispanic children: the multi-ethnic pediatric eye disease study.," *Ophthalmology*, vol. 117, no. 1, pp. 140-147, 2010.
- [15] M. I. B. G. M. P. R. K. French AN, "Prevalence and 5- to 6-year incidence and progression of myopia and hyperopia in Australian schoolchildren.," *Ophthalmology*, vol. 120, no. 7, p. 1482-1491, 2013.

- [16] P. X. S. R. M. S. S. R. E. L. Zhao J, "Refractive Error Study in Children: results from Shunyi District, China.," *Am J Ophthalmol*, vol. 129, no. 4, pp. 427-435, 2000.
- [17] N. A. M. S. E. L. Pokharel GP, "Refractive Error Study in Children: results from Mechi Zone, Nepal," *Am J Ophthalmol*, vol. 129, no. 4, pp. 436-444, 2000.
- [18] Z. J. L. Y. X. J. P. G. E. L. He M, "Refractive error and visual impairment in urban children in southern china.," *Invest Ophthalmol Vis Sci*, vol. 45, no. 3, p. 793–799, 2004.
- [19] L. D. L. R. L. J. C. K. C. E. e. a. Fan DS, "Prevalence, incidence, and progression of myopia of school children in Hong Kong," *Invest Ophthalmol Vis Sci*, vol. 45, no. 4, pp. 1071-7075, 2004.
- [20] K. B. K. R. M. S. Wang Q, "Refractive status in the Beaver Dam Eye Study," *Invest Ophthalmol Vis Sci*, vol. 35, no. 13, p. 4344–4347, 1994.
- [21] M. G. M. M. J. L. Z. K. Mutti DO, "Parental myopia, near work, school achievement, and children's refractive error," *Invest Ophthalmol Vis Sci*, vol. 43, no. 12, pp. 3633-3640, 2002.
- [22] H. S. R. D. R. K. M. I. S. W. e. a. Ip JM, "Ethnic differences in the impact of parental myopia: findings from a population-based study of 12-year-old Australian children," *Invest Ophthalmol Vis Sci*, vol. 48, no. 6, pp. 2520-2528, 2007.
- [23] H. M. M. I. Xiang F, "The impact of parental myopia on myopia in Chinese children: population-based evidence," *Optom Vis Sci*, vol. 89, no. 10, pp. 1487-1496, 2012.
- [24] F. P. J. G. S. S. Wong TY, "Refractive errors, axial ocular dimensions, and age-related cataracts: the Tanjong Pagar survey," *Invest Ophthalmol Vis Sci*, vol. 44, no. 4, p. 1479–1485, 2003.
- [25] Y. J. H. S. L. S. Lim HT, "Prevalence and associated sociodemographic factors of myopia in Korean children: the 2005 third Korea National Health and Nutrition Examination Survey (KNHANES III)," *Jpn J Ophthalmol*, vol. 56, no. 1, pp. 76-81, 2012.
- [26] C. W. H. C. W. H. C. W. C. K. e. a. Saw SM, "Nearwork in early-onset myopia," *Invest Ophthalmol Vis Sci*, vol. 43, no. 2, pp. 332-339, 2002.
- [27] R. S. C. M. H. K. P. S. S. J. e. a. Woodman EC, "Axial elongation following prolonged near work in myopes and emmetropes," *Br J Ophthalmol*, vol. 95, no. 5, p. 652–656, 2011.
- [28] R. B. Goss DA, "Relationship of accommodative response and nearpoint phoria in a sample of myopic children," *Optom Vis Sci*, vol. 76, pp. 292-294, 1999.
- [29] M. I. I. J. K. A. H. S. S. W. e. a. Rose KA, "Outdoor activity reduces the prevalence of myopia in children," *Ophthalmology*, vol. 115, no. 8, pp. 1279-1285, 2008.
- [30] T. C. W. H. Y. Y. K. H. Wu PC, "Outdoor Activity during Class Recess Reduces Myopia Onset and Progression in School Children," *Ophthalmology*, vol. 120, no. 5, pp. 1080-1085, 2013.

- [31] R. M. K. R. K. A. M. D. F. P. Sherwin JC, "The association between time spent outdoors and myopia in children and adolescents: a systematic review and meta-analysis," *Ophthalmology*, vol. 119, no. 10, pp. 2141-2151, 2012.
- [32] B. M. M. I. B. M. Megaw PL, "Diurnal patterns of dopamine release in chicken retina," *Neurochem Int*, vol. 48, no. 1, pp. 17-23, 2006.
- [33] C. M. S. E. Hung LF, "Spectacle lenses alter eye growth and refractive status of young monkeys," *Nature Medicine*, vol. 1, pp. 761-765, 1995.
- [34] M. N. O. D. Chung K, "Undercorrection of myopia enhances rather than inhibits myopia progression," *Vision Research*, vol. 42, no. 22, pp. 2555-2559, 2002.
- [35] M. G. H. J. e. a. Mutti DO, "Accommodative lag before and after the onset of myopia," *Invest Ophthalmol Vis Sci*, vol. 47, pp. 837-846, 2006.
- [36] H. S. N. F. O. H. Nakatsuka C, "Accommodative lag under habitual seeing conditions: comparison between myopic and emmetropic children," *Jap J Ophthalmol*, vol. 49, no. 3, pp. 189-194, 2005.
- [37] C. L. P. D. Fulk GW, "A randomized trial of the effect of single-vision vs bifocal lenses on myopia progression in children with esophoria," *Optom Vis Sci*, vol. 77, no. 8, pp. 395-401, 2000.
- [38] W. G. D. B. S. K. Cheng D, "Effect of bifocal and prismatic bifocal spectacles on myopia progression in children: three-year results of a randomized clinical trial," *JAMA Ophthalmol*, vol. 132, no. 3, pp. 258-264, 2014.
- [39] C. o. M. E. T. 2. S. G. f. t. P. E. D. I. 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*, vol. 52, no. 5, pp. 2749-2757, 2011.
- [40] W. J. Ticak A, "Peripheral optics with bifocal soft and corneal reshaping contact lenses," *Optom Vis Sci*, vol. 90, no. 1, pp. 3-8, 2013.
- [41] G. K. M. M. J.-J. L. Walline JJ, "Multifocal contact lens myopia control," *Optom Vis Sci*, vol. 90, no. 11, pp. 1207-1214, 2013.
- [42] L. M. W. C. Aller TA, "Myopia Control with Bifocal Contact Lenses: A Randomized Clinical Trial," *Optom Vis Sci*, vol. 93, no. 4, pp. 344-352, 2016.
- [43] H. T. O. T. Kakita T, "Influence of overnight orthokeratology on axial elongation in childhood myopia," *Invest Ophthalmol Vis Sci*, vol. 52, no. 5, pp. 2170-2174, 2011.
- [44] C. S. Cho P, "Retardation of myopia in Orthokeratology (ROMIO) study: a 2-year randomized clinical trial," *Invest Ophthalmol Vis Sci*, vol. 53, no. 11, pp. 7077-7085, 2012.
- [45] e. a. Chua WH, "Atropine for the treatment of childhood myopia. (ATOM1)," *Ophthalmology*, vol. 113, pp. 2285-2291, 2006.

- [46] H. X. K. A. e. a. Tong L, "Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine," *Ophthalmology*, vol. 116, pp. 572-579, 2009.
- [47] C. W. C. Y. e. a. Chia A, "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*, vol. 119, pp. 347-354, 2012.
- [48] S. L. J.-J. L. Bullimore MA, "The risk of microbial keratitis with overnight corneal reshaping lenses," *Optom Vis Sci*, vol. 90, no. 9, pp. 937-944, 2013.
- [49] S. R. F. F. Vitale S, "Increased Prevalence of Myopia in the United States Between 1971-1972 and 1999-2004," *Arch Ophthalmol*, vol. 127, no. 12, pp. 1632-1639, 2009.
- [50] Z. Q. Li J, "Insight into the molecular genetics of myopia," *Mol Vis*, vol. 23, p. 1048–1080, 2017.
- [51] W. S. S. K. L. S. Qiu M, "Association between Myopia and Glaucoma in the United States Population," *Invest Ophthalmol Vis Sci*, vol. 54, no. 1, p. 830–835, 2013 .