

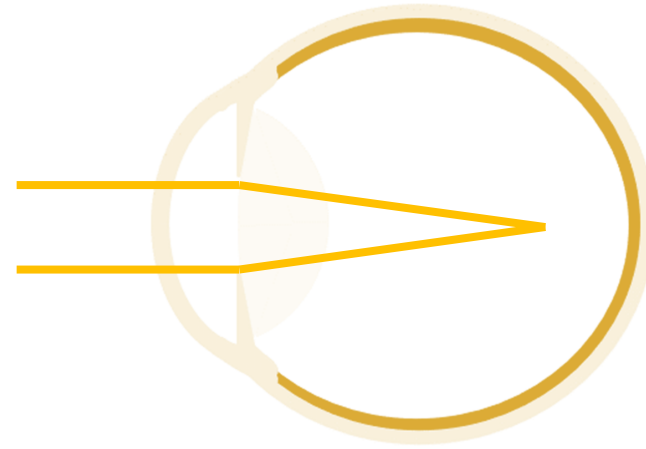
Focus on Myopia and Rising Incidence

The Big Questions in Myopia

Noel Brennan, *PhD*

Xu Cheng, *MD, PhD*

Monica Jong, *PhD*



Summary

- Definition- is myopia a ‘disease’?
- How accurate are projections of future myopia prevalence?
- What is the prevalence of myopia in US school children right now?
- What can be done to delay onset or slow progression of pathologic myopia in the hundreds of millions of people at risk (and how do we get resources to drive research into developing treatments?)
- How does the retina detect the sign of defocus?
- Do electronic devices really affect myopia onset and progression?
- What does the retinal dioptric map look like during various types of near work? What is the role of indoor light levels in myopia?
- What should the public health approach to myopia management be?
- How effective will myopia management be in reducing the public health burden?
- How do we activate parents, practitioners, institutions and agencies to address the myopia issue?
- Should uncorrected refractive error be a focus here? The solution is available, it is just a question of marshalling resources.



Definitions

Should we call juvenile-onset myopia ‘primary myopia’?

As opposed to secondary myopia, which may be due to syndromes, diabetes, cataracts etc.

Is the IMI definition adequate?

That definition is strictly optical, does not address the nature, the underlying mechanism or the potential consequences of myopia.

Is myopia a ‘disease’?

It arguably fits the definition.

Important distinction in attracting appropriate attention/funding. Parallels with, say, diabetes which, on its own, is just a number (blood glucose level), but is considered a disease and places the individual at risk of complications.

An authoritative statement is needed.

Can myopia be considered to be ‘progressive’?

Like many progressive diseases, it may stabilize but there is always the risk of progression to pathologic myopia and vision loss at all levels of myopia. There is no safe level of myopia.

Is the term ‘high myopia’ helpful or harmful?

It is a very well accepted term and concept— but there is no clear discontinuity in risk of complications and it serves to underplay the risk in low and moderate myopia.

Special Issue | February 2019

IMI – Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies

Daniel Ian Flitcroft; Mingguang He; Jost B. Jonas; Monica Jong; Kovin Naidoo; Kyoko Ohno-Matsui; Jugnoo Rahi; Serge Resnikoff; Susan Vitale; Lawrence Yannuzzi

Investigative Ophthalmology & Visual Science February 2019, Vol.60, M20-M30.
doi:<https://doi.org/10.1167/iovs.18-25957>



Managing Myopia: A Clinical Response to the Growing Epidemic is endorsed by the following organizations: American Optometric Association, Singapore Optometric Association, American Academy of Optometry, Johnson & Johnson Vision.



MANAGING MYOPIA
A Clinical Response to the Growing Epidemic

“Myopia is a chronic, progressive disease characterized by excessive eye elongation, risk of associated sight-threatening complications, and a negative-powered refractive error.”

Prevalence

Are projections of prevalence for 2050 accurate?

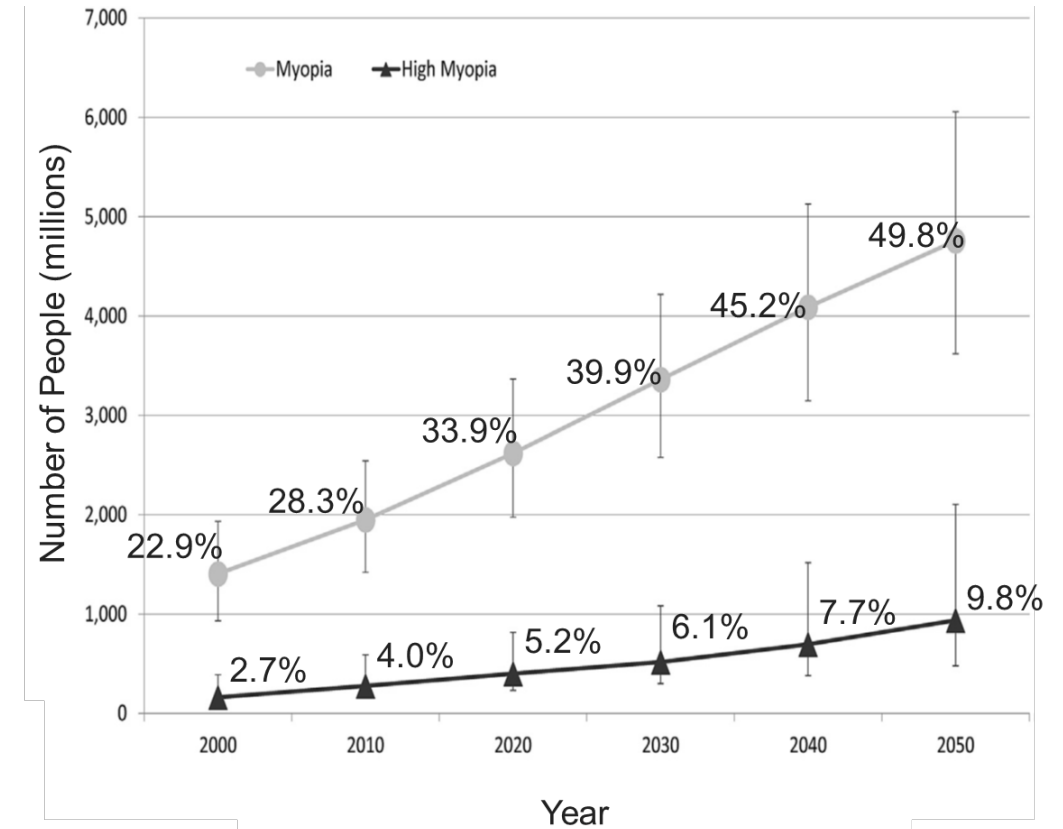
While the analysis seems solid, data underlying the projections are weak. If the projections are correct, in 2050, the USA should have higher myopia prevalence than East Asia now. And we know that myopia is a major public health issue in East Asia right now. Further, current USA prevalence should look similar to what East Asia did in 1990. Is that reasonable?

What is the current prevalence of myopia in United States schoolchildren?

To make realistic projections for future decades, data are urgently needed. Propose epidemiological study.

What do we need to get better projections?

What about beyond 2050?



Holden et al. Ophthalmology 2016; 123:1036

Prevalence

Are projections of prevalence for 2050 accurate?

While the analysis seems solid, data underlying the projections are weak. If the projections are correct, in 2050, the USA should have higher myopia prevalence than East Asia now. And we know that myopia is a major public health issue in East Asia right now. Further, current USA prevalence should look similar to what East Asia did in 1990. Is that reasonable?

What is the current prevalence of myopia in United States schoolchildren?

To make realistic projections for future decades, data are urgently needed. Propose epidemiological study.

What do we need to get better projections?

What about beyond 2050?

Table 1. Prevalence of Myopia Estimated for Each Global Burden of Disease Region between 2000 and 2050

Region	Prevalence (%) in Each Decade					
	2000	2010	2020	2030	2040	2050
Andean Latin America	15.2	20.5	28.1	36.2	44.0	50.7
Asia-Pacific, high income	46.1	48.8	53.4	58.0	62.5	66.4
Australasia	19.7	27.3	36.0	43.8	50.2	55.1
Caribbean	15.7	21.0	29.0	37.4	45.0	51.7
Central Africa	5.1	7.0	9.8	14.1	20.4	27.9
Central Asia	11.2	17.0	24.3	32.9	41.7	47.4
Central Europe	20.5	27.1	34.6	41.8	48.9	54.1
Central Latin America	22.1	27.3	34.2	41.6	48.9	54.9
East Africa	3.2	4.9	8.4	12.3	17.1	22.7
East Asia	38.8	47.0	51.6	56.9	61.4	65.3
Eastern Europe	18.0	25.0	32.2	38.9	45.9	50.4
North Africa and Middle East	14.6	23.3	30.5	38.8	46.3	52.2
North America, high income	28.3	34.5	42.1	48.5	54.0	58.4
Oceania	5.0	6.7	9.1	12.5	17.4	23.8
South Asia	14.4	20.2	28.6	38.0	46.2	53.0
Southeast Asia	33.8	39.3	46.1	52.4	57.6	62.0
Southern Africa	5.1	8.0	12.1	17.5	23.4	30.2
Southern Latin America	15.6	22.9	32.4	40.7	47.7	53.4
Tropical Latin America	14.5	20.1	27.7	35.9	43.9	50.7
West Africa	5.2	7.0	9.6	13.6	19.7	26.8
Western Europe	21.9	28.5	36.7	44.5	51.0	56.2
Global	22.9	28.3	33.9	39.9	45.2	49.8

	2020 East Asia	2050 Nth America
Myopia	51.6%	58.4%
High Myopia	13.8%	14.7%

Prevalence

Are projections of prevalence for 2050 accurate?

.While the analysis seems solid, data underlying the projections are weak. If the projections are correct, in 2050, the USA should have higher myopia prevalence than East Asia now. And we know that myopia is a major public health issue in East Asia right now. Further, current USA prevalence should look similar to what East Asia did in 1990. Is that reasonable?

What is the current prevalence of myopia in United States schoolchildren?

To make realistic projections for future decades, data are urgently needed. Propose epidemiological study.

What do we need to get better projections?

What about beyond 2050?

Estimated prevalence of myopia by age stratified by country for East Asians, and (2) stratified by continent for South Asians

	Prevalence (%) of myopia by age				Year
	5 years	10 years	15 years	18 years	
Australia	1.9	13.6	40.6	—	2005
China	3.9	24.9	59.0	71.9	2005
Hong Kong	9.2	45.3	78.2	86.4	2005
Japan	1.7	12.2	37.6	51.7	1990
Malaysia	4.6	28.4	63.2	75.3	1990
Mongolia	0.3	2.7	10.8	17.7	2003
Singapore	14.9	59.0	86.2	91.7	2005
Taiwan	10.1	48.0	80.0	87.6	2005
USA	4.9	—	—	—	2005
Sth Asians by continent					
In Sth Asia	3.6	6.4	9.1	10.3	2005
Not in Sth Asia	20.4	31.6	40.5	43.8	2005

Complications

Will complications of myopia become the biggest cause of vision impairment globally?

Already, “pathologic myopia is the leading cause of irreversible blindness in Taiwan, Japan, and China”. Since most cases of the myopia epidemic are people born after 1970, the oldest are in their early fifties. Since incidence is highest after 60 years of age, this portends a ‘tsunami’ of disease in coming decades.

What about the Western World?

No evidence of a spike in incidence of MMD in the US yet but, given timelines, that is not surprising.

What can be done to delay onset or slow progression of pathologic myopia/myopic macular degeneration?

The most serious complication of myopia, MMD, “is the only leading cause of blindness without an established treatment”. Aside from anti-VEGF for myopic CNV, surgical treatment for retinal detachment and traction maculopathy and the intrusive technique of scleral buckling, treatments are inadequate. There is no safe level of myopia— there are hundreds of millions of myopes already, with a large proportion facing the prospect of vision impairment. **ACTION IS NEEDED.**

Can we predict whose MMD will progress?

Because of risks involved with interventions, retinal specialists would like to know who is likely to progress.

Is peri-papillary atrophy a useful biomarker for pathological myopia?

Is there hope in development of cross-linking or drugs?

What are the key differences between myopic optic neuropathy and glaucoma?

Special Issue | May 2021

IMI Pathologic Myopia

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

Investigative Ophthalmology & Visual Science May 2021, Vol.62, 5. doi:<https://doi.org/10.1167/iovs.62.5.5>

“...pathologic myopia is the leading cause of irreversible blindness in Taiwan, Japan, and China.”



QJM: An International Journal of Medicine, 2019, 1–5

doi: 10.1093/qjmed/hcz076
Advance Access Publication Date: 26 March 2019
Commission

COMMISSION

We can't afford to turn a blind eye to myopia

C.M. Bourke^{1,2}, J. Loughman³, D.I. Flitcroft^{1,2}, E. Loskutova³ and C. O'Brien¹

Myopic maculopathy “is the only leading cause of blindness without an established treatment and therefore leads to inevitable loss of vision in some myopes, even at a young age.

Risk Factors I

What are the key environmental factors involved in the myopia epidemic?

At the front end, myopia is an optics problem. Does the committee have the expertise to investigate the optical component properly?

Is peripheral hyperopia the real driver of axial elongation?

Animal studies suggest so but there are limited human data.

What outdoor characteristics delay myopia onset?

Bright light slows growth indiscriminately (open loop), whereas the optical field leads to a 'visually' guided refractive state (closed loop).

Does outdoor activity slow myopic progression?

There is evidence that time outdoors delays myopia onset. Although not widely acknowledged, there is some evidence that it also slows progression.

What can we do to lessen the impact of education?

There is compelling evidence that intensity of education is a risk factor for myopia. The key mechanistic elements of education aside from likely reduced time spent outdoors are not known.

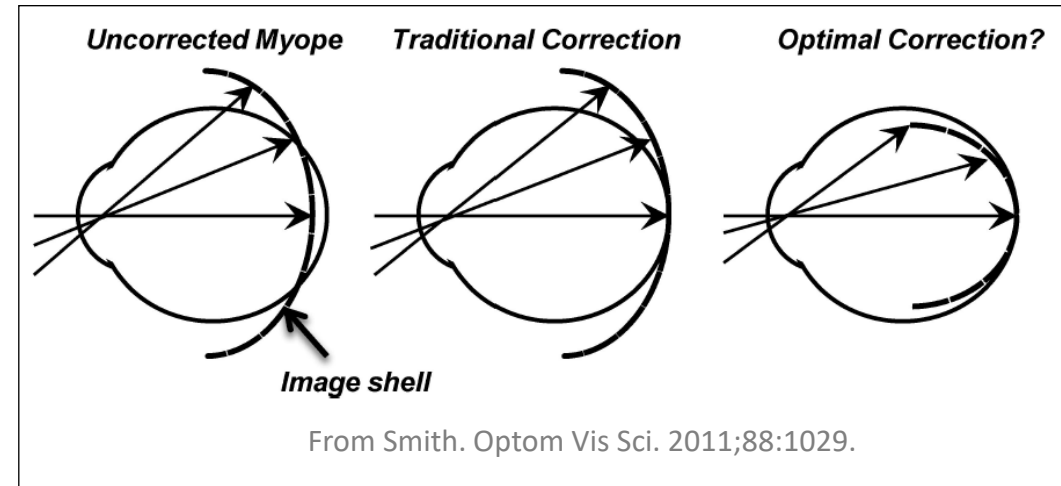
Environmental
Factors



Optical
Stimulus



Biological
Pathways



Received: 16 March 2023 | Accepted: 1 June 2023

DOI: 10.1111/opo.13185

ORIGINAL ARTICLE

OPO THE COLLEGE OF OPTOMETRISTS

Relative peripheral hyperopia leads to greater short-term axial length growth in White children with myopia

Rebecca E. Leighton | Karen M. Breslin | Patrick Richardson | Lesley Doyle | Sara J. McCullough | Kathryn J. Saunders

Risk Factors I

What are the key environmental factors involved in the myopia epidemic?

At the front end, myopia is an optics problem. Does the committee have the expertise to investigate the optical component properly?

Is peripheral hyperopia the real driver of axial elongation?

Animal studies suggest so but there are limited human data.

What outdoor characteristics delay myopia onset?

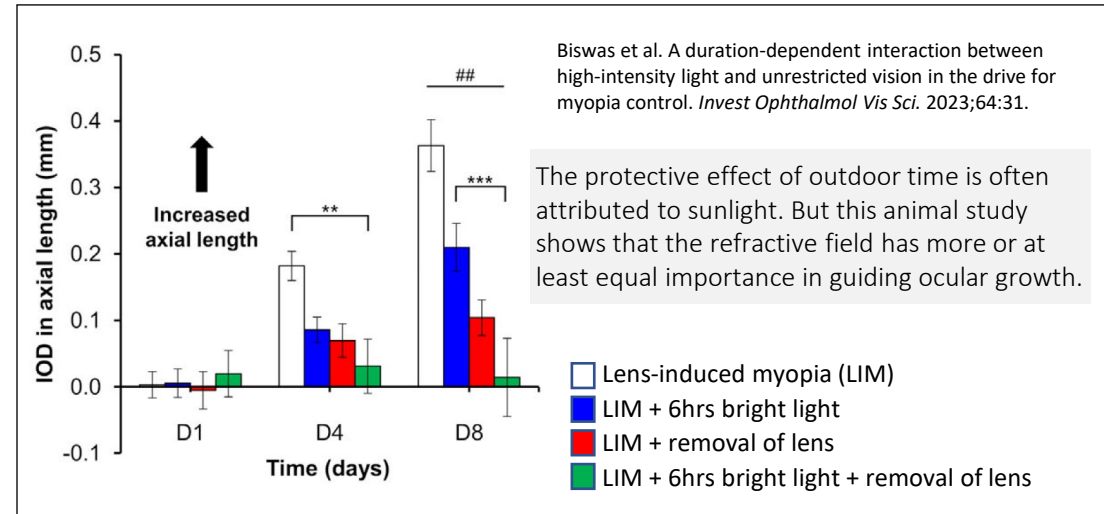
Bright light slows growth indiscriminately (open loop), whereas the optical field leads to a 'visually' guided refractive state (closed loop).

Does outdoor activity slow myopic progression?

There is evidence that time outdoors delays myopia onset. Although not widely acknowledged, there is some evidence that it also slows progression.

What can we do to lessen the impact of education?

There is compelling evidence that intensity of education is a risk factor for myopia. The key mechanistic elements of education aside from likely reduced time spent outdoors are not known.



OPO OPHTHALMIC & PHYSIOLOGICAL OPTICS
THE JOURNAL OF THE COLLEGE OF OPTOMETRISTS
Ophthalmic & Physiological Optics ISSN 0275-5408

POINT-COUNTERPOINT

Does sunlight (bright lights) explain the protective effects of outdoor activity against myopia?

Ophthalmic & Physiological Optics 33 (2013) 368–372

Professor Flitcroft argues convincingly for a closed loop control system to guide ocular growth.

Effect of Outdoor Activities in Myopia Control: Meta-analysis of Clinical Studies

Li Deng, PhD^{1*} and Yi Pang, MD, OD, PhD²

Optom Vis Sci 2019;96:276–282. doi:10.1097/OPX.0000000000001357

The authors present a valid case that outdoor activity slows progression as well as onset

Risk Factors I

What are the key environmental factors involved in the myopia epidemic?

At the front end, myopia is an optics problem. Does the committee have the expertise to investigate the optical component properly?

Is peripheral hyperopia the real driver of axial elongation?

Animal studies suggest so but there are limited human data.

What outdoor characteristics delay myopia onset?

Bright light slows growth indiscriminately (open loop), whereas the optical field leads to a 'visually' guided refractive state (closed loop).

Does outdoor activity slow myopic progression?

There is evidence that time outdoors delays myopia onset. Although not widely acknowledged, there is some evidence that it also slows progression.

What can we do to lessen the impact of education?

There is compelling evidence that intensity of education is a risk factor for myopia. The key mechanistic elements of education aside from likely reduced time spent outdoors are not known.

Myopia and international educational performance

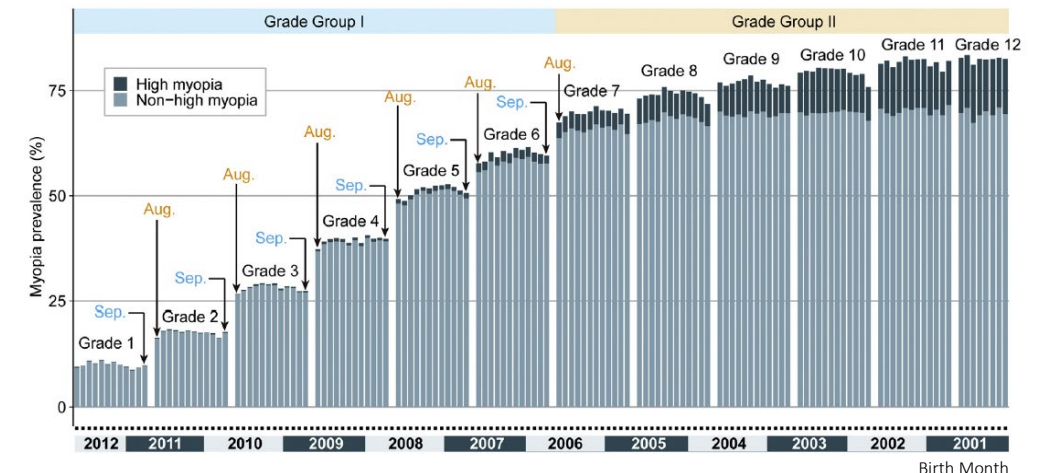
Ian G Morgan^{1,2} and Kathryn A Rose³

Ophthalmic & Physiological Optics **33** (2013) 329–338

Education and myopia: assessing the direction of causality by mendelian randomisation

Edward Mountjoy,^{1,2} Neil M Davies,^{1,2} Denis Plotnikov,³ George Davey Smith,^{1,2} Santiago Rodriguez,^{1,2} Cathy E Williams,² Jeremy A Guggenheim,³ Denize Atan⁴

BMJ 2018;361:k2022



The most striking link between education and myopia comes birth month analysis. In China, school entry is highly regulated. Multiple studies show this effect: Xu et al. (Ophthalmology 2021;128:1652), He et al. (BMJ Open 2021;23:e048450), Ding et al. (IOVS 2022;63:15 and IOVS 2023;64:25), Zhang et al. (JAMA Open 2022;5:e229545).

Risk Factors 2

What role do electronic devices play in myopia onset and progression?

There is no evidence base to support the proposition that electronic devices impact myopia onset or progression. Correlation does not equal causation. **The statement of task implies a causal relationship.**

1. The timelines do not match. The first evidence of a myopia epidemic is from Taiwan in 1983. There is no evidence of a bump in prevalence or progression following the introduction of smart devices (2007).
2. The optics don't match. A handheld device will induce peripheral retinal myopia, not hyperopia, the proposed theory of onset and progression

Is there a covariate like reduced outdoor time that creates an effect?

A randomized intervention study to examine the role of near work on electronic devices is needed and feasible.

What if any role does accommodative lag play in myopia development?

Recent evidence suggests that measured lag is largely an artefact of measurement technique. Should its role should be disregarded?

Does the understanding of the role of genetics in myopia and high myopia provide any viable role in stemming the myopia epidemic?

Is there any evidence for a genetic basis to the higher prevalence among East Asians, or is it all cultural? Is the known risk factor of parental refractive status genetic or can it be explained by environment?



Wikicommons, Said El Jamali [Creative Commons Attribution-Share Alike 4.0](#)

Journal of Vision (2021) 21(3):21, 1–18

Lags and leads of accommodation in humans: Fact or fiction?

Vivek Labhishetty, Steven A. Cholewiak, Austin Roorda,
Martin S. Banks

Mechanisms

What does the retinal dioptric map look like during various types of near work?

Indoor environments are complex optically. Can we correlate the retinal dioptric map (visual field plus ocular error) with abnormal eye growth?

How does the retina detect the sign of defocus?

What characteristics of the optical signal are being processed by the retina to guide growth? Is it an aberration-derived pattern of blur? Is it color? How are on-off signals interpreted? How does the retina put all of this information together to know which way to grow?

What criterion does the feedback mechanism use to determine an endpoint for eye growth? Is it acuity, is it contrast? Which spatial frequency channels are involved?

The eye grows to neutralize large refractive errors (eg -10D in animals) so high spatial frequency input would not seem to be necessary. Yet the eye can also grow very accurately to neutralize refractive error perhaps suggesting high spatial frequency involvement.

What role do the different layers of the eye play in axial elongation-retina (which cells?), choroid, sclera, Bruch's membrane?

Is sagittal elongation of the eyeball due to new formation and elongation of Bruch's membrane in the equatorial region? Does hypoxia as a result of thinning of the choroid play a role in myopia development and/or pathologic myopia?

What is the chemical signal cascade that leads to axial elongation?

1040-5488/15/0011-1284/0 VOL. 16, NO. 11, PP. 1284-1291
OPTOMETRY AND VISION SCIENCE
Copyright © 2013 American Academy of Optometry

ORIGINAL ARTICLE

Spherical Aberration and the Sign of Defocus

Larry N. Thibos*, Arthur Bradley†, Tao Liu‡, and Norberto López-Gil†

scientific reports

Myopia: why the retina stops inhibiting eye growth

[Barbara Swiatczak](#) & [Frank Schaeffel](#)

Scientific Reports 12, Article number: 21704 (2022) |

Current Biology 16, 687–691, April 4, 2006

What Image Properties Regulate Eye Growth?

Robert F. Hess,^{1,*} Katrina L. Schmid,²
Serge O. Dumoulin,³ David J. Field,⁴
and Darren R. Brinkworth²

Progress in Retinal and Eye Research
Available online 28 December 2022, 101156

Myopia: Histology, clinical features, and potential implications for the etiology of axial elongation

Jost B. Jonas, Rahul A. Jonas, Mukharram M. Bikbov, Ya Xing Wang, Songhomitra Panda-Jonas

Experimental Eye Research 219 (2022) 109071

Candidate pathways for retina to scleral signaling in refractive eye growth

Dillon M. Brown^{a,b}, Reece Mazade^{a,b}, Danielle Clarkson-Townsend^{b,c,d,e}, Kelleigh Hogan^{a,b},
Pooja M. Datta Roy^{a,b}, Mabelle T. Pardue^{a,b,*}

Public Health

What is the current and projected personal health and social burden of myopia?

What is the current and projected financial burden of myopia?

Can we accurately predict who will become myopic?

Refractive error by age provides best predictive power for myopia onset. So, do we need to worry about other risk factors in predicting onset?

Should we treat children to prevent them from becoming pre-myopic?

Should we have screening programs to examine all 6-year-olds under cycloplegia?

What is the cost-benefit ratio of preventive program to delay myopia onset?

Should we treat all at risk to delay onset?

If so, how?

In order to reduce the public health burden of myopia, do we need to treat all young myopes to slow progression?

Does single vision correction actually promote myopia progression?

How do we educate, motivate and activate practitioners, parents, institutions and agencies to act?

Original Investigation

Prediction of Juvenile-Onset Myopia

Karla Zadnik, OD, PhD; Loraine T. Sinnott, PhD; Susan A. Cotter, OD, MS; Lisa A. Jones-Jordan, PhD; Robert N. Kleinstei, OD, MPH, PhD; Ruth E. Manny, OD, PhD; J. Daniel Twelker, OD, PhD; Donald O. Mutti, OD, PhD; for the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study Group

JAMA Ophthalmol 2015;133:683-9.



Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children

The Academy's Task Force on Myopia

Bobek S. Modjtahedi, MD,^{1,2} Richard L. Abbott, MD,³ Donald S. Fong, MD,^{1,2} Flora Lum, MD,⁴ Donald Tan, MD,⁵ on behalf of the Task Force on Myopia

Ophthalmology. 2021;128:816-826

“...although higher degrees of myopia carry a greater risk of visual impairment to the individual, the population-based burden of lower degrees of myopia remains considerable.”

Graefes Arch Clin Exp Ophthalmol (2017) 255:189–195
DOI 10.1007/s00417-016-3529-1

NEUROPHTHALMOLOGY

Effect of uncorrection versus full correction on myopia progression in 12-year-old children

Yun-Yun Sun¹ • Shi-Ming Li¹ • Si-Yuan Li² • Meng-Tian Kang¹ • Luo-Ru Liu³ • Bo Meng⁴ • Feng-Ju Zhang¹ • Michel Millodot⁵ • Ningli Wang¹

Interventions

What are effective ways to delay myopia onset?

By what amount can we realistically reduce progression?

How much difference will we actually make if we slow progression, given that treatment effect is a modest fixed, not percentage, amount?

What do we do with atropine?

How does it actually work? Are there better drugs targeting the same mechanisms? There is an extraordinary spread in reported data for 0.01% atropine. Why? Nonetheless, 0.01% is demonstrably less effective than other interventions in reputable studies— what is the optimal dosage? How do we steer clinicians to better treatments?

How can we accelerate market approvals for products?

What improvements to clinical trial protocols should be instituted? Can we accurately predict 3-year outcomes from 1-year data?

How should a clinician choose a treatment and what evidence is there to support holistic/personalized treatment?

Who should provide treatment? What should collaborative care models look like?



Progress in Retinal and Eye
Research

Volume 83, July 2021, 100923



Efficacy in myopia control

Noel A. Brennan^{a 1} , Youssef M. Toubouti^{a 1}, Xu Cheng^{a 1},
Mark A. Bullimore^{b 1}

DOI: 10.1111/opo.13120

ORIGINAL ARTICLE

OPO THE COLLEGE OF
OPTOMETRISTS

The future of clinical trials of myopia control

Mark A. Bullimore¹ | Noel A. Brennan² | Daniel Ian Flitcroft^{3,4}

Ophthalmic Physiol Opt. 2023;43:525-533.

Uncorrected Refractive Error

What proportion of uncorrected refractive error is due to myopia?

How much of the productivity loss is specifically due to myopia?

The solution is available- how do we marshal resources to deliver needed care?

Is this an appropriate question for the committee to be asking?

It seems to be more a question for public health officials than scientists and it is a different question to the actual problem of primary myopia?

OPHTHALMIC EPIDEMIOLOGY
2023, VOL. 30, NO. 4, 331–339
<https://doi.org/10.1080/09286586.2022.2127784>

REVIEW ARTICLE

WHO Vision 2020: Have We Done It?

Dalia Abdulhussein^a and Mina Abdul Hussein^b