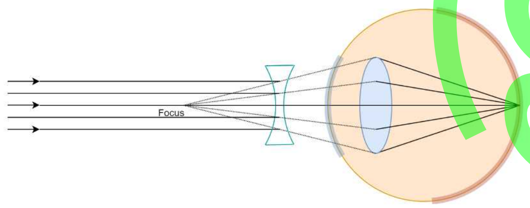

A Novel Adaptive Framework explaining Axial Shortening for Physiological Myopia

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0. Abstract

Current understanding is lacking when it comes to explaining plethora of existing observations about physiologic Myopia. We aim to propose an alternative framework to explaining these observations along with mounting counter evidences describing significant axial shortening (beyond measurement error threshold) taking into account the interplay of multiple physiological factors.

Careful characterization based on observations related to Myopia lead us to predict the breakthrough refractive state equivalences of our Continuous Adaptation Theory (CAT). The framework of CAT predicts physiological Myopia as an adaptative response of the eye. By extension, the same adaptive mechanism responsible for onset of Myopia (in emmetropic eyes) is also predicted to be responsible for Myopia progression (in myopic eyes) and can be repurposed by inducing hyperopic adaptation for Myopia management and even possible emmetropization in most cases.

The breakthrough variation on light therapy combined with behavioural interventions towards myopia management when implemented could result in first clinical observations of sustained long-term axial shortening translating into actual benefits to vision from myopia reversal.

0.1 Keywords

Axial Shortening, Progression, Myopia Management, Emmetropization

0.2 Ethics declarations

The author declares no competing interests.

0.3 Abbreviations

ILS – Ideal Lens System, RDS – Relative Dioptre Scale, AL – Axial Length, CAT – Continuous Adaptation Theory, ADV – Actual Distance Viewing

1. Introduction

Myopia – also termed near-sightedness/short-sightedness is a refractive condition widely regarded as irreversible with a suspected multifactorial aetiology lacking any viable long-term solution[1]. It is estimated that by 2050, half of the world's population will be myopic if the current trends continue unabated[2]. These worrying trends point towards an urgent need for interventions that can reverse/stabilize or at least slow down long-term rate of Myopia progression. Extreme axial elongation[3] resulting from highly severe Myopia is associated with dramatically increased risk of vision threatening complications (even after appropriate refractive compensation) including but not limited to glaucoma, retinal tears that can lead to retinal detachment, and macular degeneration[4].

The primary hypothesis behind this article is viability of emmetropization for Physiological Myopia compared to progressively malignant nature of pathological Myopia. There are mounting evidences that seemingly contradict existing assumptions about irreversible nature of Myopia and hint at the existence of a viable protocol that can induce emmetropization[5]. The objective of this article is to undertake careful characterization of a myopic eye's refractive state utilizing a mixed mode approach using both optics and incorporating experimental results/observations in order to find possible improper isolation of independent variables.

Article selection for documenting experimental results/observations for literature review used terms associated with mostly physiological Myopia on PubMed. In an attempt to maintain quality necessary for developing a theoretical framework, only article reporting significant physical observations were considered. In our bid to eliminate possible sources of confusion, we have strived to follow the guidelines outlined in (IMI – Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies[6]).

1. Carr BJ, Stell WK. The Science Behind Myopia. 2017 Nov 7. In: Kolb H, Fernandez E, Nelson R, editors. Webvision: The Organization of the Retina and Visual System [Internet]. Salt Lake City (UT): University of Utah Health Sciences Center; 1995-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470669/
2. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016 May;123(5):1036-42. doi: 10.1016/j.ophtha.2016.01.006. Epub 2016 Feb 11. PMID: 26875007.
3. Pugazhendhi S, Ambati B, Hunter AA. Pathogenesis and Prevention of Worsening Axial Elongation in Pathological Myopia. Clin Ophthalmol. 2020 Mar 18;14:853-873. doi: 10.2147/OPTH.S241435. PMID: 32256044; PMCID: PMC7092688.
4. Williams K, Hammond C. High myopia and its risks. Community Eye Health. 2019;32(105):5-6. PMID: 31409941; PMCID: PMC6688422.
5. Wang W, Jiang Y, Zhu Z, Zhang S, Xuan M, Tan X, Kong X, Zhong H, Bulloch G, Xiong R, Yuan Y, Chen Y, Zhang J, Zeng J, Morgan IG, He M. Axial Shortening in Myopic Children after Repeated Low-Level Red-Light Therapy: Post Hoc Analysis of a Randomized Trial. Ophthalmol Ther. 2023 Apr;12(2):1223-1237. doi: 10.1007/s40123-023-00671-7. Epub 2023 Feb 15. PMID: 36790672; PMCID: PMC10011250.
6. Flitcroft DI, He M, Jonas JB, Jong M, Naidoo K, Ohno-Matsui K, Rahi J, Resnikoff S, Vitale S, Yannuzzi L. IMI - Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies. Invest Ophthalmol Vis Sci. 2019 Feb 28;60(3):M20-M30. doi: 10.1167/iovs.18-25957. PMID: 30817826; PMCID: PMC6735818.

1.1 Conventions and terminology used in this article

Throughout this article, we will utilize prefixes like *compensated* myopic/hyperopic eye or suffixes like a myopic/hyperopic/presbyopic eye *wearing prescription* to denote an eye using refractive interventions differentiating it from a naked eye without any intervention. The mention of the word infinity or symbol ∞ can be taken to mean optical infinity at a distance of 10 m or greater (≤0.1 D).

Before reading, familiarity with scientific jargons and their meanings is paramount – assumption, definition, theory, prediction and its subsequent verification by experiments, facts, results, limited-scope, consistency etc. We have strived to provide terminologies and abbreviation whenever applicable at the beginning of each section.

2. Literature Review/Background

The primary objective of this article is to answer the questions:

Propose cause/reason/combination of environmental factors behind Myopia
Why so far there has been still no well established cause of Myopia?
Why is Myopia considered irreversible and what can be the reasons?

Literature review follows eyes -> physiological myopia (including its onset and progression) -> causes of Myopia -> effects of myopia on eyes -> current management and control methods

2.1 Physiologic Myopia and Pathologic Myopia

Physiologic Myopia is the defined as the proper inability to bring distant objects into focus compared to an emmetropic eye (image formation behind the retina even after relaxing accommodation). All observed instances of myopic refractive error can be termed either physiologic or pathologic/degenerative Myopia[7]. Even high degree of refractive error from physiologic Myopia (increasing risk of sequelae) must be distinguished from Pathologic Myopia[8]. Additionally, Pathological complications that can accompany highly severe forms of physiologic Myopia must be distinguished from Pathologic Myopia itself. Pathologic myopia is often associated with high myopia and complications of the fundus, however complications (esp. posterior staphyloma) have been observed to occur in eyes without high myopia and even in emmetropic individuals[9].

For the scope of the article, Physiologic Myopia refers to presentation of Myopia lacking pathologic consequences. This is important from the standpoint of consistent classification for Myopia – Myopia can

7. Grosvenor T. A review and a suggested classification system for myopia on the basis of age-related prevalence and age of onset. Am J Optom Physiol Opt. 1987 Jul;64(7):545-54. doi: 10.1097/00006324-198707000-00012. PMID: 3307441.
8. https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/1666440799
9. Kyoko Ohno-Matsui, Pei-Chang Wu, Kenji Yamashiro, Kritchai Vutipongsatorn, Yuxin Fang, Chui Ming Gemmy Cheung, Timothy Y. Y. Lai, Yasushi Ikuno, Salomon Yves Cohen, Alain Gaudric, Jost B. Jonas; IMI Pathologic Myopia. Invest. Ophthalmol. Vis. Sci. 2021;62(5):5. doi: https://doi.org/10.1167/iovs.62.5.5.

be either classified physiological or pathological but not both in the sense that Physiological Myopia can develop pathological complications later on implying difference in underlying mechanism and possibly control/management approaches.

2.2 Myopia onset and its progression

Myopia onset usually occurs in the early childhood. However, there are sufficient studies that disagree with the myopia stabilization hypothesis by documenting evidences of adults becoming Myopic after enrolling into college.

The onset of Myopia is usually viewed separately from progression of Myopia. This translates into a disease like presumed aetiology of Myopia where worsening Myopia is viewed as its natural course of progression. This standpoint is mostly justified in the absence of any viable long-term methods demonstrating the ability to slow or stabilize Myopia progression (myopia control[10]) or possibly reverse it. However, there is still no viable long-term method that directly targets axial elongation due to Myopia.

Most of the literature

2.3 Multi factorial causes behind Myopia

2.3.1 Genetics

For decades, investigations was primarily focused on genetic causes of Myopia.

There are multiple studies stating Myopia to be somewhat associated with Genetic factors but evidences are mounting that physiological Myopia might not be that dependent on genetic factors at all. At most, there can be genetic susceptibility towards physiological Myopia in the face of mostly missing heritable evidences for physiological Myopia[11]. Then there are findings that children with myopia are more likely to have myopic parents. Of note is one particularly striking aspect of the studies where reports of insignificance association of near work or outdoor activity with myopia (possibly stabilized Myopia in the absence of further details) coincides with not quantifying progressive cases of Myopia separately from stabilized Myopia [[12], [13]].

10. Smith MJ, Walline JJ. Controlling myopia progression in children and adolescents. Adolesc Health Med Ther. 2015 Aug 13;6:133-40. doi: 10.2147/AHMT.S55834. PMID: 26316834; PMCID: PMC4542412.
11. Milly S. Tedja, Annechien E. G. Haarman, Magda A. Meester-Smoor, Jaakko Kaprio, David A. Mackey, Jeremy A. Guggenheim, Christopher J. Hammond, Virginie J. M. Verhoeven, Caroline C. W. Klaver, for the CREAM Consortium; IMI – Myopia Genetics Report. Invest. Ophthalmol. Vis. Sci. 2019;60(3):M89-M105. doi: https://doi.org/10.1167/iovs.18-25965.
12. Yam JC, Tang SM, Kam KW, et al. High prevalence of myopia in children and their parents in Hong Kong Chinese Population: the Hong Kong Children Eye Study. Acta Ophthalmol. Epub ahead of print 24 January 2020. DOI: 10.1111/aos.14350.
13. Low W, Dirani M, Gazzard G, et al. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. Br J Ophthalmol 2010; 94: 1012–1016.

It is very difficult to isolate physiogical variables from all these studies on parental Myopia. It is very much unclear how much of a role genetics play towards progression of Myopia after accounting for the possibility that myopic children share most of the same physiological environment with their parents.

2.3.2 Near Work and the Recent discovery of its association with outdoor exposure

Another study properly considering Myopia progression reports environmental factors as significant[14].

Evidences are emerging that environmental physiological factors might play a crucial role in Myopia.

2.4 Effects of physiologic Myopia on human eyes and animal models of Myopia

The exact aetiology of myopia is still unclear however what happens during development of myopia can be said to be extremely well documented from animal models of Myopia and ocular biometry.

2.4.1 Animal Models of Myopia and Form Deprivation studies

There is large pool of studies documenting outcomes of inducing experimental myopia in animals. It is important to expect only a subset of these observations to actually apply to humans.

It has been observed that during development, the eye develops and responds to visual stimulus demonstrating feedback control mechanisms at work.[15]

Both hyperopia and myopia resulted in young chicks when convex and concave lenses were used to introduce defocus indicating that the animal eye has the capability to respond and compensate for the induced defocus.

Efforts to induce FDM (Form Deprivation Myopia) were successful even when the optic nerve has been cut indicating that the eye can fall back to other mechanisms when it comes to deciding course of adaptation. Experimental Myopia induced via these methods quickly subsided and emmetropia was achieved once external factors were removed suggesting that the built in mechanism is able to quickly detect and adapt to changes in the external environment.

There is considerable natural evidence regarding hemi-retinal form deprivation influencing local axial changes in infant monkeys before developmental eye-growth is completed. This study concluded that effects of form deprivation on refractive development in primates are mediated by presumably retinal

14. Lim DH, Han J, Chung TY, Kang S, Yim HW; Epidemiologic Survey Committee of the Korean Ophthalmologic Society. The high prevalence of myopia in Korean children with influence of parental refractive errors: The 2008-2012 Korean National Health and Nutrition Examination Survey. PLoS One. 2018 Nov 26;13(11):e0207690. doi: 10.1371/journal.pone.0207690. Erratum in: PLoS One. 2018 Dec 20;13(12):e0209876. PMID: 30475837; PMCID: PMC6261017.
15. Winawer J, Zhu X, Choi J, Wallman J. Ocular compensation for alternating myopic and hyperopic defocus. Vision Res. 2005 Jun;45(13):1667-77. doi: 10.1016/j.visres.2004.12.013. PMID: 15792842.

mechanisms integrating visual signals in a spatially restricted manner[16]. In chicks, hemiocular occlusion lead to similar observations.

2.4.2 The argument for distinguishing Axial elongation from eye-growth

That Axial elongation results from uncontrolled growth of the eyes from causes yet unknown is the most commonly encountered explanation with justifications given mainly in the form of experimental studies failing to observe improvement in myopia.

When it comes to physiologic Myopia, its causes are commonly stated as multifactorial interplay of environmental, lifestyle and physiological factors.

When it comes to axial elongation, animal models of Myopia indicate that retina does most of the work.

Genetics is also frequently mentioned as myopic individuals have more chances of a myopic parent. At the same time, care must be taken because older studies normally do not account for this distinction between physiological and pathological Myopia. However, the increasingly environmental association of Myopia with outdoor activity has led researchers to believe that at most genetics can result in predisposition towards physiologic myopia unlike the mostly hereditary nature of many cases of pathological Myopia.

However, there is plenty of evidence that multiple people even with significant near work habits do not become Myopic.

For instance, studies investigating under-correction of refractive prescription saw enhancement instead of inhibition of myopia progression compared to the full correction group [17, 18].

However Myopia still shows strong correlations with urban lifestyle, higher education, and the intensive visual near-work (defined as eyes working at or near their accommodation limit) that comes with it (including but not limited to reading, writing and time spent looking at displays whether PC/Laptop or smartphones/tablets)[19]. The study also calls for targeted workplace measures to reduce occupational exposure and mitigations.

16. Smith EL 3rd, Huang J, Hung LF, Blasdel TL, Humbird TL, Bockhorst KH. Hemiretinal form deprivation: evidence for local control of eye growth and refractive development in infant monkeys. Invest Ophthalmol Vis Sci. 2009 Nov;50(11):5057-69. doi: 10.1167/iovs.08-3232. Epub 2009 Jun 3. PMID: 19494197; PMCID: PMC2778320.
17. Chung K, Mohidin N, O'Leary DJ. Undercorrection of myopia enhances rather than inhibits myopia progression. Vision Res. 2002 Oct;42(22):2555-9. doi: 10.1016/s0042-6989(02)00258-4. PMID: 12445849.
18. Yazdani N, Sadeghi R, Ehsaei A, Taghipour A, Hasanzadeh S, Zarifmahmoudi L, Heravian Shandiz J. Under-correction or full correction of myopia? A meta-analysis. J Optom. 2021 Jan-Mar;14(1):11-19. doi: 10.1016/j.optom.2020.04.003. Epub 2020 Jun 2. PMID: 32507615; PMCID: PMC7752985.
19. Dutheil F, Oueslati T, Delamarre L, Castanon J, Maurin C, Chiambaretta F, Baker JS, Ugbolue UC, Zak M, Lakbar I, Pereira B, Navel V. Myopia and Near Work: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2023 Jan 3;20(1):875. doi: 10.3390/ijerph20010875. PMID: 36613196; PMCID: PMC9820324.

It is a possibility that Myopia might require multiple causes in combination.

After multiple decades of being considered and treated mostly as an irreversible condition, there is a recent influx of mounting evidences that myopia might not be irreversible as previously thought.

Human eye starts forming around third week of gestation and the process is mostly finished by the tenth week[20]. The eyes continue to develop after birth around the age of three years until it attains adult emmetropic size. This growth matches the eye's axial length with the focal components in order to form images at optical infinity without the need for accommodation (emmetropization process).

Describing axial elongation as uncontrolled eye-growth is contradictory from the standpoint of eye-growth alone. Axial elongation differs from the aforementioned actual all around developmental (globe) growth of the eye in the sense of mostly lateral and posterior pole elongation of the eye attached to retina – hence the term axial.

There might be possibility of axial changes arising out of environmental and behavioral factors primarily.

This distinction of axial elongation separate from eye growth is crucial to explain instances of focally controlled ocular growth in nature. For instance, in infant monkeys and chicks, hemiocular occlusion leads to hemiretinal elongation indicating local control of scleral growth [[21],].

That environment plays a key role in the development of Myopia via altering the equilibrium of homeostatic control mechanism inside the eye has been suspected for decades[22]. It has also been observed that these adaptive vision mechanism are a consistent feature across species[23].

However, one particular trend that must be noted was progression of Myopia in school aged children[24] and even adults during the confinement due to COVID-19 pandemic. Even stabilized adult myopic eyes reported Myopia progression.

consistent with increased prevalence of work from home and lockdown requirements.

20. Ludwig PE, Lopez MJ, Czyz CN. Embryology, Eye Malformations. [Updated 2022 Apr 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482496/
21. Smith EL 3rd, Huang J, Hung LF, Blasdel TL, Humbird TL, Bockhorst KH. Hemiretinal form deprivation: evidence for local control of eye growth and refractive development in infant monkeys. Invest Ophthalmol Vis Sci. 2009 Nov;50(11):5057-69. doi: 10.1167/iovs.08-3232. Epub 2009 Jun 3. PMID: 19494197; PMCID: PMC2778320.
22. Josh Wallman, Jonathan Winawer Homeostasis of Eye Growth and the Question of Myopia 2004/08/19 doi: 10.1016/j.neuron.2004.08.008
23. Chakraborty, R., Ostrin, L.A., Benavente-Perez, A. and Verkicharla, P.K. (2020), Optical mechanisms regulating emmetropisation and refractive errors: evidence from animal models. Clin Exp Optom, 103: 55-67. https://doi.org/10.1111/cxo.12991
24. Wang J, Li Y, Musch DC, et al. Progression of Myopia in School-Aged Children After COVID-19 Home Confinement. JAMA Ophthalmol. 2021;139(3):293–300. doi:10.1001/jamaophthalmol.2020.6239

All these observation together indicate that a rigorous adaptive process might be at work behind physiological Myopia.

2.5 Current Myopia control and management tactics

In the context of this article, Myopia control/management refers to interventions concerned with stabilization/reversal of Myopia only and should be distinguished from existing modes of refractive intervention such as lenses, contacts and surgical procedures whose primary goal is to improve vision by compensating for the defocus resulting from Myopia (subjective refraction[25]). The term compensation is more appropriate than using the term 'correction' when it comes to refractive interventions. There can be no fundamental difference between refraction induced by glasses, contacts or refractive surgeries from the standpoint of Ray optics.

2.5.1 Ortho-K and Atropine

2.5.2 Light Therapies

The two most promising and widely recommended management options – Atropine administration and Ortho-K suffer from rebound effects. The very observation of myopia returning to baseline levels confirms that these management strategies do not address the underlying cause affecting axial elongation and shouldn't be treated as such.

There is some promising advancement of management strategies towards achieving axial shortening in the form of light therapies. Light therapies build upon the observed safety of Sunlight acting as protecting agent against Myopia progression and shields children from becoming Myopic in the first place.

3. Refractive conditions of the eye

Precise characterization of the refractive state of a myopic/hyperopic/presbyopic eye demands Ray optics. The preliminary material supplied with this article serves as an in-depth refresher for the same. This article requires familiarity with the ideal lens system (ILS from now on) along with the concept of myopic/hyperopic shift in observation range from introduced defocus/screen distance changes and how observation ranges are represented on the Relative Dioptre Scale (RDS from now on).

3.1 Lumped Lens consideration of the human eye

Our main goal is quantifying changes to the observation range from refractive conditions. Instead of taking the traditional approach that has historically been attempts to precisely model the complex ocular

25. Kaur K, Gurnani B. Subjective Refraction Techniques. [Updated 2022 Dec 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK580482/

components present inside the eye, we have chosen the easier route of studying systems like the ILS for the human eye.

A labelled diagram[26] of the human eye is given below in Figure 3.1 for reference.

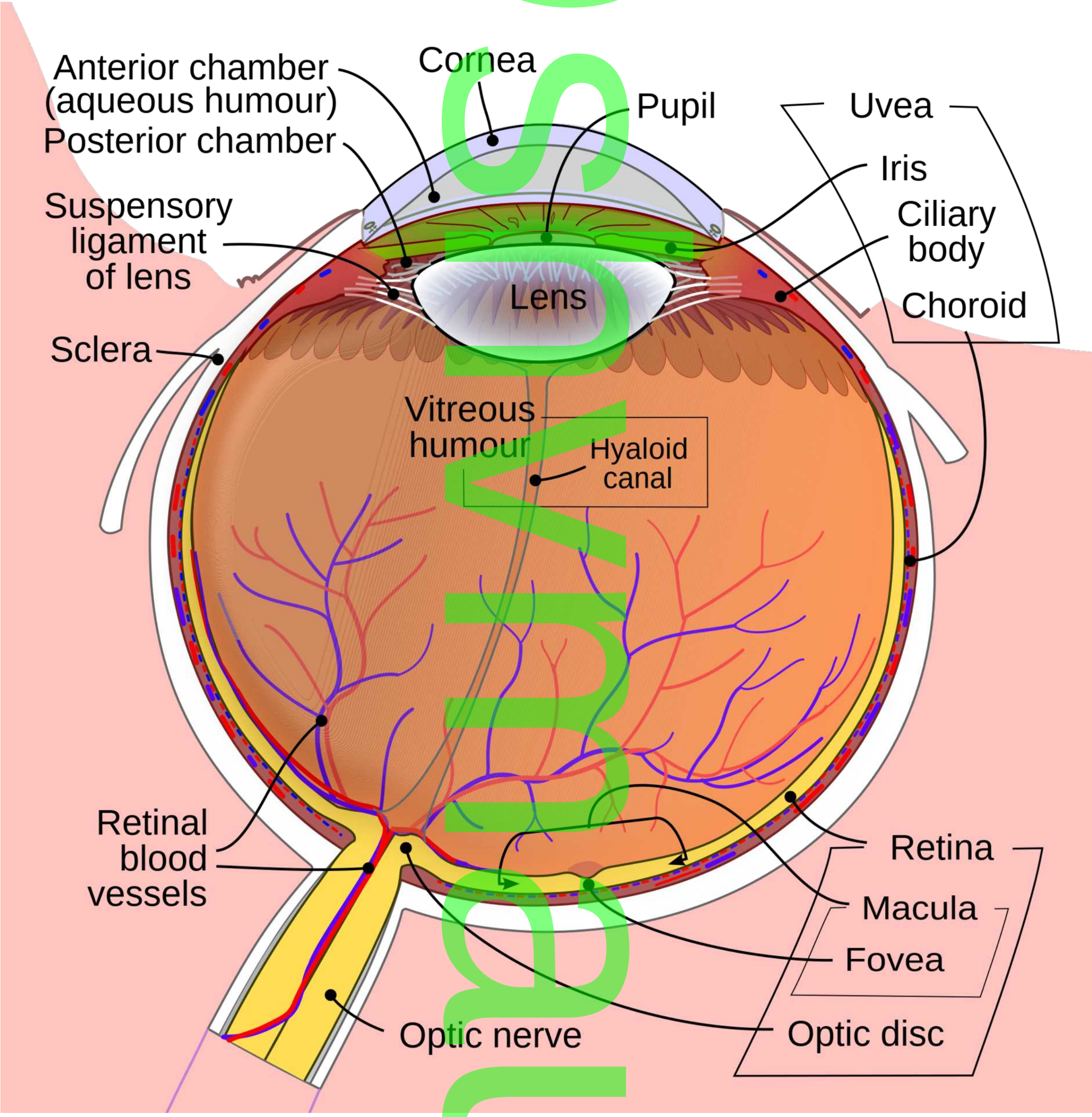

Figure 3.1 Labelled diagram of the human eye. It shows the lower part of the right eye after a central and horizontal section.

The role ocular components play inside the eye are explained in the order in which a light ray entering the eye traces its path towards photoreceptors on the retina.

Cornea → Aqueous humor → Eye lens → Vitreous humor → Photoreceptors on the Retina

26. Image: Rhcastilhos. And Jmarchn., CC BY-SA 3.0 <https://creativecommons.org/licenses/by-sa/3.0>, via Wikimedia Commons

The Pupil is a hole in the Iris acting like aperture in the ILS. The aqueous & vitreous humors act as an optical medium for light travel – any non-destructive/physiological changes to the index of the refractive media can be described as power changes, leaving us with remaining ocular components of the eye as:

Cornea → Eye lens → Photoreceptors on the Retina

The cornea and eye lens play the role of two fixed and variable power optical element with the retina acting as an image sensor. The cornea, the eye lens, and the mediums around them combined together converge light rays onto a spot on the retina forming an inverted image just like the ILS[27]. For our considerations, this has been assumed as a 'lumped lens' with refractive power of cornea and eye lens combined together and the retina acting as an image screen. The imaginary distance of retina from the optical centre of lumped lens will be referred throughout this article as Retinal Distance (RD from now on) and the same should be treated as screen distance equivalent of the eye. Any introduction of external defocus in the form of refractive intervention (glasses, contacts etc.) will be assumed to respect the power addition law. Our simplification are valid in actual real-world conditions for defocus lower than -5 D (Section 3.6).

Long term changes to the axial length from Myopia[28] involve the cornea (changes to the corneal curvature and ACD) and the posterior scleral shape involving physical distancing of the retina[29]. For our limited purposes, these changes to ocular components have been incorporated into the lumped lens consideration as shown in Table 1 below.

Table 1: Lumped lens consideration of the eye

Ocular component	Lumped Lens consideration
Accommodation of the eye lens due to ciliary muscle action	Instantaneous/Short-term Accommodation of the lumped lens
Long term changes to the corneal curvature	Long term accommodative shift of the lumped lens
Long term changes to the Anterior Chamber Distance	Long term increase in distance between retina and the lumped lens
Long term changes to the	

27. Sánchez López de Nava A, Somani AN, Salini B. Physiology, Vision. [Updated 2022 Jul 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538493/
28. van ALPHEN G. On emmetropia and ametropia. Opt Acta (Lond). 1961;142(Suppl):1-92. PMID: 13860704.
29. Jonas JB, Jonas RA, Bikbov MM, Wang YX, Panda-Jonas S. Myopia: Histology, clinical features, and potential implications for the etiology of axial elongation. Prog Retin Eye Res. 2022 Dec 28:101156. doi: 10.1016/j.preteyeres.2022.101156. Epub ahead of print. PMID: 36585290.

posterior Scleral shape	

3.2 Observation range of an Emmetropic eye

While the far-point of an emmetropic is ideally fixed at optical ∞, a representative value can be taken as the near-point of an emmetropic human eye without any loss of generalisation. For this article, we have taken this to be 25 cm for the sake of simplicity. It represents the closest distance of continuous focus an adult emmetropic eye is able to maintain without immediate fatigue/discomfort under daily circumstances. This value has been represented with a red dashed vertical line at the +4 D mark on the RDS. An elder person might not be able to observe objects this close due to presbyopia. Throughout this article, use of the word emmetropic without any prefix additionally means *an emmetropic eye with normal accommodation ability* (≥ 4 D).

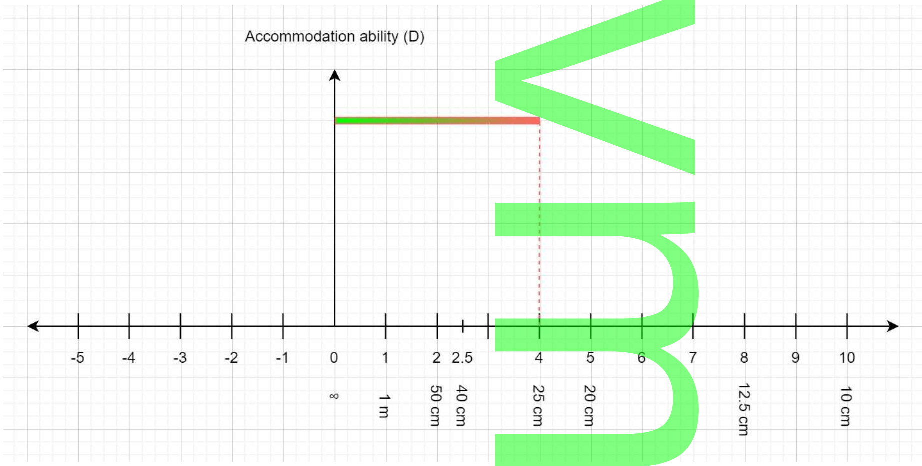

Figure 3.2 The observation range of an emmetropic eye (observation range: 25 cm up to ∞)

Because accommodation is facilitated by the ciliary muscle, the left end of observation range corresponds to relaxation (focusing at far-point) while the right end corresponds to maximum ciliary muscle contraction. All observation ranges can be divided into two distinct regions as shown in Figure 3.3 assuming the presence of a neutral point.

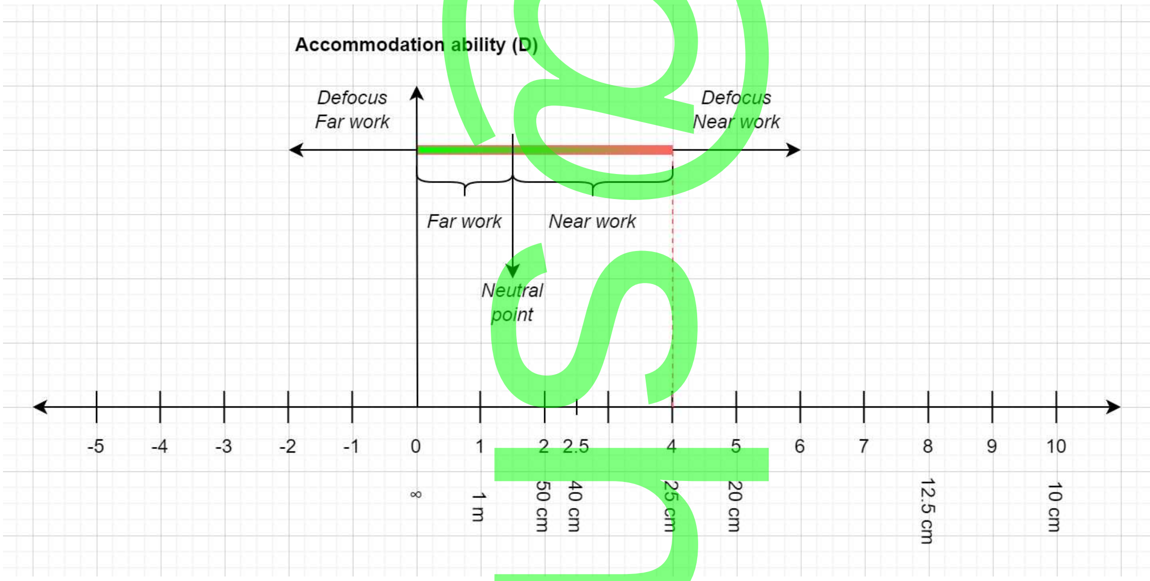

Figure 3.3: Observation range demarcation

This neutral point separates the observation range into two subsets – corresponding to far-work beyond the neutral point [d_{far}, $d_{neutral}$) and Near-work closer than the neutral point ($d_{neutral}$, d_{near}]. Once outside the observation range, defocus far work can be defined as ($-\infty$, d_{far}) and defocus near work as (d_{near}, ∞). It must be noted that these classifications apply regardless changes to the observation range.

3.3 Myopia/Hyperopia

It is important to note that for all eyes with refractive error, a best possible refractive compensation can be determined resulting in an observation range closely resembling an emmetropic eye (Figure 3.2).

Assuming the power addition law holds, this refractive compensation can then be 'subtracted' from the pseudo-emmetropic observation range giving the uncompensated observation range of the eye. Simply put, by knowing the near and far-points of a myopic/hyperopic eye after proper refractive compensation, its actual observation range can be determined by 'negating' the prescription. Astigmatism, floaters, and aberrations due to retina/refractive media can affect final image quality even with best possible refractive compensation. Visual acuity (resolution) is a property primarily associated with the retina that must be distinguished from defocus resulting from refractive conditions like Myopia or hyperopia[30].

30. Ji Hyun Kim, Hye Sun Lee, Na Rae Kim, Gong Je Seong, Chan Yun Kim; Relationship Between Visual Acuity and Retinal Structures Measured by Spectral Domain Optical Coherence Tomography in Patients With Open-Angle Glaucoma. Invest. Ophthalmol. Vis. Sci. 2014;55(8):4801-4810. doi: https://doi.org/10.1167/iovs.13-13052.

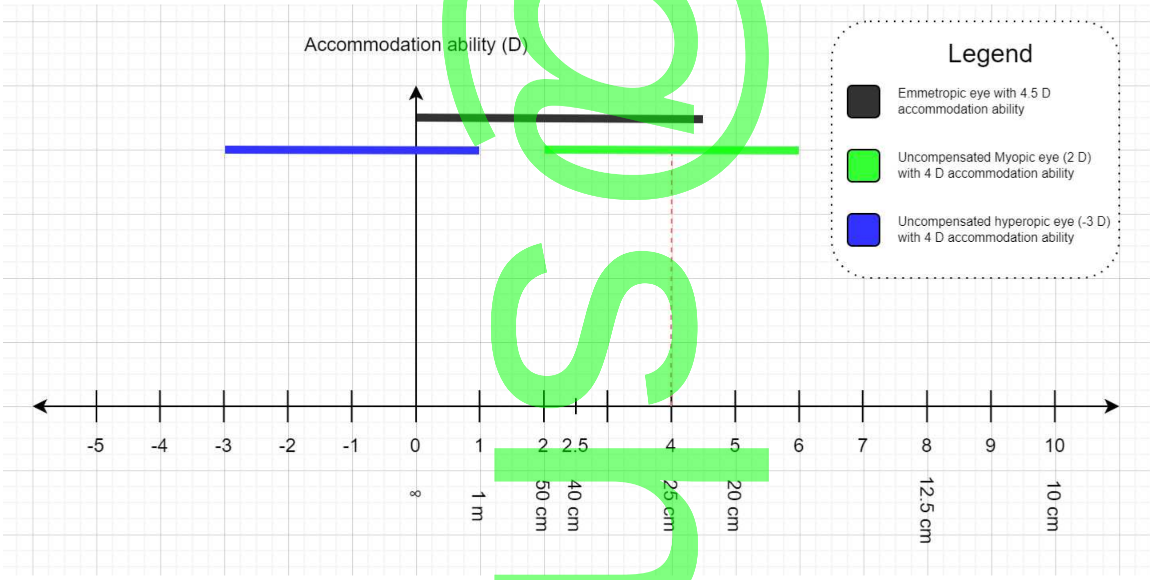

Figure 3.4: Myopic and Hyperopic observation ranges on the RDS

It can be stated that physiologic **Myopia** is a refractive condition in which the eyes' far point (the maximum distance at which the eye can **focus properly**) is closer than/no longer located at optical infinity.

Similarly, physiological Hyperopia can stated as a refractive condition in which the far point is situated well beyond optical infinity. Hyperopia/far-sightedness primarily results from axial changes to the eyeball such that images of closer objects are formed behind the retina.
Both physiological Myopia and Hyperopia mostly involve the screen shift mode like the ILS and they're compensated by defocus mode of refractive intervention.
Hyperopia is much less commonly encountered than Myopia. Prebyopia unlike Myopia or Hyperopia involves changes to the accommodation ability of the eye.

It should be now intuitive and easy to understand how appropriate compensation restores pseudo-emmetropia for aforementioned refractive conditions. It is evident that Myopic eyes require hyperopic shift in observation range for emmetropization and vice-versa.

3.4 Focusing vs. Exposing & Actual vs. Apparent focus

Having already differentiated between image distance and screen distance for ILS, one can extend this distinction in the context of exposing and focusing for the eyes too. This is necessary in order to be able to indicate the physical possibility that can involve for instance, an eye **focused** at infinity but **exposed** to a nearby white wall. The focusing part is extremely important as it enables us to efficiently dismiss other prevalent but wrong explanations for refractive conditions. Alternatively, an eye can be exposed to all possible distance but focused only within its observation range.

Even if a myopic eye is exposed to and observing infinity, it will still be *focused* at a point closer than infinity. The characteristic blur due to Myopia/Hyperopia results from *exposing* eyes to distances farther/closer their respective far/near-point. Thus, Myopia and Hyperopia should actually be seen as inability to focus distinct from eye conditions impacting visual acuity regardless of distance.

We will refer to focusing after refractive interventions as *apparent* focus to distinguish it from *actual* focusing without refractive intervention. The term **apparent focusing** refers to the focusing involving the eye and lens combined while **actual focusing** refers to unassisted focusing involving only the eyes.

It is obvious that for ***apparent*** focus at some distance, a myopic eye must ***actually*** focus at a distance closer than the said distance. For a hyperopic eye to achieve apparent focus at the same distance, it must actually focused farther than the distance in question. Refractive interventions in this context act as a mapping between actual and apparent observation ranges of the eye.

A diagram explaining this for the case of Myopia is given in Figure 3.5:

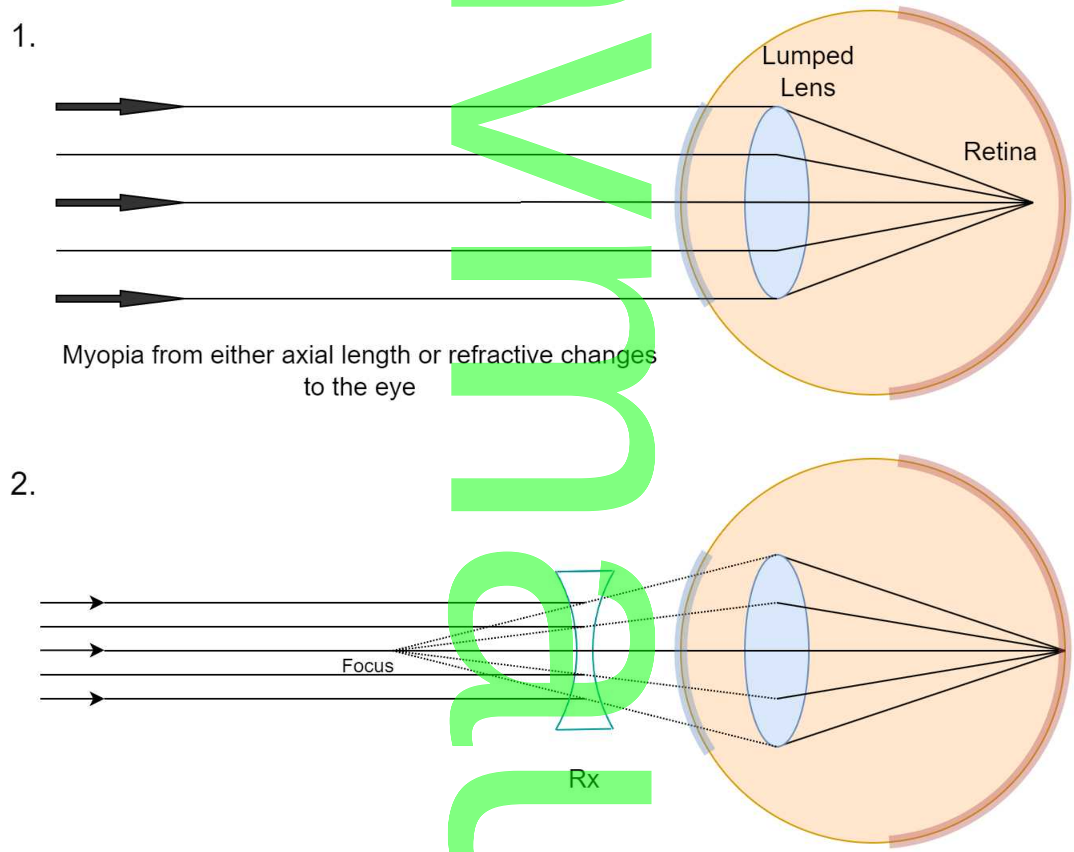

Figure 3.5 A diagram showing how refractive intervention compensate for Myopia.

In Ray optics speak, the introduced prescription introduces additional divergence to the incoming light rays shifting the resulting image plane to coincide with the retinal plane. It is intuitive to see how the compensated eye is actually focused at a distance closer than the apparent focusing distance.

3.5 Sign and severity designation of a refractive state

From the standpoint of Ray Optics, using (+)[31] sign for degree of Myopia encodes the true 'compensating' behaviour refractive interventions with opposite (-) sign have on the myopic observation range. This sign conventions allows for natural interpretation of statements reporting information about under-prescription without confusion such as "A person with 2.5 D Myopia wearing -2.0 D under-prescription."

Presbyopia is reduction in accommodation ability resulting in an additional (+) compensation requirement for observing closer distances and needs to be denoted with a negative sign just like Hyperopia.

According to WHO, High Myopia is defined at 5.0 D spherical equivalent or more. Other literature define High Myopia to start at 6.0 D spherical equivalent or more.

We have substantially demonstrated that Myopia being mostly axial in nature affects observation range mainly due to SPH defocus imposed on the eye. In the interest of scientific rigor, we have chosen to treat SPH and CYL components separately for this article. It is clear from the strictness of focusing criteria that a myopic eye is not in a position to focus beyond its far-point and a hyperopic eye is unable to focus closer than its near-point. The position of these points compared to an emmetropic eye determines the severity of myopia/hyperopia. These considerations lead us to propose defining refractive state severity on the basis of (threshold) lack of overlap between the actual observation range and its best compensated counterpart as shown below in Figure 3.6. The value of the overlap factor is the identical to the value required for threshold Myopia (≥0.5 D according to WHO).

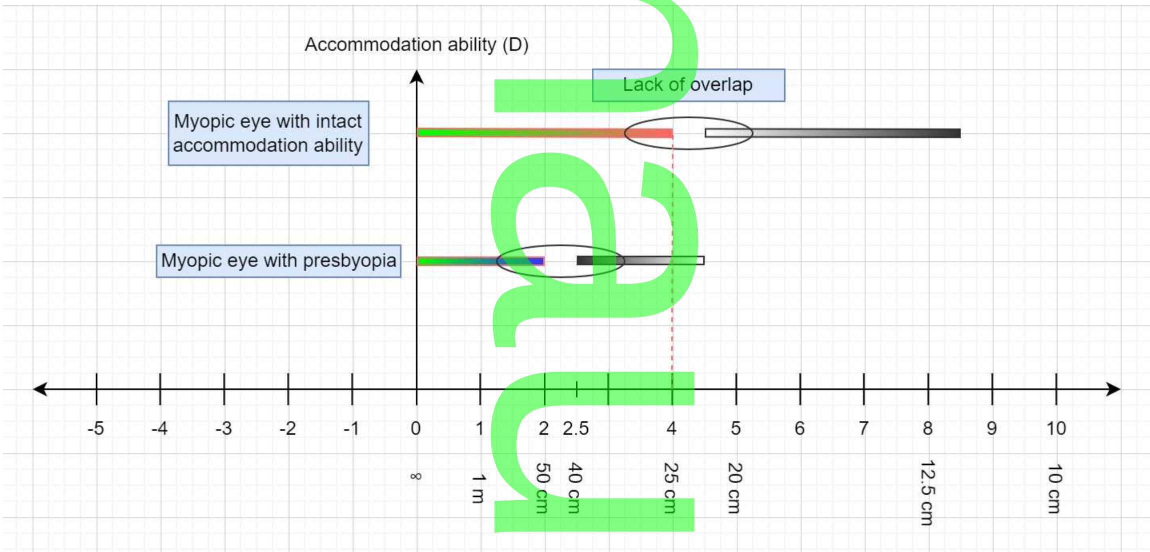

Figure 3.6: The 'overlap' criteria for determining severity of Myopia. The observation range in grey represents the uncompensated observation range without any refractive interventions.

The following arguments favour our overlap criteria for deciding severity of refractive states:

31. Fredrick DR. Myopia. BMJ. 2002 May 18;324(7347):1195-9. doi: 10.1136/bmj.324.7347.1195. PMID: 12016188; PMCID: PMC1123161.

1. Encodes the observation that a person satisfying the criteria is unable to focus at any 'reasonable' working distance without refractive intervention. Conversely, subjects with low myopia can focus closer than their far-point comfortably without refractive compensation because of the overlap.

2. Yields nearly equivalent classification as the existing scientific consensus values deviating only in the presence of Presbyopia.

3. Results in consistent threshold determination for both Myopia and Hyperopia.

4. Predicts an increase in risk posed by refractive conditions with age due to onset of Presbyopia. A borderline severe case of Myopia in adulthood can become severe myopia after some time.

5. Severity of Myopia depends on factors affecting observation range which may or may not be significantly affected by actual refractive errors like astigmatism in practice. This is one of the reasons behind avoiding 'spherical equivalents' in the first place.

Severe Myopia indicates the difficulty faced by eye's extraocular muscles when focusing close to its near-point (for highly severe myopia, even the far-point may be beyond reach of convergence without refractive compensation).

3.6 Distance between optical system (eye/camera) and introduced lens

Introducing a lens in this context means placing the lens (in the form of glasses/contacts) close to the optical centre of an optical system including the human eye.

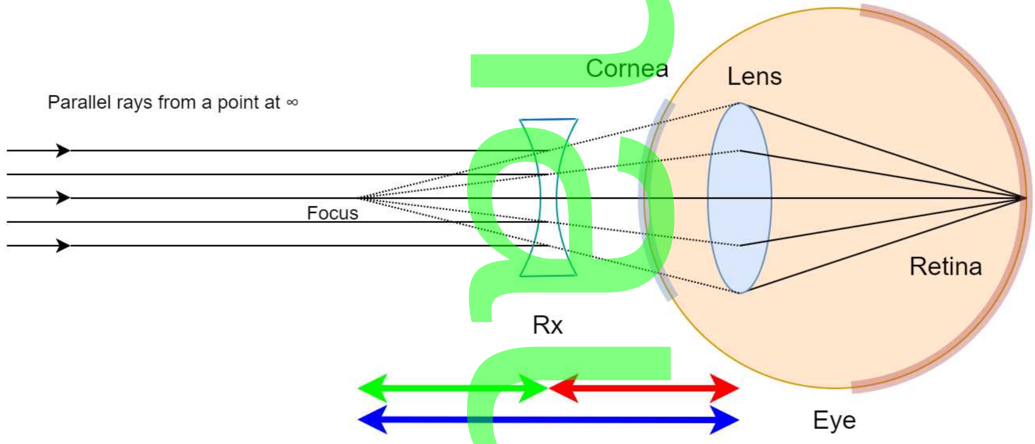

Figure 3.7 Calculating power difference due to distance between external lens and eye (highly exaggerated)

Consider the myopic eye in Figure 3.7, unable to focus beyond 51 cm (shown by blue). Let's assume the eyeglasses place the lens at a distance of 1 cm from the eye (red). For contacts, this distance becomes even closer. It is clear in this case that the diverging lens must make the object at infinity appear 50 cm in front of the lens (green) such that the eye achieves apparent focus at infinity.

$$lens\ distance\,(m) - \frac{1}{power\ of\ external\ lens} = \frac{1}{power\ of\ refractive\ condition}$$

The degree of Myopia comes out to be ~1.96 D. The diverging (-) lens required for compensating Myopia in this case comes out to be -2.0 D. The difference between them is smaller than the commercially available power increments available for prescription lenses which is usually not lesser than 0.25 D. The distance between eye and lens becomes significant only when we start dealing with higher powers for severe Myopia (~5 D). In case of an eye with 20 D Myopia, the power of lens required to compensate it keeping distance same comes out to be -25 D which is significant.

4. Discussions: Proposed Aetiology for physiological Myopia

This section builds the theoretical framework of our Continuous Adaptation Theory (CAT) describing ocular adaptive changes.

4.1 Changes to Accommodation-convergence reflex in Myopia

Human eyes form a stereoscopic pair for depth perception which necessitates the presence of simultaneous convergence[32]. Convergence is basically the simultaneous tilting of the axis of both eyes towards the object point in focus to form an aligned image. We'll only focus upon convergence aspects related to Myopia and characterize how the accommodation-convergence reflex must differ for myopia compared to emmetropic subjects.

For an adult emmetropic eye focusing on an object equidistant from both eyes, the relation between convergence angle θ and the accommodated power of eye is governed by $\theta = \sin^{-1}\left(\frac{IPD \times Accommodation\ Power}{2}\right)$, where IPD (InterPupillary Distance) has been used as distance between axis of two eyes. The angle between the respective image planes depicted in blue happens to be the sum of convergence angle for both eyes shown in Figure 4.1.

32. Linton P. Does vision extract absolute distance from vergence? Atten Percept Psychophys. 2020 Aug;82(6):3176-3195. doi: 10.3758/s13414-020-02006-1. PMID: 32406005; PMCID: PMC7381460.

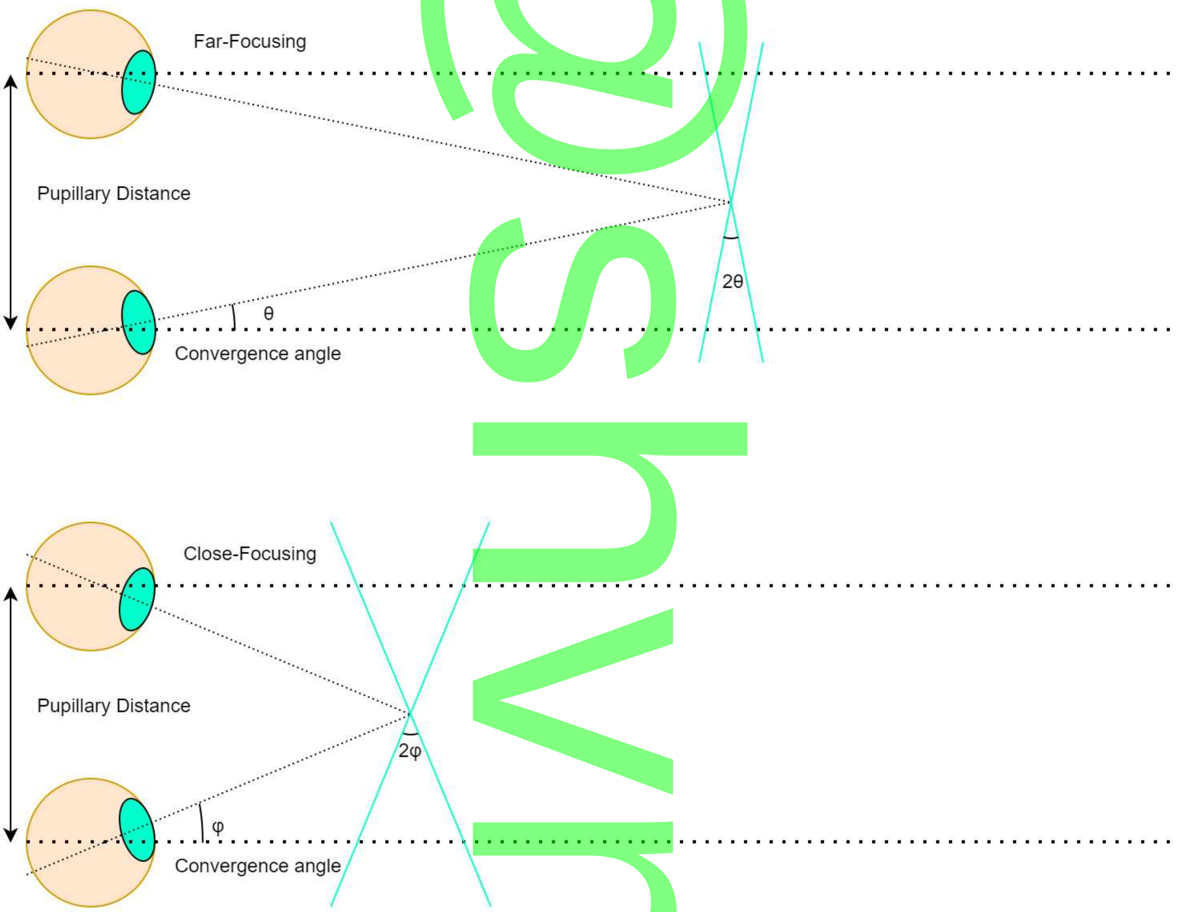

Figure 4.1 Depiction of convergence with observed distance compared to observing at infinity. Note the increasing angle between the image planes shown in blue as focusing distance gets closer.

Using avg. IPD of 63 mm gives 1.8°±0.1° of convergence angle for each eye per Dioptre of Accommodation. For focusing at 20 cm (+5 D accommodation, convergence is ~ 9°.

The increasing angle between the image planes corresponding to each eye as focusing distance comes closer must also be noted. The roughly cylindrical nature of image plane distortion with its axis normal to the line joining both eyes suggests its association with astigmatism. It predicts presence of baseline levels of astigmatism in emmetropic subjects mainly involved with significant near-work. It needs to be investigated how this particular form of cylindrical distortion affects the ocular biometry.

It is possible that fully compensating for this form of astigmatism can result in experienced discomfort and development of further astigmatism in subjects – (progression of astigmatism). Astigmatism of this form is best left slightly uncompensated unless it perceptibly affects visual acuity.

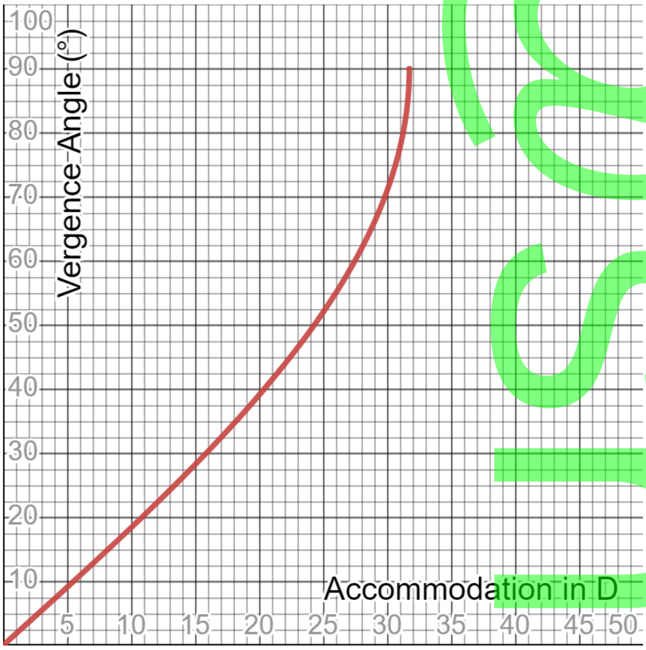

Figure 4.2: A plot of convergence angle with accommodation (IPD: 63 mm)

As can be seen from Figure 4.2, the reflex acts in a linear fashion even beyond the usually encountered accommodation ability for the eye (+4 to +5 D). It is not a mere coincidence that the range of ciliary accommodation falls mostly inside the contraction range of extraocular muscles responsible for convergence. Extraocular muscles responsible for convergence start hitting their limits at close-up distances characteristic of severe myopia necessitating refractive interventions and the same is accounted for in definitions of severe Myopia.

For an emmetropic eye with its far-point close to infinity, the reflex acts at all observed distances. The same applies to a pseudo-emmetropic eye also with best possible refractive compensation. For an uncompensated Myopic eye with its far-point no longer at infinity, accommodation begins only when convergence 'reaches' distances closer than the far-point. For distances beyond the myopic far-point, the eyes continues to maintain their relaxed state. This can be termed as introduction of **convergence lag** due to Myopia[33]. In both cases, it can be said that the reflex starts acting only when the observed distances reach closer than the far-point of the eye whether myopic or emmetropic.

We suspect that conflict[34] of the accommodation-convergence reflex plays a crucial role influencing reports of initial discomfort associated with wearing under or over-prescribed lenses. The common observation of discomfort stabilizing in few days suggesting that the convergence reflex could also get recalibrated within this time-frame.

33. Labhishetty V, Cholewiak SA, Roorda A, Banks MS. Lags and leads of accommodation in humans: Fact or fiction? J Vis. 2021 Mar 1;21(3):21. doi: 10.1167/jov.21.3.21. PMID: 33764384; PMCID: PMC7995353.
34. Yao Zhou, Jufan Zhang, Fengzhou Fang, Vergence-accommodation conflict in optical see-through display: review and prospect, Results in Optics, Volume 5, 2021, 100160, ISSN 2666-9501, https://doi.org/10.1016/j.rio.2021.100160.

4.2 Variable time-scale adaptive processes of the eye

A lot has been already described about accommodation in multiple texts. Put simply, contraction of ciliary muscle relaxes the suspensory ligaments holding the eye lens, allowing it to become thicker resulting in the shortening of focal length necessary for observing closer distances. Accommodation happens to be a very short-term (almost instantaneous) response due to ciliary muscle action. The ciliary muscle is relaxed when accommodation is not needed. A high-quality video of accommodation in action[35] can be accessed here: https://youtu.be/1yIpyitm6eE

Processes that result in axial changes take place on a relatively long-term time frames mostly due to changes involving the cornea, and the outermost scleral shape of the eye which is non-muscular in nature requiring time-scales of months and longer. Commonly encountered Myopia involves changes mostly axial in nature.

There are two ways in which the observation range of the ILS can be shifted: by accommodative shift due to defocus or by changing screen distance. The same is applicable for the Lumped Lens consideration and by extension the human eye. We have already reviewed how retinal distancing occurs during Myopia as a component of AL elongation. It is expected that accommodative-shift of some sort also takes place inside the eye during the course of Myopia.

This accommodative-shift contributing towards the non-axial component of transient myopia has to involve the ciliary body because only the ciliary muscle mechanically attaches to and changes the focal length of the eye lens. Myopic accommodative shift can thus be termed as state change in ciliary muscle translating into increased relaxed and accommodated power of the eye lens.

Prediction P1: We predict that the aforementioned accommodative shift acts as a medium-term (happening on the time-scale of days to weeks) **bridging** process between (short-term) accommodation and long-term axial changes. P1 also implies the existence of a biological pathway capable of responding to and alleviating transient state shifts in the ciliary muscle by inducing axial changes.

This prediction is strengthened from the distinct but continuous structures of iris, the ciliary body and the choroid (the layer between the retina and the sclera) comprising the uvea. It is well known that Choroidal thickness exhibits inverse association with the AL changes and the same can be incorporated as well[36].

4.3 Observation range shift due to Myopia

The eye experiences continuous changes to its observation range while undergoing refractive state changes. From the observation range of a Myopic eye and multiple real-world observations, it can be said that a

35. Goldberg D. Computer-animated model of accommodation and theory of reciprocal zonular action. Clin Ophthalmol. 2011;5:1559-1566 https://doi.org/10.2147/OPTH.S25983

36. Lee SS, Alonso-Caneiro D, Lingham G, Chen FK, Sanfilippo PG, Yazar S, Mackey DA. Choroidal Thickening During Young Adulthood and Baseline Choroidal Thickness Predicts Refractive Error Change. Invest Ophthalmol Vis Sci. 2022 May 2;63(5):34. doi: 10.1167/iovs.63.5.34. PMID: 35616928; PMCID: PMC9150825.

myopic eye gains additional close-range vision capability while *sacrificing* capability to observe distant objects as shown in Figure 4.3.

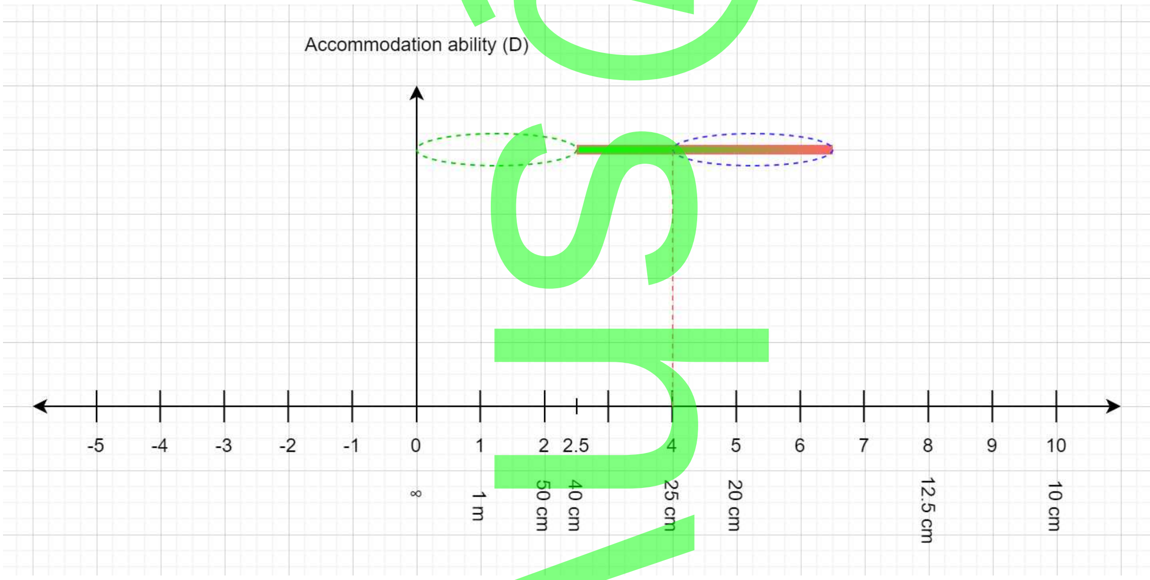

Figure 4.3: Compared to an emmetropic eye, the gained close-range observation capability by a Myopic eye (2.5 D) is shown with an blue oval while its sacrificed observation range for distance objects is shown with a green oval.

The blue oval denotes the distances between myopic near-point and emmetropic near-point while the green oval denotes distances between myopic far-point up to infinity (its emmetropic counterpart). It is evident that power gained at the near end (right) should be equal to the power lost at the far end (left) of the observation range.

Prediction P2: We assume that the human eyes try to adapt continuously towards the **exposed** visual stimulus in order to alleviate accommodation load on ciliary muscle. Eyes can respond to stimulus from accommodative load, defocus or even pathological factors. The scope of CAT is self-limited to non-pathological factors only.

The adaptive framework of our theory and the eyes as an organ dedicated towards visual perception means terming environmental factors that are optical in nature such as object distance (accommodation), contrast, brightness/intensity (affecting the pupil) or their combination as physiological factors. Factors not optical in nature, for instance: genetic abnormalities, birth defects/congenital anomalies and environmental factors different from physiological ones mentioned above such as, toxins, trauma, and other unidentified factors internal to the eye should be treated as pathological factors in the framework of CAT.

It might even be possible to derive assumption P2 from other elementary assumptions in the near-future but will not be attempted here. Because the ciliary accommodation ability is limited, presence of an under-utilised extreme of observation range should result in an even stronger adaptive response. For Myopia, this extreme of the observation range corresponds to focusing at distant objects. The aforementioned observation of Myopia initiation/progression resulting from the eye gaining additional close-range capability while sacrificing capability to observe distant objects can be explained as shift in equilibrium resulting from adaptive requirements from close-range stimulus driven by under-utilisation of distant vision capability. This can be understood by the simultaneous 'push-pull' analogy for shifting of observation range. For myopia, accommodative load can be said to 'pull' while underutilisation of distant vision capability exerts 'push' on the observation range. Push or pull in isolation is insufficient towards causing changes to the observation range.

This answers the first among many unexplained mysteries of Myopia: Why it is observed that some people do not experience Myopia even with 'significant' near-work habits[37]? We now have an answer in the form of sufficient utilisation of distant vision keeping in check the adaptation due to near-work. We predict no net shift in an eye sufficiently utilising both ends near and far of its observation range. It also explains why long-duration near-work correlates[38] with Myopia but is not sufficient towards being a cause for Myopia with the simple implication being under-utilisation of distant vision capability (not the same as near-work) should also be correlated with Myopia. This is also corroborated by multiple review studies[39] on Myopia.

Simply put, under-utilisation of distant vision capability is a more important consideration factor for Myopic adaptation in CAT resulting in the observation range of the eye (continuously) shifting *away* from observing farther distances *towards* closer distances. An eye doing long-duration near-work but also sufficiently utilising distance vision capability should only be signalling eye-strain from long-duration near-work without becoming Myopic. It also hints that emphasis towards proper utilisation of distance vision capability must form an essential requirement for management of Myopia.

4.4 The mechanism behind Myopic adaptation

We have previously described adaptative processes differing in the time-scale of operation work in the eye. These short-term, medium term and long-term processes together are responsible for maintain the refractive state of the eye in accordance with the environment. We have also described how the observation range of an emmetropic eye shifts during the development of Myopia.

The onset of Myopia has been mainly predicted to result from the ciliary muscle 'tiring' out during long-duration near-work and developing some form of (accommodative) spasm in the ciliary (pseudomyopia[40]).

37. Low W, Dirani M, Gazzard G, Chan YH, Zhou HJ, Selvaraj P, Au Eong KG, Young TL, Mitchell P, Wong TY, Saw SM. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. Br J Ophthalmol. 2010 Aug;94(8):1012-6. doi: 10.1136/bjo.2009.173187. Epub 2010 May 14. PMID: 20472747; PMCID: PMC4041336.
38. Huang HM, Chang DS, Wu PC. The Association between Near Work Activities and Myopia in Children-A Systematic Review and Meta-Analysis. PLoS One. 2015 Oct 20;10(10):e0140419. doi: 10.1371/journal.pone.0140419. PMID: 26485393; PMCID: PMC4618477.
39. Lagrèze WA, Schaeffel F. Preventing Myopia. Dtsch Arztebl Int. 2017 Sep 4;114(35-36):575-580. doi: 10.3238/arztebl.2017.0575. PMID: 28927495; PMCID: PMC5615392.
40. Khalid K, Padda J, Pokhriyal S, Hitawala G, Khan MS, Upadhyay P, Cooper AC, Jean-Charles G. Pseudomyopia and Its Association With Anxiety. Cureus. 2021 Aug 24;13(8):e17411. doi: 10.7759/cureus.17411. PMID: 34589322; PMCID: PMC8459808.

Doing near-work closer to the focusing limit of the ciliary muscle should theoretically bring faster exhaustion of the ciliary. This accommodation requirement of the ciliary should then translate into an adaptive requirement towards Myopia. Defocus near work should result in faster adaptation due to accommodative stress and defocus adaptation both.

Without 'suitable' interventions, the ciliary muscle starts developing accommodative-shift (in the medium-term time-span of days to weeks) in order to relieve the accommodative stress caused by long-duration near-work. It can be expected that a person with myopic ciliary shift should possess markedly better capability of doing near work for a longer time period along with suppression of near-work induced eye-stress.

Myopic shift in the ciliary could also result in discouragement towards utilisation of distance vision capability in the form of excessive tear formation, rapid/uncontrolled blinking, increased sensitivity towards bright lights and signalled discomfort (HARE[41]) establishing a subtle feedback loop that should promote further progression of Myopia.

Prediction P1 stated earlier is essential towards explaining this missing link between how accommodative requirements from near-work translate into eventual long-term axial changes during Myopia. The under-utilisation of distant vision capability in the presence of accommodative shift lets long-term adaptive processes to initiate Axial Changes in order to alleviate this myopic shift as long as the shift in ciliary is maintained. The subsidence of external factors forcing myopic adaptation results in equilibrium being established again with the ciliary gradually returning to its previous state with the axial changes in place observed as stabilization of Myopia.

Because accommodative-shift is a novel construct towards understanding Myopia, physical details about shift in the ciliary are hard to come by. We speculate that the reported observation of ciliary body thickening[[42], [43]] in Myopic subjects can serve as an indicator for myopic ciliary shift.

We've already mentioned that a component of astigmatism should result from increasing angle between image planes resulting from closer observation distances in section 5.1.a. Another form of astigmatism can be said to result from changes that the ciliary undergoes and then reverses during the process of developing accommodative shift factored with changes to retina and cornea from long-term AL changes. The

41. Christopher J, Priya Y, Bhat V, Sarma G. Characteristics of Headache in Children Presenting to Ophthalmology Services in a Tertiary Care Center of South India. Cureus. 2022 Feb 1;14(2):e21805. doi: 10.7759/cureus.21805. PMID: 35251869; PMCID: PMC8890450.
42. Bailey MD, Sinnott LT, Mutti DO. Ciliary body thickness and refractive error in children. Invest Ophthalmol Vis Sci. 2008 Oct;49(10):4353-60. doi: 10.1167/iovs.08-2008. Epub 2008 Jun 19. PMID: 18566470; PMCID: PMC2994597.
43. Dinesh Kaphle, Katrina L. Schmid, Leon N. Davies, Marwan Suheimat, David A. Atchison; Ciliary Muscle Dimension Changes With Accommodation Vary in Myopia and Emmetropia. Invest. Ophthalmol. Vis. Sci. 2022;63(6):24. doi: https://doi.org/10.1167/iovs.63.6.24.

‘recalibration’ of the accommodation-convergence reflex as introduction of convergence lag mentioned earlier is also predicted to happen alongside myopia.

An important consequence of the Continuous Adaptation theory is that it does away with the ‘eye-growth’ dichotomy and simultaneously explains many contradictions in the commonly accepted age-bound theory for Myopia progression and stabilization during mid-twenties. Keeping up with the ‘unconventional’ theme of this article’s explanations about Myopia, this argument too is supported from the observation that average human eyes stop growing and attain[44] their full adult size by three years.

This suggests at the possibility that Myopia stabilization happening during mid-twenties should boil down purely to changes brought by environmental and lifestyle factors from attaining adulthood and conscious improvements in viewing habits including eye-strain awareness during long duration near-work. Put simply, existing theories explaining Myopia are lacking when it comes to explaining observations like the surge in Myopia during COVID-19 in adults[45]. It also makes it trivial to explain why some subjects can still experience continued ‘Myopia progression’ throughout their adult lives.

4.5 Influence of lighting conditions on Myopia

This section aims to describe the influence environmental lighting levels have on Myopia.

The pupil of the iris[46] evolved as an aperture control mechanism to regulate the amount of light entering the eye. [Pupil size[47] in adults varies from 2 to 4 mm in diameter in bright light to 4 to 8 mm in the dark.] We will refer to environmental lighting conditions in terms of how it relatively affects the pupil size in healthy eyes: pupil constricted (bright) and pupil dilated (dim/dark) lighting conditions. The pupil is fully dilated in the absence of light.

From the lumped lens consideration, the dilated pupil’s shallower Depth of Field should result in extra accommodation demand on the ciliary in dim lighting conditions for the same observed distance. It is well known at this point that near-work under pupil dilated lighting conditions is correlated with Myopia[48]. There is also an established body of research on Myopia being the ‘default’ behaviour of various species of

44. Bhardwaj V, Rajeshbhai GP. Axial length, anterior chamber depth-a study in different age groups and refractive errors. J Clin Diagn Res. 2013 Oct;7(10):2211-2. doi: 10.7860/JCDR/2013/7015.3473. Epub 2013 Oct 5. PMID: 24298478; PMCID: PMC3843406.
45. Kohmarn T, Srisurattanamethakul N, Watcharapalakorn A, Poyomtip T, Poolsanam C. Outbreak of COVID-19-Related Myopia Progression in Adults: A Preliminary Study. Clin Optom (Auckl). 2022 Aug 4;14:125-131. doi: 10.2147/OPTO.S374155. PMID: 35959467; PMCID: PMC9359493.
46. Bloom J, Motlagh M, Czyz CN. Anatomy, Head and Neck, Eye Iris Sphincter Muscle. [Updated 2022 Jul 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532252/l
47. Spector RH. The Pupils. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990. Chapter 58. Available from: https://www.ncbi.nlm.nih.gov/books/NBK381/
48. Muralidharan AR, Lança C, Biswas S, Barathi VA, Wan Yu Shermaine L, Seang-Mei S, Milea D, Najjar RP. Light and myopia: from epidemiological studies to neurobiological mechanisms. Ther Adv Ophthalmol. 2021 Dec 19;13:25158414211059246. doi: 10.1177/25158414211059246. PMID: 34988370; PMCID: PMC8721425.

animal eyes when subjected to form deprivation in dim/dark environments [49,50 and 51]. Retinal Ganglion Cells (RGCs) are known to play a crucial role in influencing[52] adaptive processes of the eye in this regard.

Prediction P3: We suggest that there is a high chance that less than adequate levels of light (pupil dilated lighting conditions) during near-work accelerates the adaptation towards Myopia described in the previous section by utilising pathways similar to FDM. We've already pointed out how adaptive requirements from long-duration near-work and under-utilisation of distant vision capability combined constitute adaptive requirements towards Myopia. In this context, less than adequate lighting levels can be said to accelerate the rate of Myopic adaptation. This should explain why highly myopic people can show sensitivity to bright lighting visual environment which normally do not affect ordinary emmetropic individuals.

Inadequate lighting as a factor should be the last remaining puzzle piece in our understanding of physiological factors affecting Myopia. Because low light levels result in reduction of available light information, it also implies increased risk of alignment errors and visual aberrations thereby making Myopic adaptation inherently 'inferior' in this regard.

4.6 Equivalences in observation range and behaviour for an emmetropic eye and an eye compensated for Myopia

The behaviour shown by an emmetropic eye an eye compensated for Myopia can be subdivided into two parts – Equivalence of observation range shift and equivalence of observation range itself.

4.6.1 Equivalence of observation range shift

A myopic shift (towards right) in observation range should appear similar whether it happens to an emmetropic eye (termed onset of Myopia) or previously myopic eye (termed Myopia progression).

This equivalence compels us to suggest that (combined environmental and behavioural) factors causing onset of Myopia in an emmetropic eye should be responsible for Myopia progression in a compensated Myopic eye as well. Myopia progression is 'onset of Myopia' in an eye already compensated for Myopia.

It also means equivalence in behaviour of an emmetropic eye and a myopic eye with stabilized Myopia.

49. Marcus H.C. Howlett, Sally A. McFadden, Form-deprivation myopia in the guinea pig (Cavia porcellus), Vision Research, Volume 46, Issues 1–2, 2006, Pages 267-283, ISSN 0042-6989, https://doi.org/10.1016/j.visres.2005.06.036.
50. Zhou X, Lu F, Xie R, Jiang L, Wen J, Li Y, Shi J, He T, Qu J. Recovery from axial myopia induced by a monocularly deprived facemask in adolescent (7-week-old) guinea pigs. Vision Res. 2007 Apr;47(8):1103-11. doi: 10.1016/j.visres.2007.01.002. Epub 2007 Mar 9. PMID: 17350070.
51. Ji FT, Li Q, Zhu YL, Jiang LQ, Zhou XT, Pan MZ, Qu J. [Form deprivation myopia in C57BL/6 mice]. Zhonghua Yan Ke Za Zhi. 2009 Nov;45(11):1020-6. Chinese. PMID: 20137422.
52. Kim US, Mahroo OA, Mollon JD, Yu-Wai-Man P. Retinal Ganglion Cells-Diversity of Cell Types and Clinical Relevance. Front Neurol. 2021 May 21;12:661938. doi: 10.3389/fneur.2021.661938. PMID: 34093409; PMCID: PMC8175861.

4.6.2 Equivalence of observation range

Our eyes lack any special capability to distinguish between types of refractive interventions. This hints at the consideration that apparent observation range of a best compensated myopic/hyperopic (pseudo-emmetropic) eye should not differ considerably from the actual observation range of an emmetropic eye. An emmetropic eye and a pseudo-emmetropic eye are equivalent when it comes to their actual and apparent far-point respectively.

For a myopic eye to experience change in Myopia – it goes without saying that the same must be accompanied by hyperopic shifting of its far-point. We have already demonstrated experimentally that a myopic eye apparently focusing at infinity with the help of refractive compensation must be actually focused at its myopic far-point. We have termed this as ‘clamping’ of actual far-point due to worn prescription (daily use glasses/contacts or even refractive surgery) shown in Figure 4.4.

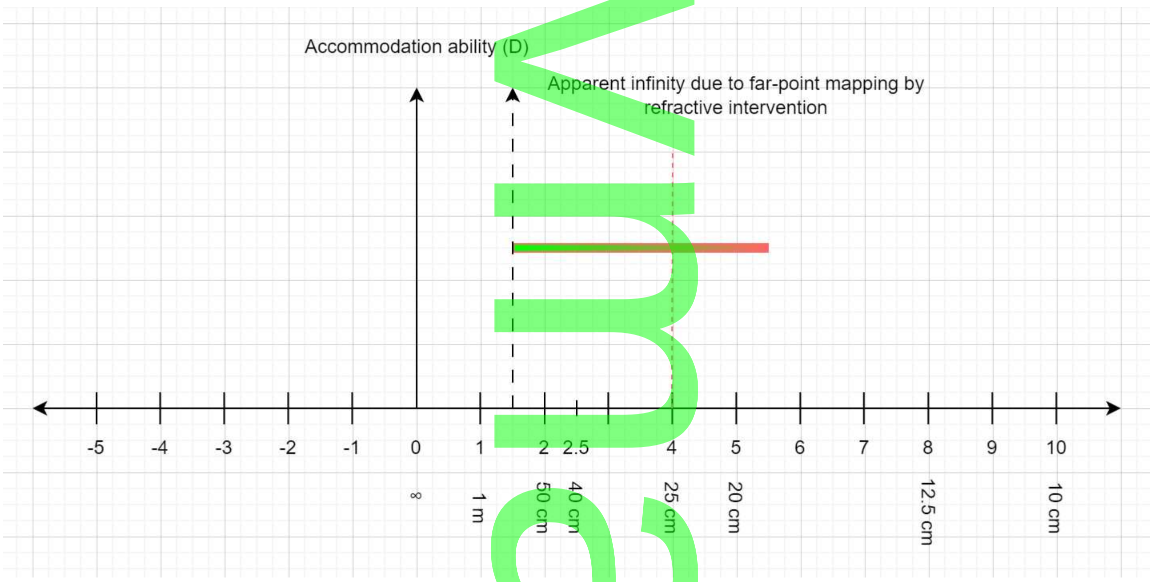

Figure 4.4: Clamped far-point of a Myopic eye due to refractive compensation

It can even be stated the other way around: expecting Myopia reversal for a pseudo-emmetropic eye whose far-point is clamped by refractive intervention is equivalent to expecting the far-point of an emmetropic eye to shift farther away (become hyperopic) from its ‘naturally clamped’ position at infinity. Nothing happens in either of the cases simply because relaxation of the ciliary muscle at the far-point does not constitutes accommodative stress towards adaptive requirement. This is the reason why it is impossible for Myopic far-point to recede beyond the clamped far-point introduced by refractive intervention in any adaptive system. It should also explain why truly physiologic hyperopic progression unlike Myopia progression is not observed.

This has a simple physical implication that inducing hyperopic adaptation should be impossible without myopic defocus. Myopic defocus is a necessary (not sufficient[53]) requirement for reversing Myopia.

From both theoretical and experimental standpoints, the widely stated observation regarding 'distance viewing with best possible refractive intervention not resulting in Myopia reduction' can not be considered conclusive towards deciding reversibility of physiological Myopia. Reversibility of Myopia depends on the behaviour shown by the eye only when complete adaptive requirements are satisfied.

The findings from these two behavioural equivalences are stated below (Table 2):

Table 2: Behavioural Equivalence between a pseudo-emmetropic eye and an emmetropic eye

Myopic eye wearing best possible refractive compensation (pseudo-emmetropic eye)	**Emmetropic eye**
No observed reversal of Myopia even after viewing distant objects with best possible refractive compensation	No observed hyperopia (shifting of far-point beyond infinity) even after viewing distant objects
Myopic adaptation is seen as Myopia progression	Myopic adaptation is seen as Onset of Myopia
Some population observes myopia stabilization even with near-work habits.	Some population observes no myopia even with near-work habits.
Apparent Far-point lies at infinity	*Actual* far-point lies at infinity

The refractive state of a physiological myopic/hyperopic eye is as '*valid*' as emmetropia from the standpoint of CAT. These equivalences and the lack of specific anomalies inside the eye should serve to distinguish physiological Myopia from pathological Myopia. Physiological myopia can not be termed as some disorder or disease. This is required from the self-consistency standpoint of our theoretical framework and the resulting behavioural equivalences.

4.7 Predicting time taken for long-term axial changes to the eye

There are two approaches to predict the time taken for long term axial changes. Both approaches should converge at same estimates.

The first approach emerges from the consideration that both myopic and hyperopic adaptation are the outcome of same adaptive process. This means myopic and hyperopic adaptations should bear rough

53. Chung K, Mohidin N, O'Leary DJ. Undercorrection of myopia enhances rather than inhibits myopia progression. Vision Res. 2002 Oct;42(22):2555-9. doi: 10.1016/s0042-6989(02)00258-4. PMID: 12445849.

similarity on the order of time-scales on which they take place. By our prediction, time required for Hyperopic adaptation can be estimated from the data on Myopia progression[54]. The observed rate of hyperopic adaptation should only be slightly faster than the progression rate of Myopia because it requires pupil constricted lighting conditions with more available information.

The second approach involves figuring out the relation between axial length of the eye with the retinal image distance from the optical centre of the eye (RD) and then employing the simple lens model's screen shift calculations. The second approach is described in detail below.

For an emmetropic eye, the RD should also be equal to the combined focal length of the lens and cornea when the eye is focused at infinity. The lens formula should then give the required shift in RD for focusing an object at the Myopic eye's far-point. To determine retinal distancing from AL measurements, we have assumed Myopic RD to be proportional to AL denoting the ratio RD/AL as β.

$$\textit{Lens relation}: \quad \frac{1}{s} - \frac{1}{u} = \frac{1}{f}$$

Here, elongated (myopic) RD serves as screen distance (s) and emmetropic eRD serves as focal length (f)

$$\frac{1}{RD} + \frac{1}{-u} = \frac{1}{f}$$

$$\textit{emmetropic } RD\ (f) = \frac{-u \times RD}{-u + RD}$$

$$\textit{if we assume } RD / AL \textit{ as } \beta \textit{ then}$$

$$\textit{Elongation in Axial Length } \Delta AL \textit{ due to Myopia} = AL - \frac{f}{\beta} = \frac{\beta \times (AL^2)}{-u + \beta \times AL}$$

For instance, a myopic eye wearing prescription of −4 D corresponding to a far − point of roughly 25 cm will give u as −25 cm for the formula.

If the axial length and degree of Myopia of a non-severe Myopic eye is known, this formula gives change in AL that must be necessary for emmetropia if β is known. Measuring the long-term rate of AL changes arising out from regular ADV sessions could then yield a rough estimate of the time for emmetropization. We want to emphasize that any calculations based on the second approach require long-term data on sustained axial shortening which is currently lacking due to the lack of any viable method to reverse Myopia in the first place.

54. Verkicharla PK, Kammari P, Das AV. Myopia progression varies with age and severity of myopia. PLoS One. 2020 Nov 20;15(11):e0241759. doi: 10.1371/journal.pone.0241759. PMID: 33216753; PMCID: PMC7678965.

4.8 Changes to Field of View due to Axial Length Changes

FoV depends on the screen distance which in the case of Lumped Lens consideration is taken as the distance of the central part of the retina (RD) from combined optical centre of the lens and the cornea. Axial elongation due to Myopia results in the physical distancing of the posterior part of retina while the region responsible for clear vision remains mostly unchanged at least for cases of non-severe Myopia.

The resulting FoV reduction can be estimated from *emmetropic AL* ÷ *myopic AL* assuming the proportionality of AL with Retinal Distance (RD). This works in a manner similar to how focal length changes affect FoV of the image in a camera. For instance, emmetropic AL of 23 mm and Myopic AL of 25 mm result in myopic FoV being roughly 0.92× (times) that of the emmetropic FoV.

Any mainstream investigation into Field-of-View characterization regarding Myopia is virtually non-existent. The closest study that considers FoV changes in highly myopic subject is the one done by {Yanming Chen; Ji Liu; Yining Shi} on visual field features venturiig in the pathological domain[55]. It is reasonable on the basis of optics alone that effects of FoV reduction start resembling 'tunnel vision effect' with highly severe Myopia. This also implies that people managing significant Myopia reversal should experience widening of their FoV.

4.9 Summing up the Continuous Adaptive Theory (CAT) for physiological Myopia

In the framework of CAT, physiological Myopia is treated as a 'valid' refractive state of the eye brought on by multifactorial integration of environmental/lifestyle factors over time. The continuously adaptive aspects are also naturally consistent with the evolution of eyes as a visual organ.

Because we have proposed Myopia as a 'valid' refractive state of the eye, a tabulation of the conditions required for myopic adaptation vs hyperopic adaptation is being provided below:

Table 3: Physiological factors required to induce adaptation

Function	Onset/Progression of Myopia	Hyperopic adaptation
Visual stimulus 'pulling' shift in adaptive equilibrium	Near work induced accommodative stress from ciliary muscle contraction	Myopic defocus under pupil constricted lighting conditions (ADV)
Visual stimulus 'pushing' shift in adaptive equilibrium	under-utilisation of distance vision capability	Near-work management and periodic breaks as signalled by the eye to alleviate

55. Yanming Chen, Ji Liu, Yining Shi; Evaluation of visual field changes of high myopic eyes in a Chinese population at northwestern China.. Invest. Ophthalmol. Vis. Sci. 2015;56(7):2952.

		accommodative stress.
Promoter Lighting Conditions	Pupil dilated	Pupil constricted
Accommodative shift in the ciliary/feedback loop	Myopic	Hyperopic
Shift in Observation Range (far-point and near-point)	Towards Right	Towards Left
Secondary refractive errors	Results in aberrations and progression of refractive errors like astigmatism	Corrects aberrations and refractive errors
Field of View	Shrinks	Expands
Time Interval	Existing Myopia progression rates	slightly faster than Myopia progression due to more light information

4.9.1 Strength and Limitations

The strength of this theory lies in predicting the development, progression and even till date lack of observed reversal of Myopia in a consistent manner in contrast with existing explanations. CAT is also the only theory of myopia in accordance with the theory of evolution via natural selection.

Because of the way CAT re-defines pathological Myopia from physiological Myopia in terms of reversibility, the theory breaks down for pathological Myopia due to unpredictable alterations to the underlying adaptive mechanism responsible for maintaining refractive state of the eye.

5. Conclusion

The framework of CAT put forward in this article might very well be the first such explanation put forward characterizing physiological Myopia in a way that manages to consistently and convincingly explain nearly all clinically observed aspects of physiological Myopia including but not limited to its onset, progression and even its apparent irreversibility so far in clinical trials so far. Because of the multi-factorial aetiology of physiological Myopia, the theory successfully explains existing clinical trials failing to observe Myopia reversal on the inability to properly separate the underlying physiological variables.

We expect the sheer predictive prowess of CAT to continue with rapid light therapy optimisation coupled with behavioural interventions for effective Myopia management.

5.1 Key takeaways

We expect that long-term commitment along with multiple habitual and lifestyle interventions are required from candidates willing to reverse physiological myopic state near emmetropic levels. From modifying their lifestyle to reducing the impact of near-work stimulus to a minimum to not letting go of any chance of viewing distant objects during breaks – it is theoretically very simple but practically very difficult.

The author recognise the tediously slow and time intensive nature (taking months and years) for the Myopia reversal process outlined in this article. Still, we are firmly convinced that the results outlined should be of enormous utility towards maintaining post-refractive surgery outcomes and preventing Myopia progression in subjects.

At the same time we want to stress that our simple lens model can not differentiate between peripheral and central components of vision or predict myriad of other factors that can play a role towards towards promoting Myopia in the human eye.

Although this article provides a method for satisfying necessary conditions for observing stabilization and/or reversal of Myopia, the article should not be taken as against wearing glasses/contacts or refractive interventions in general. The goal of this article is to reduce subject's dependence on glasses and promote safe and minimally invasive management of Myopia.

5.2 Challenging the status quo and existing explanations for Myopia

The response of the eyes towards ADV under pupil constricted lighting conditions is so important that we feel confident declaring it as the 'discrimination' test for pathological Myopia which by definition should result in failure of the very adaptation mechanism described in this article. It also follows that pathological Myopia should be distinguished on the basis of additional complications aside from the refractive state of the eye.

We expect subjects with even long-term childhood myopia to start experiencing clear flashes within their first few session of ADV. This should serve as cementing the predictions about eyes responding and beginning to adapt within first few days of ADV sessions.

5.3 Corporate responsibility of Myopia

The key role played by accommodative-stress towards Myopia once firmly established should also mean recognising the contribution made by lack of 'official' near-work breaks in the IT sector. We expect companies and lawmakers to recognise the importance of ADV towards both preventing and managing Myopia and provide facilities and incentives for encouraging the same.

5.4 Further research

Proposing precise set of conditions that must be satisified for reversing physiological Myopia presents a massive unexplored opportunity in front of the research community. We attempt to highlight a select few of them.

1. Optimal myopic defocus under pupil constricted lighting conditions that promotes fastest rate of hyperopic adaptation.
2. Whether severity criteria mentioned in this article can actually be extended for Hyperopia and investigating implementation of Myopic adaptation for Hyperopic subjects.
3. Further optimisation of lighting environment and distant calibration target requirement for ADV.
4. Experimental studies trying to observe form-deprivation hyperopia under pupil constricted lighting conditions.
5. Investigation into the role played by mechanistic interaction of the iris with ciliary.

6. Appendix: Implementation details for Myopia Management according to CAT

Current myopia management[56] interventions including but not limited to atropine, Ortho-K, relative peripheral myopia-inducing devices, or prism/bifocals carry reports of rebound Myopia upon cessation – an indication that the underlying cause of Myopia remains unaffected as predicted by CAT.

The natural and obvious end-goal for any theory capable of consistently and convincingly explaining various counter-intuitive observations about Myopia should be its ability to arrive at a physically viable method towards significant reversal of Myopia. The following sections describe our method for Myopia management in accordance with CAT.

6.1 Predicted requirements for Reversing Myopia

If Myopia is indeed a 'valid' refractive state of the eye as a consequence of adaptation, shift in adaptive equilibrium must be induced in the opposite direction for reversing Myopia. To achieve this shift, we need to determine 'duals' or principles opposite to the ones responsible for Myopic shift.

To summarise our findings in this article, section 4.3 covers why accommodative stress from long-duration near-work coupled with under-utilisation of distant vision capability should result in Myopic shift. Section 4.5 predicts why low-light should accelerate Myopia. Section 4.6 points out how observing no reversal of Myopia even while viewing distant objects with best possible refractive compensation is not sufficient to decide irreversibility of Myopia.

56. Chuang AY. How to effectively manage myopia. Taiwan J Ophthalmol. 2017 Jan-Mar;7(1):44-47. doi: 10.4103/tjo.tjo_24_17. PMID: 29018754; PMCID: PMC5525606.

It follows that requirements towards inducing hyperopic shift should result from Myopic defocus in pupil constricted lighting environment and reduction of existing accommodative stress from near work causing myopia in the first place. This emerges from the idea that a pseudo-emmetropic eye and an eye with very low levels of Myopia should differ only in their ability to observe distant objects and the observation that relaxing ciliary muscle does not constitutes accommodative stress.

These summarised findings and their corresponding duals are given below:

Table 4: Duals of physiological factors required for myopic adaptation

Observed requirements that result in Myopic adaptation	**'Duals' for inducing Hyperopic adaptation**
Accommodative stress from near-work resulting in adaptive requirement.	Saturation levels of Myopic defocus (exposure beyond far-point)
Under-utilisation of the distance vision capability	Near-work management to reduce accommodative stress causing Myopic adaptation in the first place.
Myopic adaptation is accelerated under pupil dilated lighting conditions	Hyperopic adaptation needs pupil constricted lighting conditions

These duals form the breakthrough physical requirements for inducing hyperopic adaptation: exposure towards myopic defocus under pupil constricted lighting conditions such as those that occur on a clear sunny day and management of near work to reduce accommodative stress causing myopic adaptation in the first place. These 'duals' expand our theoretical framework that now explains why earlier attempts[57] at reversing Myopia failed so far using reduced prescription.

The distances beyond far-point (myopic defocus) that need to be observed under pupil constricted lighting conditions lie inside the green oval for a myopic eye shown in Figure 4.3. Throughout this article, we will refer to this as ADV (short for Actual Distance Viewing). Because hyperopic adaptation requires pupil constricted lighting conditions, it follows that it should also be slightly faster (Superior than Myopia) due to availability of more information in bright lighting conditions.

The framework of CAT also predicts that the eyes try to adapt continuously towards all visual stimulus that can be encountered during the day – which implies that hyperopic adaptation from distance vision should

57. García García M, Breher K, Ohlendorf A, Wahl S. To Correct or Not Correct? Actual Evidence, Controversy and the Questions That Remain Open. J Clin Med. 2020 Jun 24;9(6):1975. doi: 10.3390/jcm9061975. PMID: 32599775; PMCID: PMC7356996.

get somewhat ‘compensated’ by accommodative stress due to ‘ordinary work’ from the rest of the day. The temporal nature of this integration hints at less than ideal rate of recovery.

The adaptive nature of the process also results in an obvious implication that the requirements for Myopia reversal should be far stricter than that required for Myopia stabilization. This is the ‘dual’ of observing a subset of subjects with significant near-work habits not becoming Myopic. The dual then implies that a subset of subjects should experience stabilization of Myopia (and not reversal) even with ADV.

Most if not all of the implementation details regarding Myopia management in this article result from limited scale experimentation spanning more than a year including the entire time spent documenting and writing this article. It would have been near-impossible otherwise to gather important insights from empirical deliberations alone.

These duals already contain sufficient information to design an experimental trial for Myopia Management aimed towards observing significant Myopia reversal. The following sections are our attempts at listing necessary implementation details for the same in the form of a targeted protocol for Myopia management.

6.2 Saturation time for hyperopic stimulus and ‘relative’ lack of near work

The question of what should be the recommended time interval of myopic defocus for myopia management emerges from the observation of peaking of maximum axial length reduction (referred from now on as saturation) around 50 minutes as mentioned in [The time course of the onset and recovery of axial length changes in response to imposed defocus[58]]

“The first statistically significant reduction in axial length occurred after 40 minutes of exposure to myopic defocus, with a mean reduction of -8 ± 9 μm ($p = 0.017$). This change peaked shortly after, reaching a maximum axial length reduction of -10 ± 8 μm at 50 minutes ($p = 0.001$).”

We recognise that the article in question is not a long-term study on axial changes. But even then, the observation of a saturation time and its duration being somewhere around the ballpark of an hour should apply. The presence of a saturation time in itself is an obvious indicator that the eye takes periodic breaks. The time to achieve saturation naturally increases if done in small chunks instead of one go. This suggests that a person wanting to ensure maximum hyperopic adaptation towards reversing myopia should aim for observation time slightly more than saturation time. For preliminary trials, the initial duration of observation time for ADV to maximize saturation in the absence of further experimental data should be taken close to an hour (more than 50 min). Subjects should be encouraged to determine long-term saturation time for ADV on their own from the signals given by their eyes.

Promoting hyperopic adaptation for reversal of Myopia demands under-utilisation of near-focusing capability of the ciliary mentioned in previous section to reduce accommodative stress due to near-work as

58. Delshad, S., Collins, M.J., Read, S.A. et al. The time course of the onset and recovery of axial length changes in response to imposed defocus. Sci Rep 10, 8322 (2020). https://doi.org/10.1038/s41598-020-65151-5

much as possible. This constitutes the ‘extra requirement’ part required to reverse Myopia rather than stabilising it. This load reduction of near-work on the ciliary muscle can be done in two ways – reducing the time or increasing the distance at which near-work in closely accommodated state is done.

The former can be achieved by reducing the duration of near-work and is the obvious, most effective but largely impractical approach. The second approach refers to mitigations that reduce load on the ciliary due to near-work. This can be done by physically increasing the distance at which near-work is done or by utilising refractive interventions. This also cements the importance of taking regular breaks as signalled/indicated by the eye and looking at far-away objects during breaks. The already established recommendation[59] in the form of 20-20-20 rule is handy in this regard.

6.3 Implementation of ADV

Having elaborated the ‘saturation’ and near-work management aspect for Myopia reversal, we will now describe in detail the physical requirements for ADV. ADV as described should be seen as a targeted method for High Environmental Illuminance viewing utilizing high-intensity outdoor sunlight for imposing myopic defocus conducive towards hyperopic adaptation.

The lack of any previous large-scale experimental trial also means that the ideal value of myopic defocus for ADV is in dire need for determination. It is hard to predict whether Myopic defocus even matters at all considering the hints that eyes only respond to pupil constricted lighting without regular biometry achievable only in a highly monitored advance research setting.

It is our suggestion that familiar concept of ‘saturation’ defocus could exist for myopic defocus resulting in the eyes hitting an adaptive rate limit once defocus is greater than a certain threshold for ADV. It might also be possible that defocus isn’t considered at all if pupil-constricted lighting conditions are maintained.

This leads us to suggest that subjects with non-severe Myopia should be able to perform ADV with no prescriptive compensation at all. Our limited scale testing verified this to be indeed true. This leads us to recommend doing ADV without wearing any glasses or contacts for subjects with non-severe Myopia resulting in a greatly simplified implementation because practising ADV without refractive interventions should directly approach emmetropy (ensuring exposure to maximum possible stimulus towards emmetropization). Subjects experiencing difficulties should gradually taper their prescriptive compensation utilising the existing prescription to view distant targets during the initial days of their ADV sessions.

Due to the similar lack of any previous experimental data regarding the time interval between ADV sessions, we suggest that subjects should be doing ADV sessions consistently on a daily basis. Effective Myopia management requires augmenting daily ADV sessions with refractive intervention guidelines detailed in the next section for rest of the day.

59. Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. BMJ Open Ophthalmol. 2018 Apr 16;3(1):e000146. doi: 10.1136/bmjophth-2018-000146. PMID: 29963645; PMCID: PMC6020759.

ADV demands daily exposing entire visual field to distant 'targets objects' with good contrast involving blur from myopic defocus (observation beyond far-point by reduction or elimination of prescription power) in bright daylight until saturation. The idea behind exposing entire visual field to distant 'target objects' having good contrast under very bright lighting emerges from the concept of conveying maximum light information to the Retinal Ganglion Cells (RGCs) of the retina. When it comes to pupil constricted lighting conditions, sunlight on a clear sunny day should be our benchmark. This also means that we must exclude viewing the Sun directly because the Sun is a point object in the visual field even if one ignores the harms[60] directly viewing the Sun has on the eyes. It is imperative that the subjects keep the Sun behind them at all times to minimize risk of exposure to harmful UV radiation.

Regarding observation of distant sunlit objects, subjects should place no demands or special emphasis in the way distant objects are being observed. They should strive to observe naturally in a relaxed manner without squinting, forcing or stressing their eyes in any manner. Subjects should be encouraged to do slow walking, standing, or sitting still while performing ADV according to their convenience.

There should be no difference from the way an emmetropic or a refractively compensated (pseudo-emmetropic) subject normally observes objects at a distance. The best analogy we can give is similar to trying to read a distant signboard or resolving fine details presented by a distant structure. We expect contrasting patterns in both vertical and horizontal meridians to be useful and implore researches to come up with precise target object requirements and explore such synthetic target patterns for ADV.

Figure 6.1 Image demonstrating close to ideal calibration target for ADV

60. Chawda D, Shinde P. Effects of Solar Radiation on the Eyes. Cureus. 2022 Oct 29;14(10):e30857. doi: 10.7759/cureus.30857. PMID: 36465785; PMCID: PMC9709587.

An image showing ideal ADV environment satisfying our criteria is shown in Figure 6.1. The Sun in clear sky is behind the observer in this image and most of the objects are more than 20 m away with the farthest being more than 100 m away resulting in a good calibration target. The difference between an object at 4 m compared to an object located at 20 m is 0.2 D, a difference that can be useful for fairly low myopia.

Because the lighting requirement is for the eyes only, being under direct sunlight or doing it from a shaded place should be immaterial. The outcomes of ADV should not depend on whether the body is exposed to Sunlight or not. People residing in hot climatic conditions should be attempting ADV from a cool and shaded place to combat the sweltering heat outside. Swamp (desert) coolers are an effective option in this regard.

It remains to be seen how the strategic requirements posed by ADV pans out for myopic subjects living in inclement climatic conditions receiving little sunlight during the year. Artificial lighting that recreate the bright daylight environment might prove useful according to some suggestions. [NBK470669: "In countries where the intensity of outdoor light is generally lower, because of air pollution or short duration of natural daylight – such as Canada or Scandinavia in the winter, or Beijing year-around – sunlight therapy could be supplemented in the form of SAD lights (approved and used for Seasonal Affective Disorder)"]

6.4 Refractive compensation guidelines for Myopia management.

We have previously established that observing objects closer than the myopic far-point while wearing prescription results in more physical contraction of the ciliary muscles compared to viewing directly without wearing anything. This should also mean that glasses for non-severe Myopia should be worn on a need basis – only for vision requirements farther than the myopic near-point. As myopia reversal progresses, this far-point should get closer to ∞ reducing dependence.

In accordance with our duals established in section 6.5, refractive interventions can ensure that the subject's quality of life remains relatively unaffected from the process of managing Myopia while simultaneously ensuring that near-work incidence on ciliary muscle is minimized.

For the purpose of Myopia management as outlined in this section, conventional glasses emerge as the best piece of equipment because they are easy to wear and remove in accordance with varying refractive demands during the day, cheaper, reliable, safer for the eyes, and allow easier to manage powers in the long run compared to contacts.

Within few weeks of daily ADV sessions, it should be expected for an eye to gradually start experiencing difficulties both while wearing their normal prescription during the day (over-prescription resulting from reduction in Myopia) and in the form of subtle aversion from near-work. Such developments should result from the gradual disruption of myopic feedback loop in the ensuing weeks of daily ADV sessions. The natural course of action suggested is that refractive interventions should be implemented in the order in which they become apparent during Myopia management. Subjects should change things one at a time and that too only when indicated by the eye.

The disruption of myopic feedback loop from ADV sessions means that refractive demands of the eye become somewhat complicated and slightly reduced prescription should be needed than the regular prescription (for near-work beyond the myopic far-point) so as to lessen the feeling of eye-strain during near-work. As such situations arise, the signalled comfort of the eyes towards worn prescription should be prioritized. The eyes should signal immediate discomfort for both over and too much under-correction and the same should be avoided. As long as the worn prescription is kept within this narrow range of comfort according to the signals given by the eyes, we expect ADV to continue resulting in effective hyperopic adaptation for the eyes.

This concept of refractive intervention is an important aspect of myopia management and requires strictly individual implementation because of the varying near-work requirements of subjects, their present refractive state and preferences/tolerance to defocus. The adaptive nature of the eye makes it obvious that the refractive compensation requirements from the standpoint of reducing accommodative load for a system as dynamic as the human eye can not be accomplished using one refraction value[61]. For the ease of understanding, we have tabulated these guidelines in the table below.

Refractive compensation guidelines for Myopic candidates with non-severe Myopia.

Table 5: Tentative Refractive compensation guidelines for near-work management

Working distance	Daylight (outdoors on a sunny day)	Evening/Night
For ADV until saturation	Without wearing any prescription	NA
Long distance work	Reduced Prescription with sunglasses according to the need	Regular Prescription
Near-work at a distance just beyond the myopic far-point	Reduced Prescription	Reduced Prescription
Near-work done at a distance closer than the myopic far-point	Non-severe Myopics should be able to observe objects closer than their far-point comfortably without needing prescription	
Life-critical task such as driving,	Best Possible Refractive compensation for maximum visual acuity	

61. Sha J, Fedtke C, Tilia D, Yeotikar N, Jong M, Diec J, Thomas V, Bakaraju RC. Effect of cylinder power and axis changes on vision in astigmatic participants. Clin Optom (Auckl). 2019 Mar 19;11:27-38. doi: 10.2147/OPTO.S190120. PMID: 30936760; PMCID: PMC6431005.

operating heavy industrial machinery and other dangerous work	possible to prevent incidents and to comply with applicable local laws

Coming to the actual lenses used, we suggest 'normal' clear lenses without any special coating such as blue light blocking filters because of the reasons given below:

1. Increased costs of lenses that will need replacment eventually in the near future as Myopia reversal progresses.
2. Provides no clinically substantiated shielding against Myopia as evident from multiple research attempts into investigating their benefits[62].
3. Nearly every recent computing device with a display already has an inbuilt blue-light reduction/night-comfort feature. [Windows Night Light[63] and Apple Night Shift[64]]. The intended physical purpose of blue-light glasses is already achieved at the source level for modern computing devices.
4. We suspect that blue-light glasses can suppress the ability of the eye to signal eye-stress due to extended near-work (DES) which deters from our guidelines of regular breaks as essential in order to reduce near-work load on the ciliary muscle.
5. We also suspect that Blue-light glasses are less effective as refractive compensation than regular clear-classes due to decreased availability of light in dark conditions that can result in delayed improvement towards Myopia. For candidates wanting fast management of their Myopia, this is not something they might want.
6. Blue light lenses can not replace the utility and eye-protection offered by outdoor sunglasses under direct sunlight.

These guidelines result in a slightly more complicated answer for the most commonly asked question in myopia – "When should I wear glasses?"

These guidelines are only meant as a starting point for the trial implementation for our Myopia management method. It is expected that the eye's refractive need will change during the course of the trial as Myopia reversal progresses. The evaluation criteria always remains the fastest and safest reversal of

62. Wong NA, Bahmani H. A review of the current state of research on artificial blue light safety as it applies to digital devices. Heliyon. 2022 Aug 15;8(8):e10282. doi: 10.1016/j.heliyon.2022.e10282. PMID: 36042717; PMCID: PMC9420367.
63. https://support.microsoft.com/en-us/windows/set-your-display-for-night-time-in-windows-18fe903a-e0a1-8326-4c68-fd23d7aaf136
64. https://support.apple.com/en-in/HT207570

Myopia and we fully expect some of these tentative guidelines to fail or get superseded by further understanding gained from future trials.

6.5 The proposed mechanism for Hyperopic adaptation towards emmetropization

Section 4.4 already covers our attempts at characterizing how myopic adaptation takes place.

Onset/progression of physiological Myopia should result from accommodative stress due to near-work in pupil-dilated lighting conditions combined with significant under-utilisation of distance vision capability. This should then result in development of myopic shift in the ciliary muscle. Long term axial elongation is proposed to result from the eye's eventual attempts towards alleviating this accommodative shift in the ciliary muscle.

This section attempts to describe the mechanism of Myopia reversal based on our observations upon year long implementation of the method described in the preceding sections. For lower degree of Myopia, subject's experience should reduce to only a subset of what has been described in this section.

The initial days of ADV sessions should be relatively uneventful with slow spontaneous onset of brief moments of visual clarity (referred to as clear flashes from now on) vanishing immediately after blinking with long reset time (minutes to hours) between each consecutive clear flash. This suggests that just like Myopia, the ciliary is the first to respond to hyperopic adaptation.

Within weeks of regular ADV sessions, besides a perceptible increase in clarity, clear flashes become more frequent and longer in duration while gaining the capability to 'survive' between blinks. Subjects should be advised not to prolong blinking in order to sustain clear flashes.

This development alone with the occurrence of significant clear flashes coinciding with going outside in daylight should be enough to conclusively dispel the common hypothesis that these clear flashes result from formation of tear film[65] on the cornea or due to the diurnal variation in vision[66]. ADV can also result in transient intervals of blurrier than usual vision on some days signifying that the structures inside the eye are being repaired/rebuilt.

It can be naturally deduced from the anatomy of the eye that clear flashes must arise due to increase in focal length (decrease in power) of the eye lens because of their instantaneous nature. In the case of Myopia, adaptive requirements for closer distances result from accommodative stress on the ciliary muscle. However, the opposite of this can not be true because the ciliary muscle can not get 'tired or exhausted' in

65. Chang AY, Purt B. Biochemistry, Tear Film. [Updated 2022 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK572136/
66. Ulaganathan S, Read SA, Collins MJ, Vincent SJ. Daily axial length and choroidal thickness variations in young adults: Associations with light exposure and longitudinal axial length and choroid changes. Exp Eye Res. 2019 Dec;189:107850. doi: 10.1016/j.exer.2019.107850. Epub 2019 Oct 19. PMID: 31639338.

its relaxed state – hence the designation, overshoot in ‘negative accommodation[67]’. It also explains the commonly reported instances of ‘ciliary spasms’ in myopic people observing spontaneous brief flashes of clear vision under pupil constricted viewing conditions when not wearing their glasses. We will prefer to use the more descriptive term ‘clear flashes’ instead.

Within weeks, ADV sessions should force the establishment of a feedback loop with behaviour opposite to the previously described myopic feedback loop – resulting in perceived eye-strain/aversion towards near-work. We fully expect that experiencing discouragement from near work could serve as a reliable indicator that hyperopic adaptation is taking place. For a person experiencing active myopia progression, this process can take some extra time signifying disruption of existing myopic shift (reversible component of refractive Myopia) and development of hyperopic ciliary shift.

After regular ADV sessions spanning over longer time-frames (months), subjects should start experiencing a perceptible level of visual clarity that comes on automatically when going outside on a sunny day – a telltale marker of hyperopic ciliary shift. Long-term axial changes should soon follow to compensate this hyperopic response of the ciliary as long as under-utilisation of near-work is maintained. Measurable reduction in retinal distance starts happening after this stage is reached. This stage should continue translating into improvements to baseline vision with time as long as emmetropization is not reached.

Successful observation of hyperopic ciliary shift would also cement the bi-directional bridging nature of the accommodative shift as the precursor of long-term axial changes for both myopic and hyperopic adaptations (Prediction P2). The very observation of hyperopic ciliary shift alone should be sufficient to confirm that the predicted[68] *active emmetropization mechanism* is not different from the process described in this article inducing Myopia or Hyperopia in accordance with the imposed visual stimulus. The process of Emmetropization naturally involves ocular re-calibration for distance vision and results in eventual changes to the eyeball shape in the long-term (months). Some subjects can also report feeling changes to the extraocular eyeball muscles resulting from calibration both during and after ADV sessions.

It is equally important to mention that most of the aforementioned clarity gains during ADV sessions vanishes swiftly under pupil dilated lighting conditions. This behaviour from the eyes could be looked as a source of frustration upon witnessing the clarity gained during the day vanishing in the night. This observation is so important from the standpoint of light’s role in influencing adaptive behaviour of the eye that we predict that it should result from the mechanistic interaction of the iris restricting ‘headroom’ for negative accommodation (responsible for clear flashes), explaining why loss of clarity occurs so swiftly under pupil dilated lighting conditions. This can be termed as restrictive effect of the dilated pupil for ciliary relaxation under less-bright lighting conditions.

67. Raz A, Marinoff GP, Landzberg KS, Guyton DL. Substrates of negative accommodation. Binocul Vis Strabismus Q. 2004;19(2):71-4. PMID: 15180591.
68. Wildsoet CF. Active emmetropization--evidence for its existence and ramifications for clinical practice. Ophthalmic Physiol Opt. 1997 Jul;17(4):279-90. PMID: 9390372.

This mechanistic interaction of the iris with the ciliary should explain why Myopia has been observed as the default behaviour of the eye when subjected to form-deprivation under dim-lighting conditions[69]. A conclusive way to validate this interaction would involve inducing form-deprivation while simultaneously imposing pupil constricted lighting conditions.

6.5.1 The informal Law of physiological Myopia

Given time, a person with physiological Myopia should be able to focus at infinity without refractive interventions at par or better than their current visual performance with best possible refractive compensation.

This law encapsulates our bold prediction from CAT signifying that best possible visual acuity should be improved or maintained due to the error correcting, superior nature of hyperopic adaptation.

6.6 Precautions, Safety and candidate selection requirements

6.6.1 Candidate Selection Criteria

Managing Myopia according to our method requires active integration into daily lifestyle and trial candidates should be willing to devote the (an hour or two it takes) of their daily time towards achieving saturation requirements for ADV besides implementing near-work management aspects.

The novel nature of the idea and the lack of any widespread experimental trial means heavy emphasis on precautions as a first line of safety. We insist on limiting the first run of trials to **Non-severe** young adults only having good ocular health history without adverse event, Presbyopia, and screened for any presence of musculoskeletal disorders. Further information from the outcome of the preliminary trials on non-severe myopics will be used towards narrowing down additional requirements for candidates with severe physiological myopia and their eventual transition into non-severe Myopia if possible.

It is recommended that the candidates exercise caution during the initial transition period of the trial, starting with ‘less brighter’ objects first and take regular breaks until acclimatisation is completed within the first week. We expect the majority of candidates to experience excessive-tearing and strong aversion signals from the eyes in the form of eye-strain and minor headache during the beginning of the trial due to the aforementioned sensitivity of a myopic eye towards bright light. It is also recommended that observation duration too should be gradually ramped up towards saturation over the course of multiple days under constant monitoring so as to prevent the possibility of any adverse complications from over exertion.

69. Zhihui She, Li-Fang Hung, Baskar Arumugam, Krista M. Beach, Earl L. Smith, The development of and recovery from form-deprivation myopia in infant rhesus monkeys reared under reduced ambient lighting, Vision Research, Volume 183, 2021, Pages 106-117, ISSN 0042-6989, https://doi.org/10.1016/j.visres.2021.02.004.

6.6.2 Safety of ADV:

The only part of our method resulting in any significant stress on the eye results from ADV. Regular ADV sessions towards inducing hyperopic adaptation should have a risk profile similar to the risks associated with the onset/progression of Myopia because the same adaptive process responsible for Myopia should result in hyperopic adaptation towards emmetropization also.

We would also like to point out positive sentiments of experts about outdoor therapies like ours that involve High Environmental Illuminance trials: ["Outdoor-light therapy may offer the ideal treatment for myopia. Not only does encouraging children to play outside combat other major health concerns – such as childhood obesity, juvenile diabetes, and depression – but also, light therapy presents little to no serious health concerns or side-effects compared to those of other available myopia-treatments."[70]]

There are multiple studies demonstrating safety profile and tolerance of eyes towards light therapies with light levels far higher than that of indirect sunlight for Myopia management[71]. No serious complications have been reported in RLRL's (Repeated Low-Level Red Light) studies with periods from 6 months up to 2 years. There is even a 12-month study reporting improved accommodative function after RLRL treatment[72].

6.6.3 Important Warning for personal safety and compliance with applicable laws/regulations:

The candidates should be strictly made aware of the potential life-threatening dangers of doing critically important work involving life at risk without wearing best possible refractive correction. Put simply, safety of personal and other's lives while driving during low-light conditions such as night-time or working in dangerous conditions including but not limited to operating construction, industrial, or heavy-machinery/equipments should always be prioritized and best possible refractive compensation must always be worn under such conditions.

Candidates are expected to use fair judgement and not jeopardise their own and other's lives for Myopia management. Because ADV involves observing blur from Myopic defocus and significant reduction in visual acuity is involved, it is only imperative that personal safety must be prioritised and ADV should always be attempted in a safe environment.

70. Carr BJ, Stell WK. The Science Behind Myopia. 2017 Nov 7. In: Kolb H, Fernandez E, Nelson R, editors. Webvision: The Organization of the Retina and Visual System [Internet]. Salt Lake City (UT): University of Utah Health Sciences Center; 1995-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470669/

71. Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W, Mitchell P. Outdoor activity reduces the prevalence of myopia in children. Ophthalmology. 2008 Aug;115(8):1279-85. doi: 10.1016/j.ophtha.2007.12.019. Epub 2008 Feb 21. PMID: 18294691.

72. Chen H, Wang W, Liao Y, Zhou W, Li Q, Wang J, Tang J, Pei Y, Wang X. Low-intensity red-light therapy in slowing myopic progression and the rebound effect after its cessation in Chinese children: a randomized controlled trial. Graefes Arch Clin Exp Ophthalmol. 2023 Feb;261(2):575-584. doi: 10.1007/s00417-022-05794-4. Epub 2022 Aug 17. PMID: 35976467.