Myopia:
More than Minus Meets the Eye

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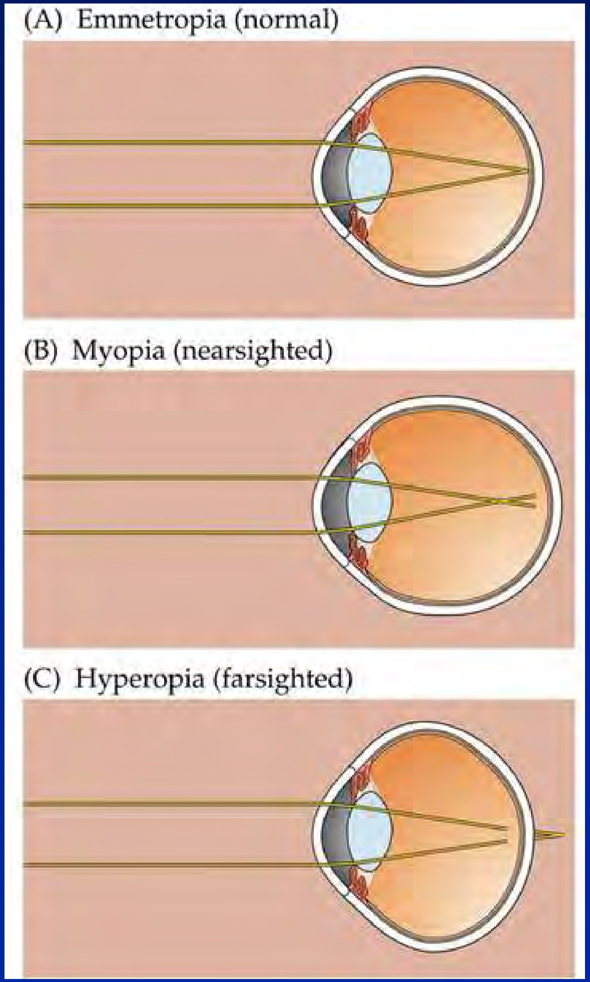
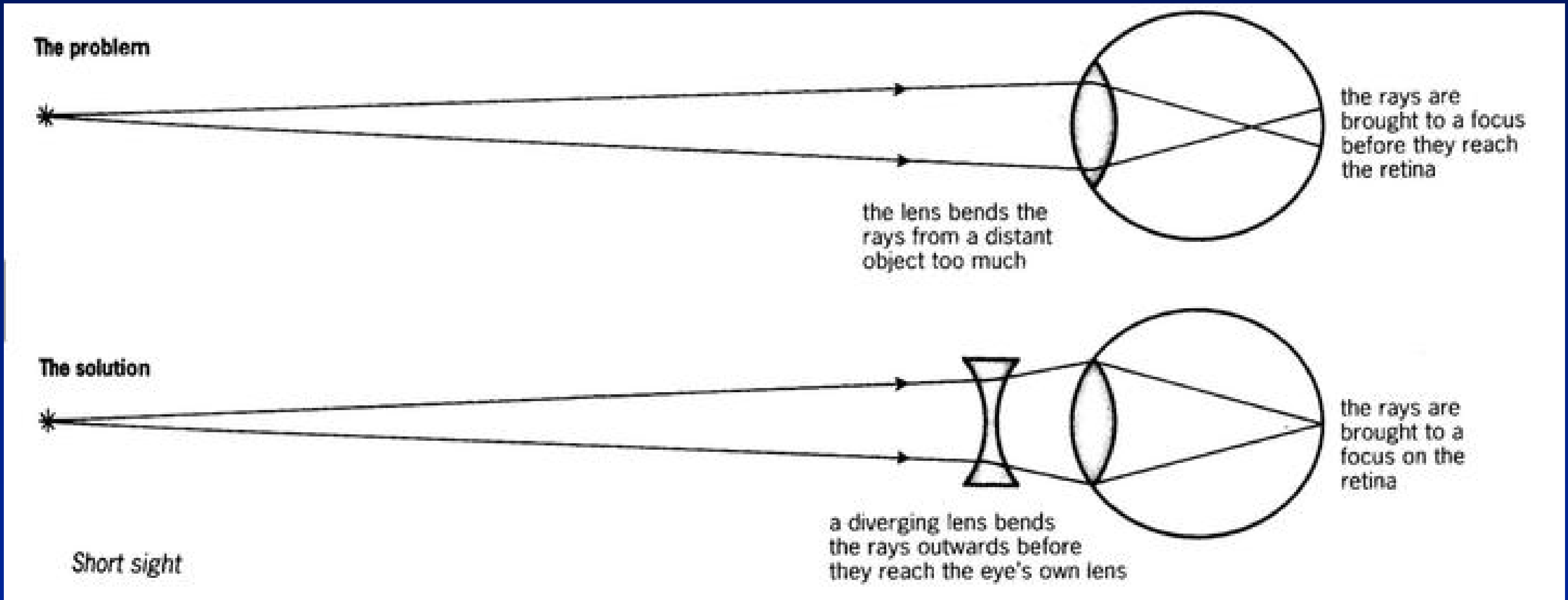
What is myopia?



What is myopia?

- Patient/parent education:
  - “Far-sighted eyes are too short; near-sighted eyes are too long.”
  - “Near-sightedness means your sight is at near.”

How do we treat myopia?

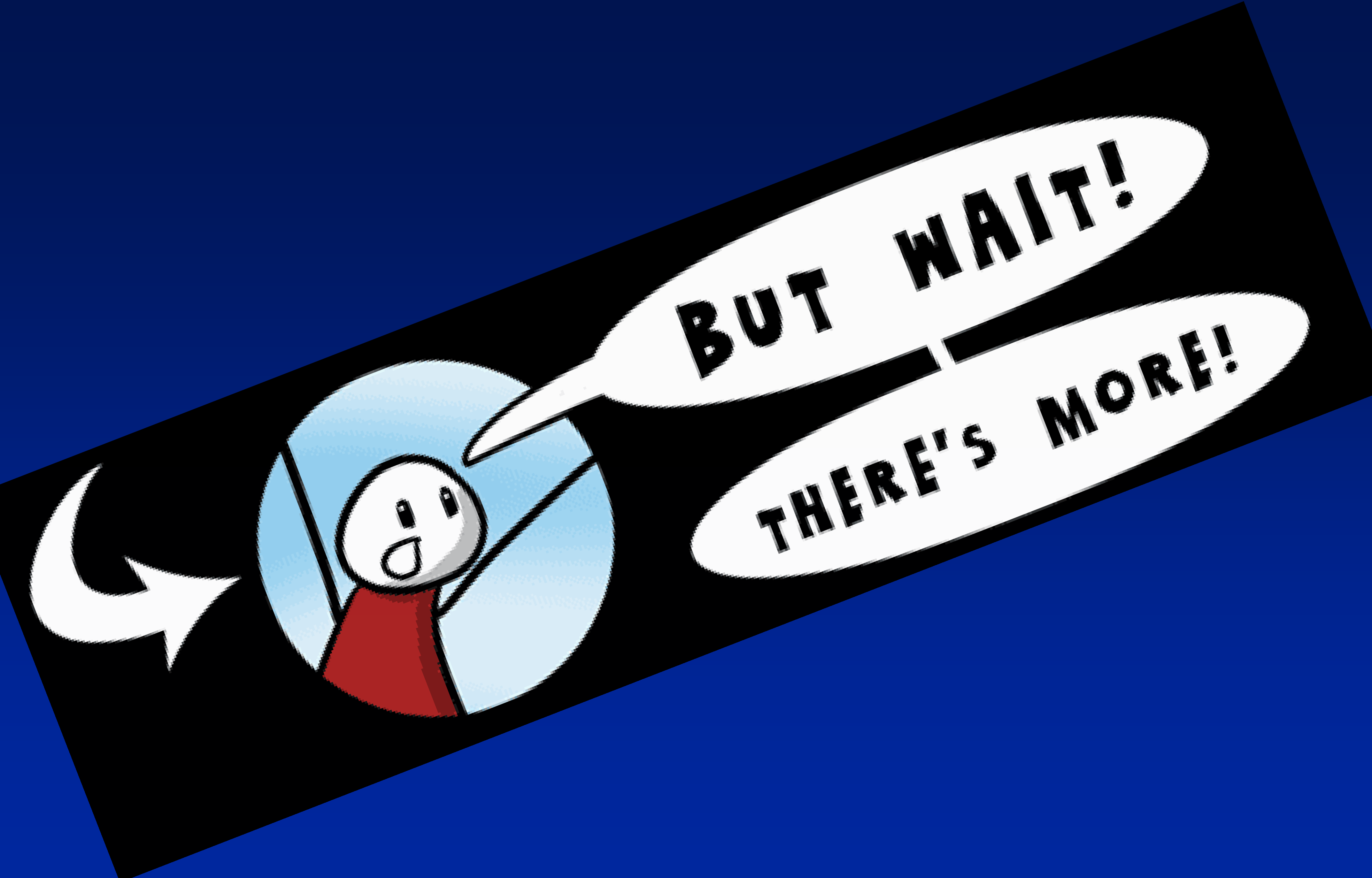


Concave lenses diverge light, allowing the light to focus more posteriorly; concave lenses minify

How do we treat myopia?

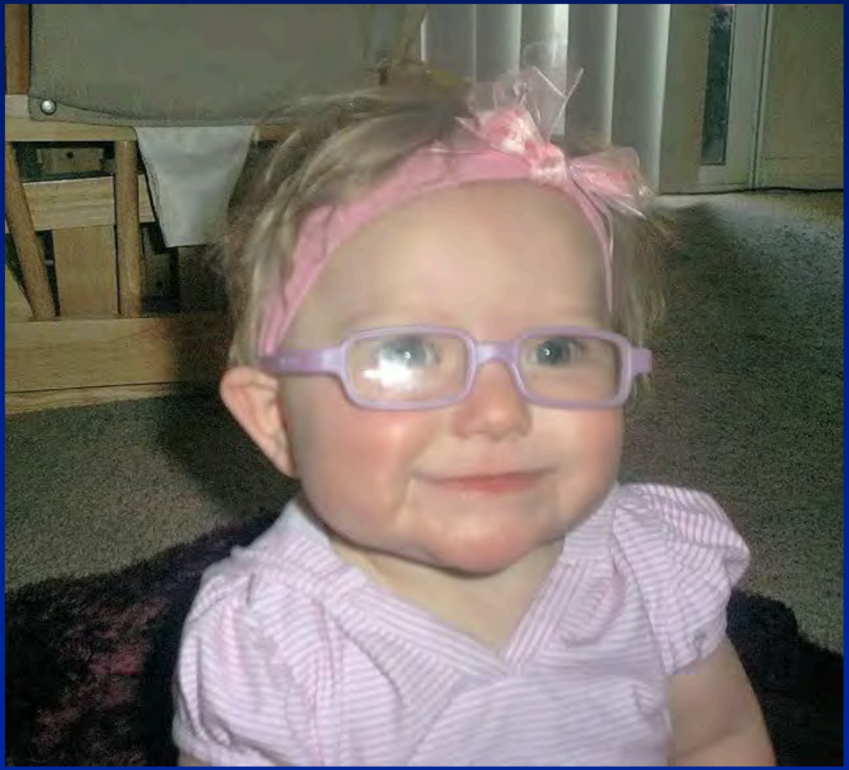
- Is he myopic?
  - How can you tell?
- Case 1
  - Subjective: -8.00 DS OD, OS
  - Wet ret: -8.00 DS OD, OS
  - Wet AR: -8.00 DS OD, OS
  - BCVA 20/20 OD, OS
  - What do you prescribe?

The End.


BUT WAIT!
THERE'S MORE!

How do we treat myopia?

- Is she myopic?
- Case 2
  - Wet ret: -8.00 DS OD, OS
  - Wet AR: -8.00 DS OD, OS
  - What do you prescribe?



  - What else do we need to know?

Myopia

- What is myopia?
- How do we treat myopia?
- What is the natural history of myopia?
- How prevalent is myopia?
  - In infancy
  - In preschoolers
  - In school-aged kids
  - In adults
- What are risk factors for myopia?
  - Race
  - Genetics
  - Parental myopia
  - Environmental Factors
    - Near work?
    - Level of education
    - Refractive Error
    - Blue light? Circadian rhythm?
  - Peripheral Hyperopic Defocus
  - Optical
    - PAL?
    - MF CL
    - Ortho-K
    - Special Specs (DIMS, DOT, HALT)
  - Environment
    - Outdoor play
  - Pharmacological
    - Atropine
    - Pirenzepine
- Food for Thought
  - Which is better?
  - Is there better?
    - RLRL?
  - Is it worse?
    - Education?
    - Prevalence of Myopia since 2010?
- Myopia in Infancy

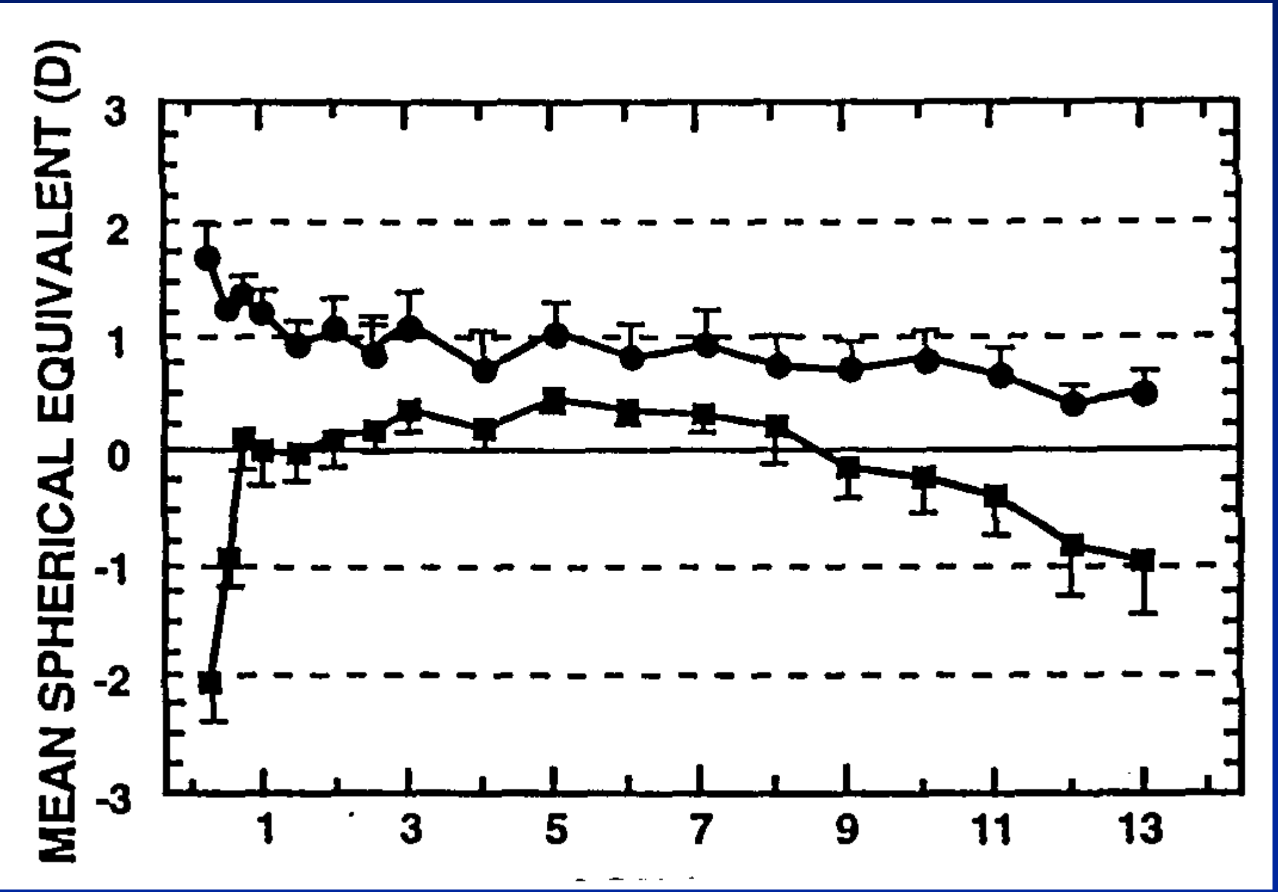
What is the natural history of myopia? (Longitudinal data by non-cyclo Ret)

Gwiazda, Thorn, Bauer and Held, 1993, longitudinal data

n=20 hyperopic infants

n=31 myopic infants

Age in years



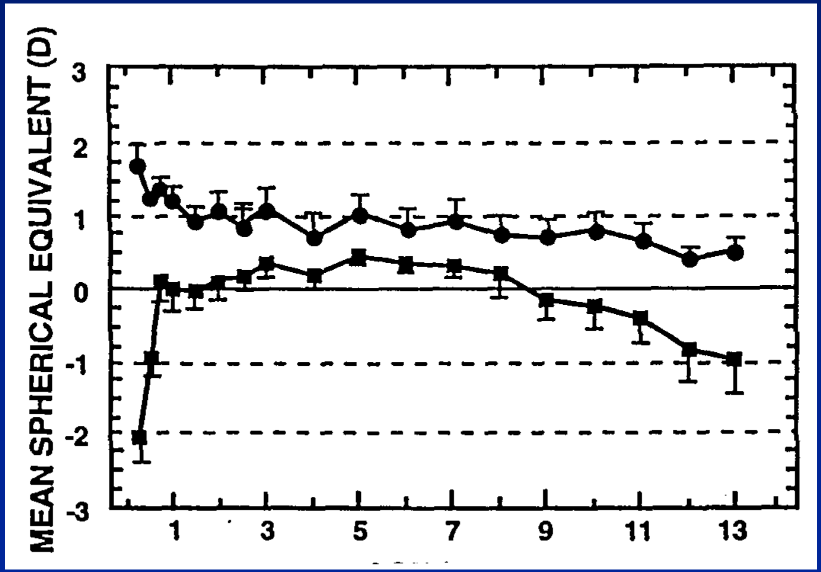
What is the natural history of myopia? (Longitudinal data by non-cyclo Ret)

Gwiazda, Thorn, Bauer and Held, 1993, longitudinal data

- 31 myopic infants got less myopic on average

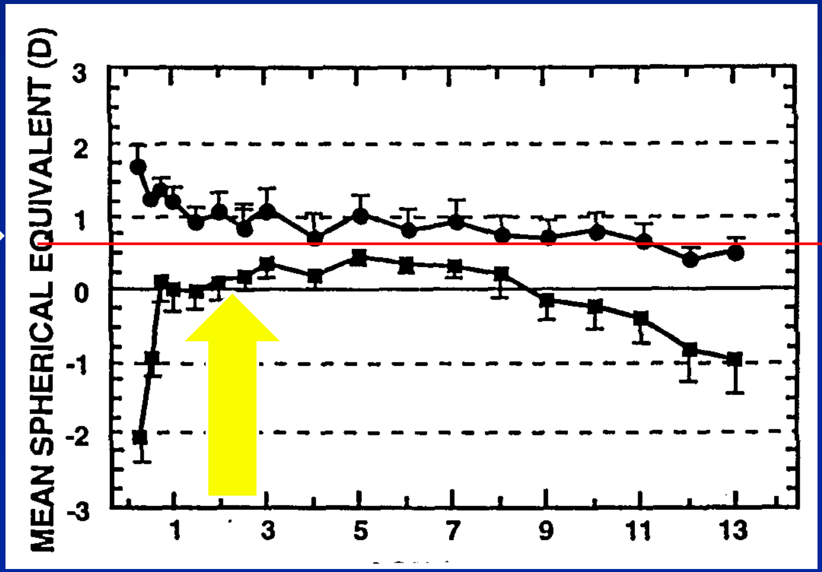
- 20 hyperopic infants got slightly less hyperopic on average

- “**emmetropization**”

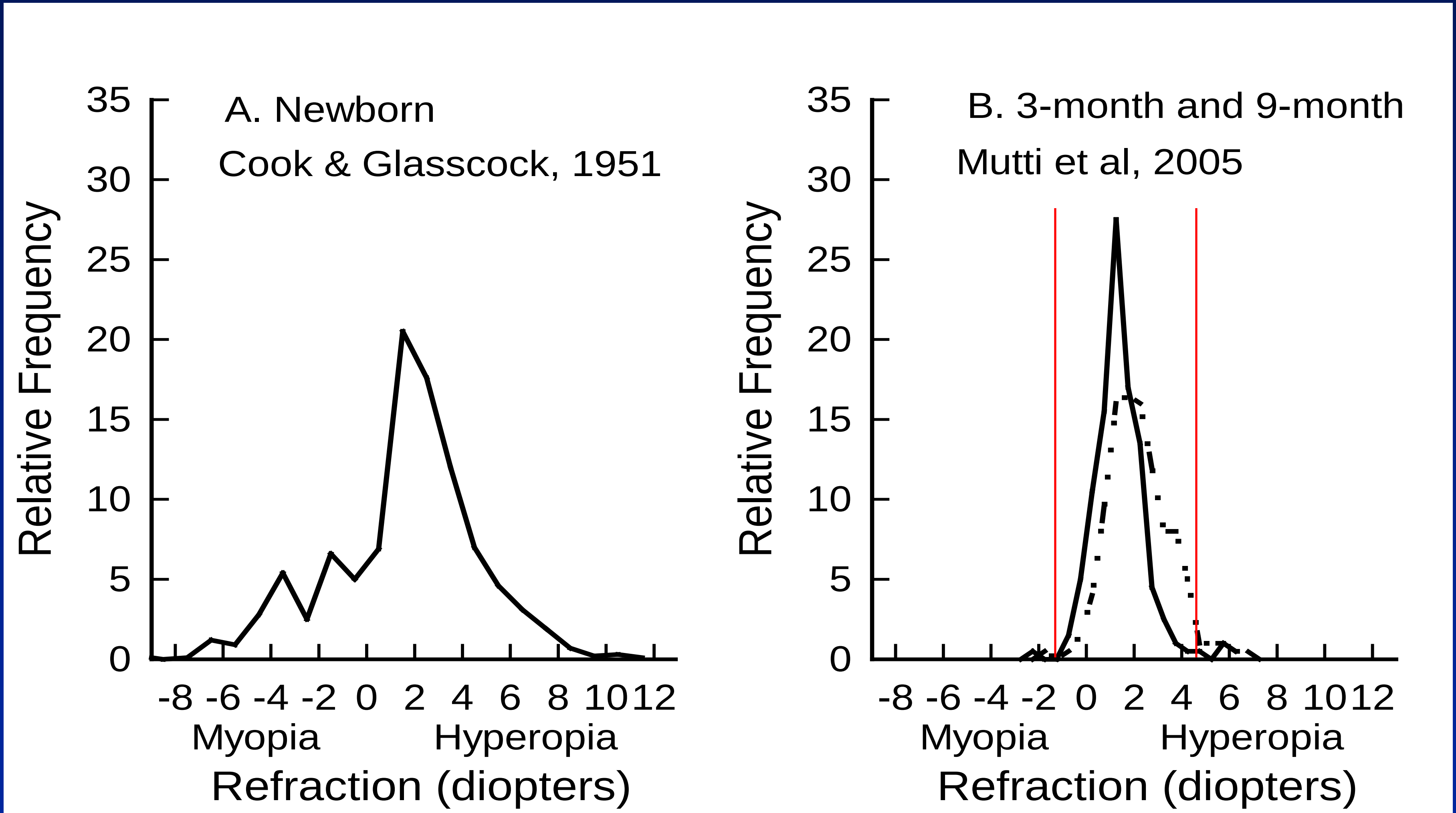


Emmetropization: a mechanism inherent to the human eye that guides eyes to good focus

- Children "emmetropize"
  - Broad refractive error distribution at birth becomes narrow
  - By 1-2 years, most children have little refractive error

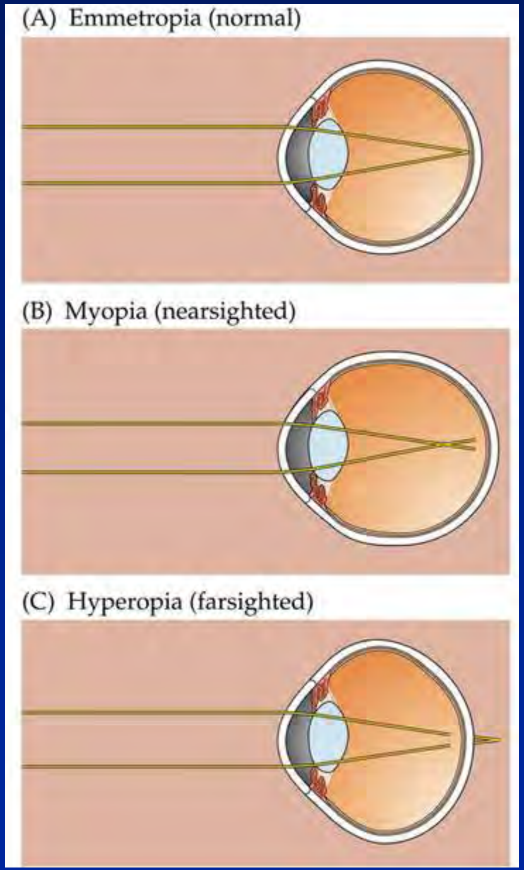


Emmetropia: Broad Distribution Becomes Narrow



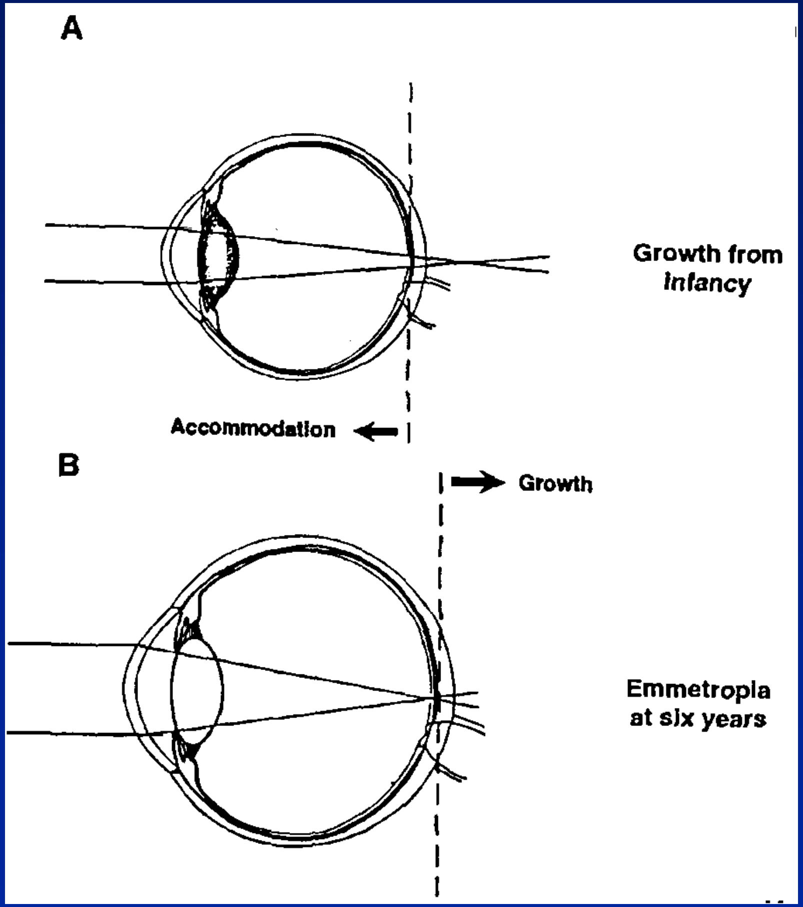
Emmetropia

- How does emmetropization occur?
  - The environment (refractive error) engages the emmetropization mechanism to guide eye growth to emmetropia

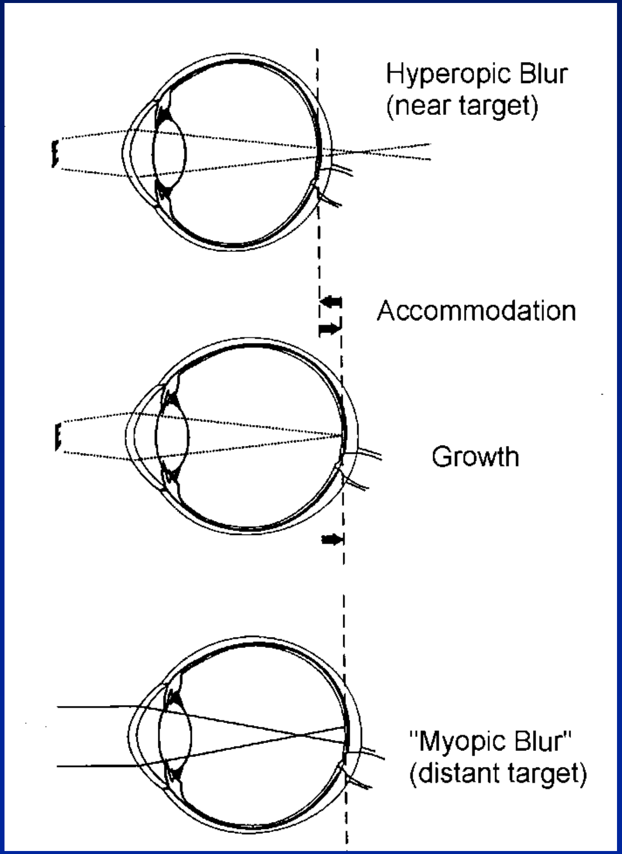

(A) Emmetropia (normal)
(B) Myopia (nearsighted)
(C) Hyperopia (farsighted)

Theory of Myopia Development

Emmetropization



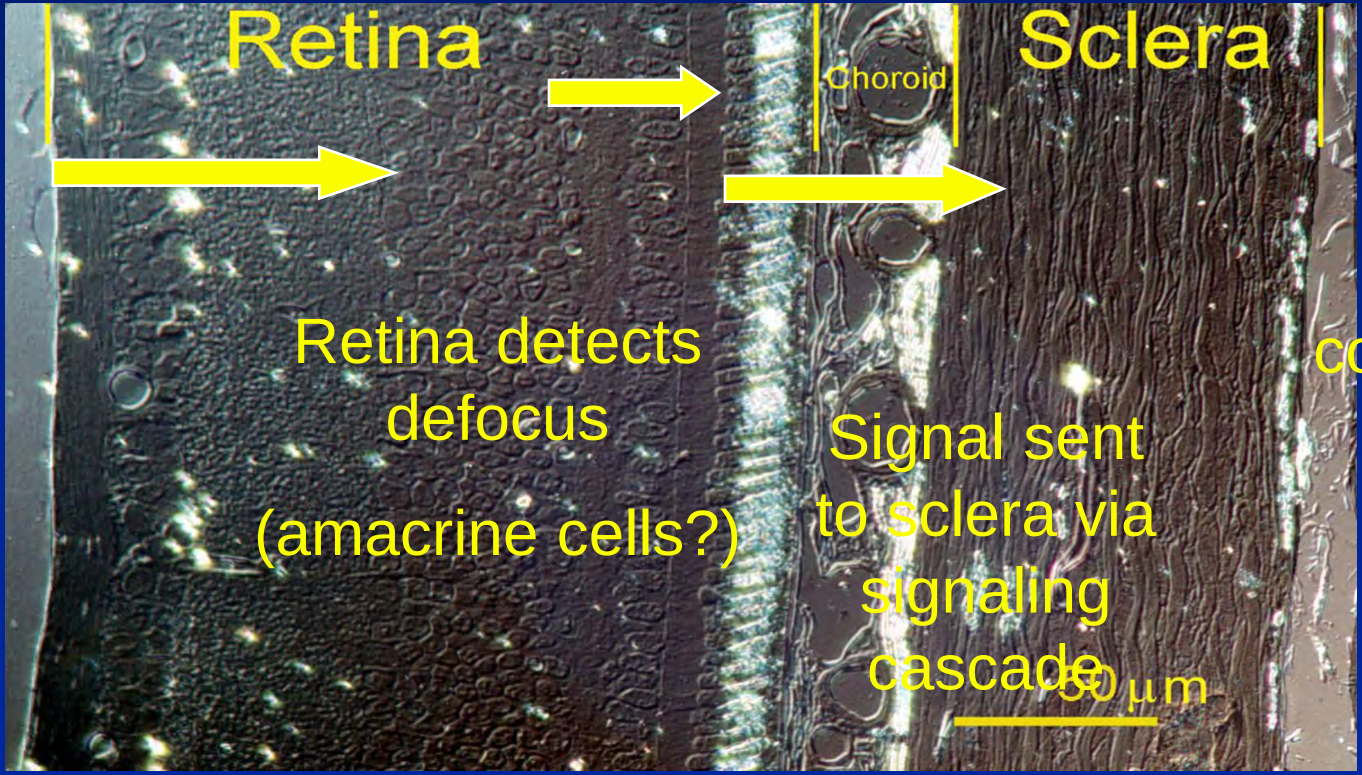
"Myopization"



Direct Emmetropization Pathway

(T. Norton slide)

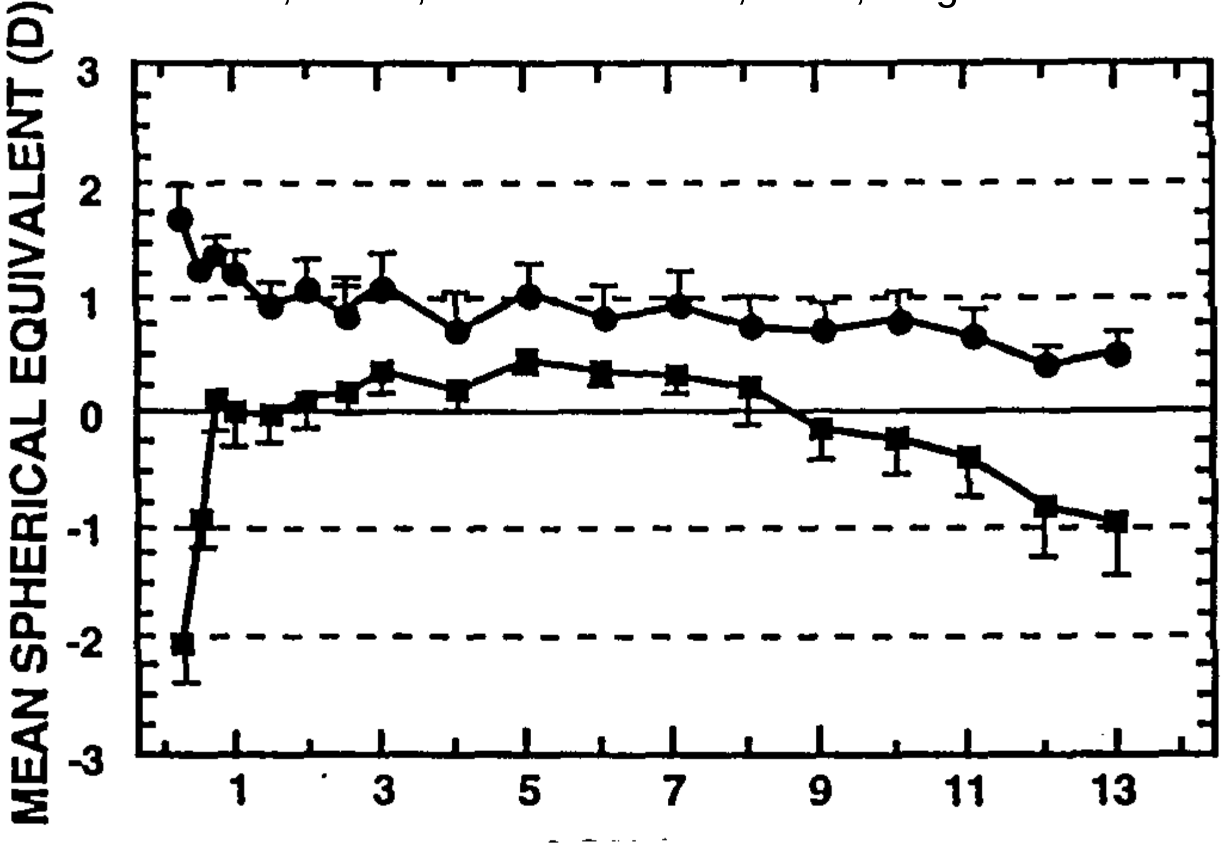
- Retinal “go” (from hyperopia) and “stop” (from myopia) signals
- Communicated through RPE & choroid
- modulate the axial length of the eye to position the retina close to the focal plane.



Scleral changes control axial length

What is the natural history of myopia? (Longitudinal data by non-cyclo Ret)

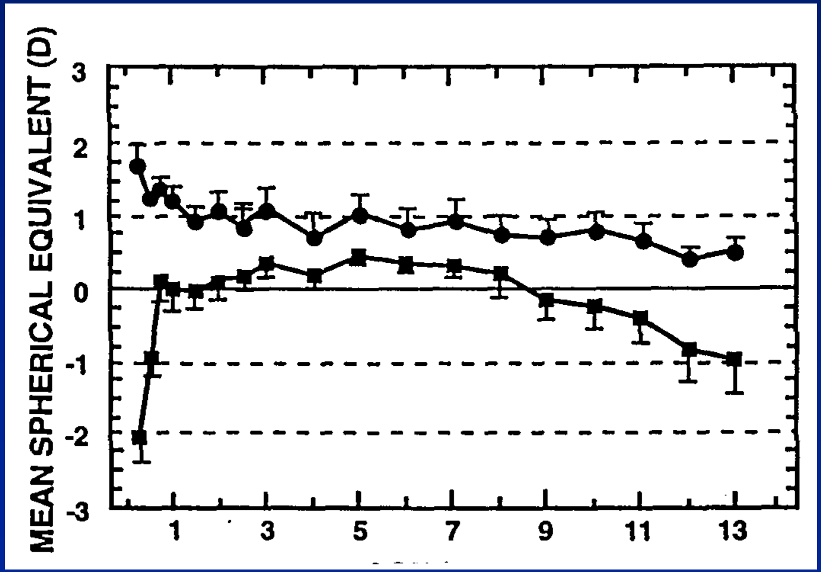
Gwiazda, Thorn, Bauer and Held, 1993, longitudinal data



What is the natural history of myopia? (Longitudinal data by non-cyclo Ret)

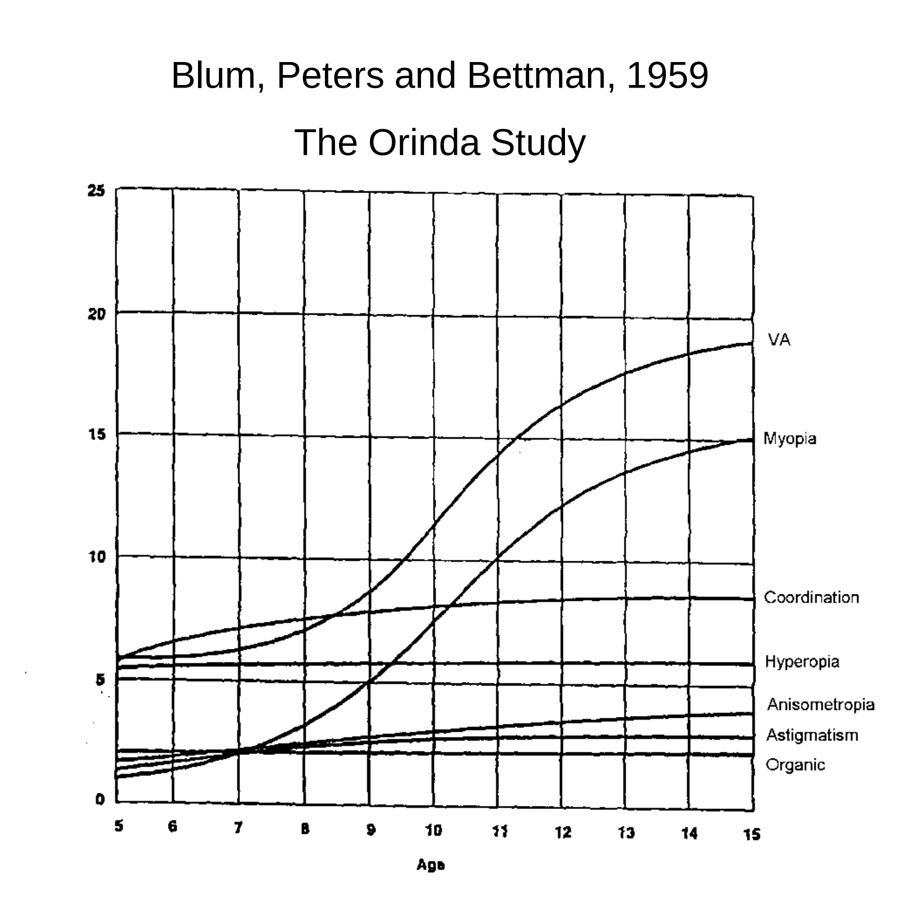
Gwiazda, Thorn, Bauer and Held, 1993, longitudinal data

- Hyperopic infants tended to become hyperopic kids
  - Far-sightedness stayed about the same in school years
- Myopic infants tended to become myopic kids
  - Near-sightedness got worse in school years
- "Myopia results from a complex combination of genetic and environmental factors"



Age in years

Myopia becomes most common refractive error



When do kids get near-sighted?

- Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE)
  - Multi-center NIH grant also, 5,000+ kids
    - Watched elementary school aged kids (age 6 to 14 years)
    - Kleinstein, J. Sims (UAB!)
  - Average age of onset of myopia ~11 years (7 to 16) (Kleinstein 2012)

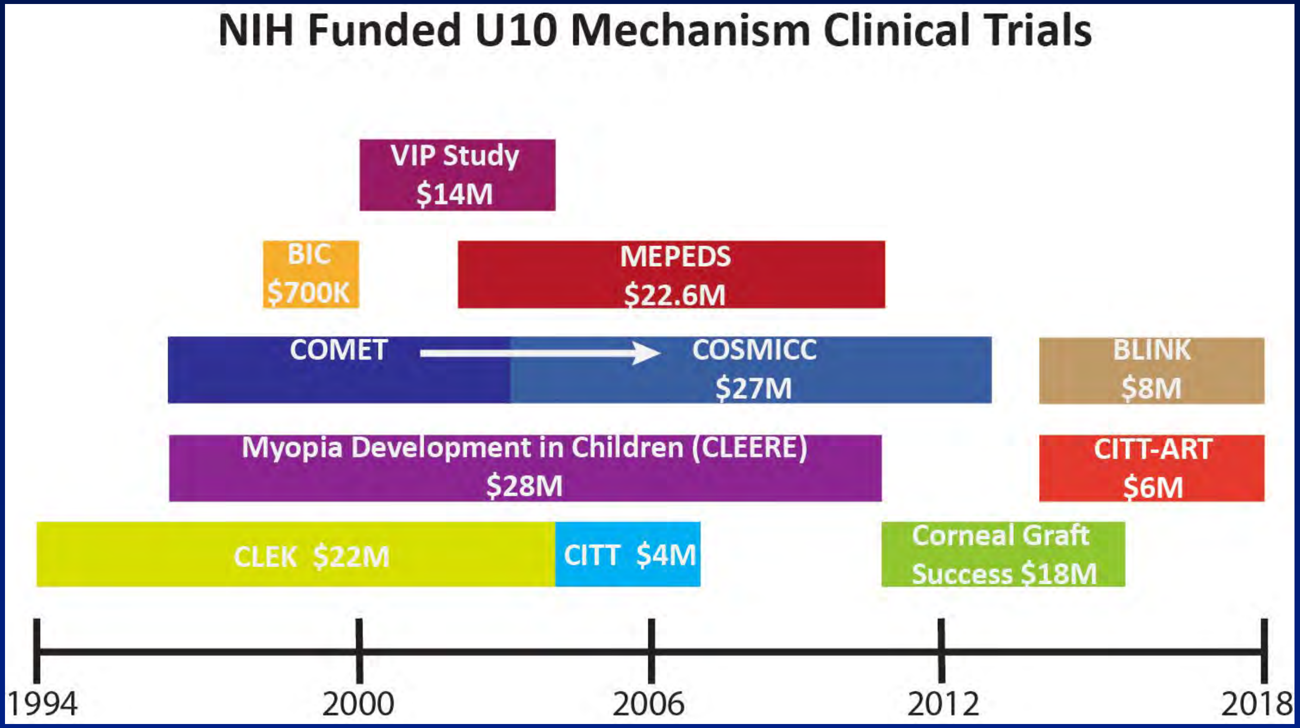
Table 3. Data on the Youngest Age at Which Myopia Was Observed

	Myopia Definition, No. (%) of Participants	
Age, y	Spherical Equivalent −0.50 D or More (n = 1006)	Both Principal Meridians −0.75 D or More (n = 749)
7	25 (2.5)	11 (1.5)
8	80 (8.0)	59 (7.9)
9	150 (14.9)	100 (13.4)
10	175 (17.4)	122 (16.3)
11	161 (16.0)	136 (18.2)
12	157 (15.6)	112 (15.0)
13	142 (14.1)	111 (14.8)
14	91 (9.0)	80 (10.7)
15	23 (2.3)	12 (1.6)
16	2 (0.2)	6 (0.8)

Abbreviation: D, diopters.

Once near-sighted, what happens?

- Correction of Myopia Evaluation Trial (COMET)
  - 4 centers: PCO (Salus); UH; NECO; UAB
  - 469 kids aged 6 to 11 years old
  - -1.25 to -4.50
    - Monitored for 14 years (1997 to 2011) (!)
    - UAB: 118/133 (89%) at year 14 (!)
  - PAL’s vs. SV (Year 1 to 5)
  - Natural History of Myopia (Year 5 to 14)
  - November 20, 1995-November 30, 2015
    - Gwiazda, Marsh-Tootle, Norton



BIC: Bifocals in Children
BLINK: Bifocal Lenses in Nearsighted Kids
CITT: Convergence Insufficiency Treatment Trial
CITT-ART: Convergence Insufficiency Treatment Trial Attention & Reading Trial
CLEERE: Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error
CLEK: Collaborative Longitudinal Evaluation of Keratoconus

Corneal Graft: Effect of Corneal Preservation Time on Long-Term Graft Success
COMET: Correction of Myopia Evaluation Trial
COSMICC: Collaborative Observational Study of Myopia in COMET Children
MEPEDS: Multi-Ethnic Pediatric Eye Disease Study
VIP: Vision in Preschoolers

Data from NIHRePORT

NIH Support - UAB Clinical Pediatric Optometry: 1997-present

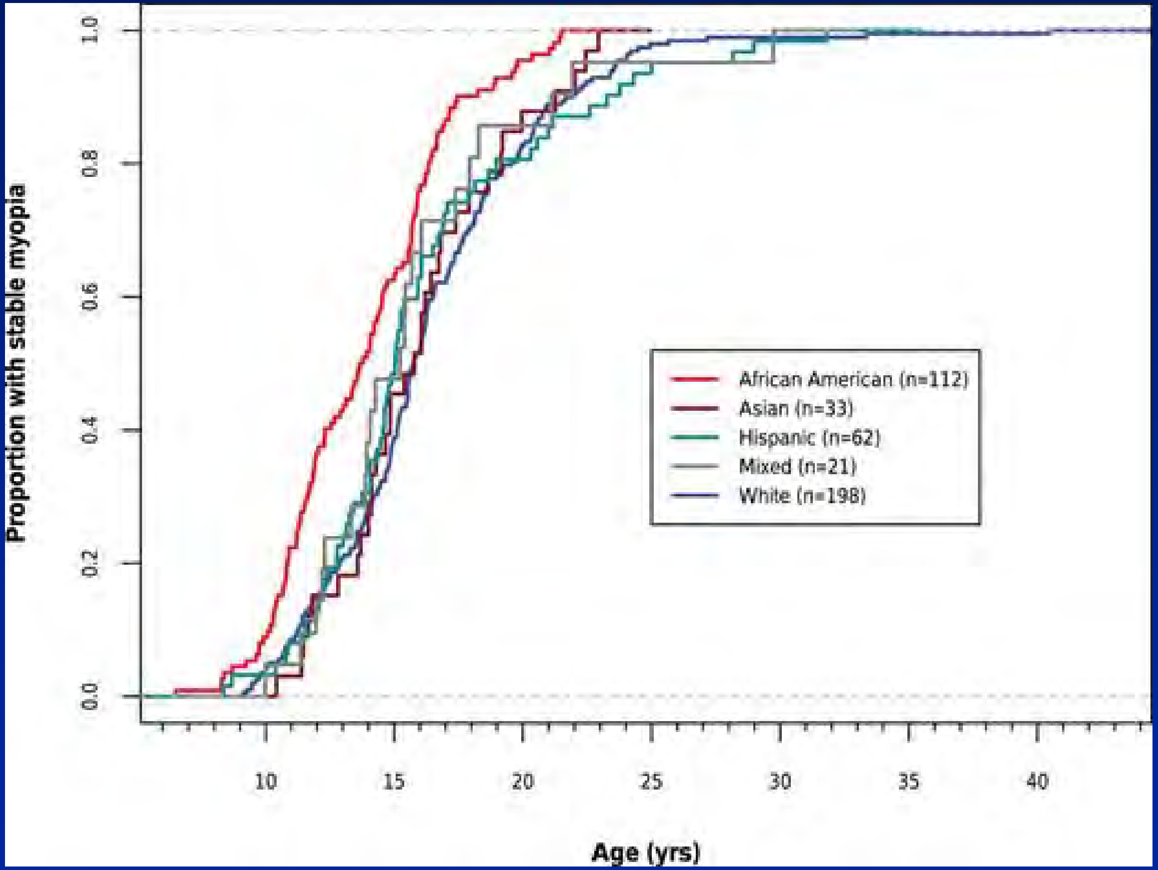
- **UG1 proposal** – Drs. Katherine Weise, M. Heath Hale
  - Convergence Insufficiency Treatment Trial – Concussion (**January 2016 to present?**)
- **U10**– Drs. Kristine Hopkins (PI), Marcela Frazier, Sarah Lee, Wendy Marsh-Tootle, Katherine Weise
  - Convergence Insufficiency Treatment Trial – Attention and Reading Trial (CITT-ART) (**August 2014-present**)
- **U10** - Pediatric Eye Disease Investigator Group (PEDIG) – Drs. Kristine Hopkins (local PI), Katherine Weise, Tamara Oechslin, Maggie Bailey, Marcela Frazier, Ann Marie Arciniegas-Bernal, (formerly Dr. Robert Rutstein, Dr. Wendy Marsh-Tootle, Sarah Lee)
  - >300 Pediatric OMD and OD
  - Executive Committee: Mayo, Duke, Johns Hopkins, SCCO, UABSO
  - EY011751 **(1997-present)**
- **U10** – Dr. Wendy Marsh-Tootle (PI), Drs. Katherine Weise, Marcela Frazier, Lei Liu
  - Correction of Myopia Evaluation Trial+ (COMET): 118/133 (89%) retention at year 14
  - Multi-center Ocular Observations in Non-myopic Subjects (MOONS)
  - EY11756, EY11754, EY11805, EY11752, EY11740, EY11755 **(1998-2013)**
- **RO1** – Dr. Wendy Marsh-Tootle (with T. Walls, MD)
  - Multi-modal physician intervention to detect amblyopia
  - R01 EY015893 **(2005 to 2011)**
- **U10 –** Dr. Kristine Hopkins (PI), Drs. Marcela Frazier, Katherine Weise
  - Convergence Insufficiency Treatment Trial
  - EY014659-02 **(2005-2011)**
- **NIH Loan Repayment Program** (mentor-sponsored research X 0.50 FTE)
  - Dr. Wendy Marsh-Tootle, mentor
    - Dr. Marcela Frazier (2005-2009)
    - Dr. Katherine Weise (2003-2007)
    - Dr. Sarah Lee (2013-present)

COMET

- Near-sightedness tends to grow
- Average change per year (Gwiazda J 2003):
  - 0.50 D
- Average period of growth
  - 9 years
    - Near-sightedness tends to grow for about 9 years
  - Earlier onset, faster progression
- When does it stop growing?

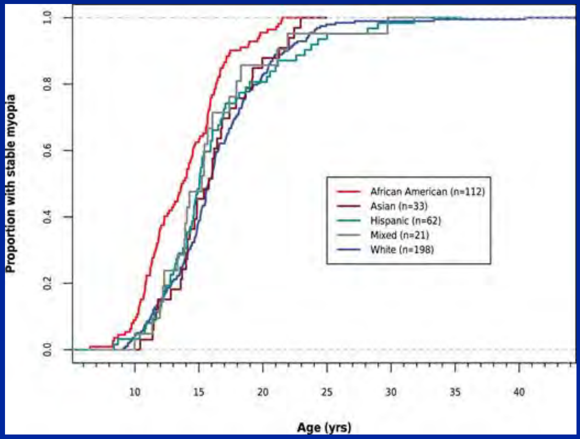
What is the natural history of myopia? When does the eye stop growing?

COMET Group; Norton T; IOVS 2013



COMET

- Average age at stabilization (COMET 2013)
  - 15.6 (4.17) years
    - 48% were stable by age 15 years
    - 77% were stable by age 18 years
    - 90% were stable by age 21 years
    - 96% were stable by age 24 years
- Average myopia at stabilization
  - -4.87 (2.01) D



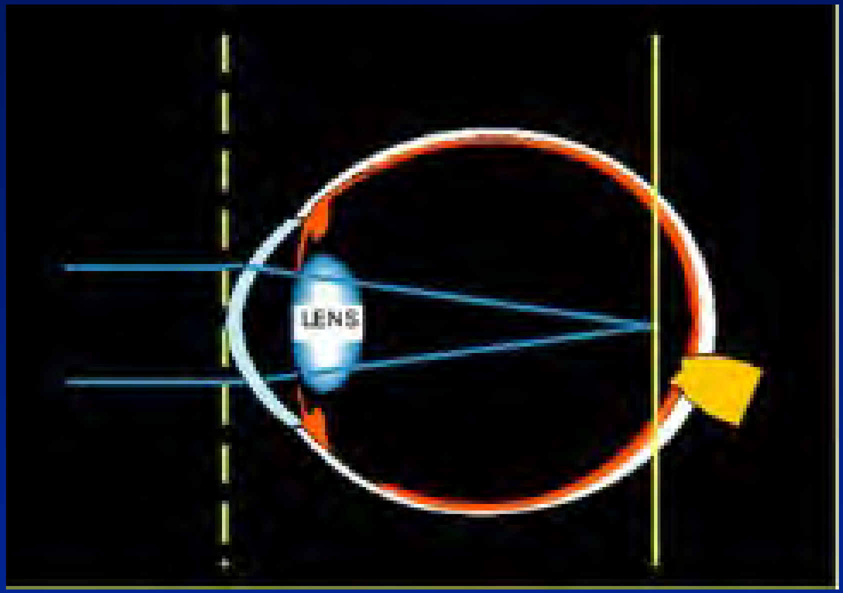
The End?

What’s all the fuss about?

Dad: I’ll just wait for LASIK.

Side-effects of Being Myopic

- Increased risk of
  - Glaucoma
  - Retinal detachment
  - Choroidal degeneration
  - Cataract



- Mainly due to eye shape and globe expansion

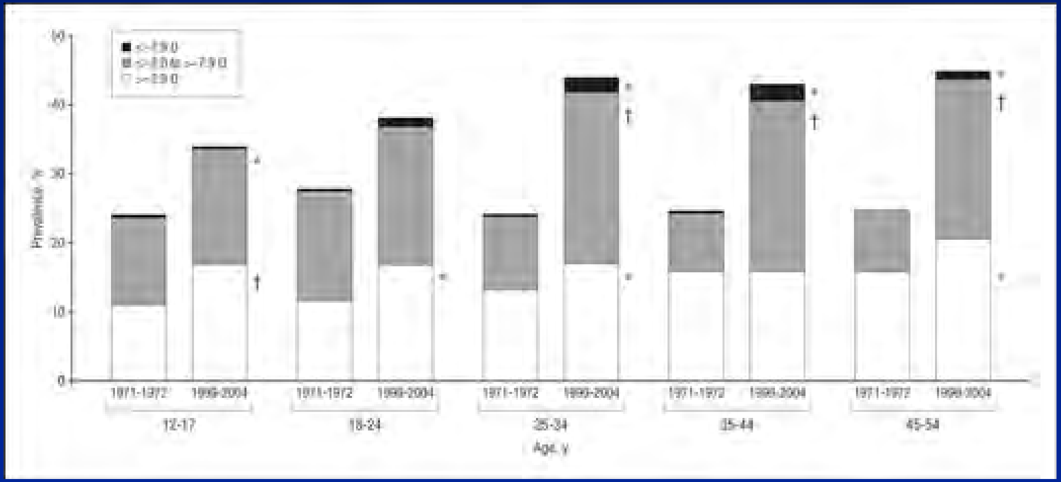
What's all the fuss about? (Is there more?!?)

Prevalence of Myopia

- US
  - 33.1% (Vitale S 2008)
    - N = 14,213 aged 20 years and older, 1999-2004 National Health and Nutrition Examination Survey (NHANES) ;
      - 12,010 with non-cyclo refractive error
      - Myopia = Sph Eq $\leq$1.00 D

Prevalence of Myopia

- US (Vitale S 2009)
  - **41.6%** in 1999-2004 vs. **25.0%** in 1971-1972



- Algorithm: Lensometry, PH VA, presenting VA, ret
  - Myopia = Sph Eq. <0.-00
  - 12-54 years

Prevalence of Myopia

Wen G 2013: Multi-Ethnic Pediatric Eye Disease Study (MEPEDS)

- Population-based sample
- aged 6-72 months
- N = 3008
- Los Angeles County and Riverside County, California
  - 1501 NHW children: 1.2%
  - 1507 Asian children: 3.98%
- Cycloplegic AR (<1.0 D = myopia)

Dirani M 2010:Strabismus, Amblyopia and Refractive Error in Singaporean Children (STARS)

- Population-based sample
- aged 6 to 72 months
- N = 3009
- Southwest Singapore
  - 11%
- Cycloplegic ref (<0.50 D)

Prevalence of Myopia

- Singapore
  - 81.6% (Koh V 2014)
    - N = 15,085 aged 19.5 +/- 1.4 years
    - 2009-2010
    - Non-cyclo AR (<-0.50 D sph Eq)
  - 38.9% (Pan CW 2013)
    - N = 10,033 adults > 40 years
    - Subjective refraction

"Myopia Generation?"

Myopia Risk Factor: Race

- Among US adults sampled in 1999-2004 vs. 1971-1972 (Vitale; Arch Ophthalmol 2009 127(12):1632)

	Now	Then	% increase	P value
Overall	41.6%	25.0%	166%	<0.001
Females	45.8%	27.1%	169%	“
Males	37.4%	22.8%	164%	“
Whites	43.0%	26.3%	163%	“
Blacks	33.5%	13.0%	258%	“
≤ -7.9 D	1.6%	0.2%	800%	“

- Some suggest the disproportionate increase in higher amounts of simple myopia indicate these cases are more susceptible to environmental factors

Prevalence of Myopia

Changes of cases between 2000 and 2010

Year	Value	Short Value
2000	30,357,202	30,357
2010	34,119,279	34,119

12% increase

- https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/nearsightedness-myopia-data-and-statistics/nearsightedness-myopia-tables (website last updated Feb. 7, 2020)

Prevalence of Myopia: 2020

Projections for myopia (2010-2030-2050)

Year	All	White	Black	Hispanic	Other
2010	34,119,279	27,391,291	2,204,294	2,724,715	1,798,978
2030	39,094,141	28,034,771	2,840,018	5,177,235	3,042,117
2050	44,496,229	27,787,556	3,380,636	8,695,907	4,632,129
Total Population	142,648,393	103,846,437	15,190,777	14,901,369	8,709,810

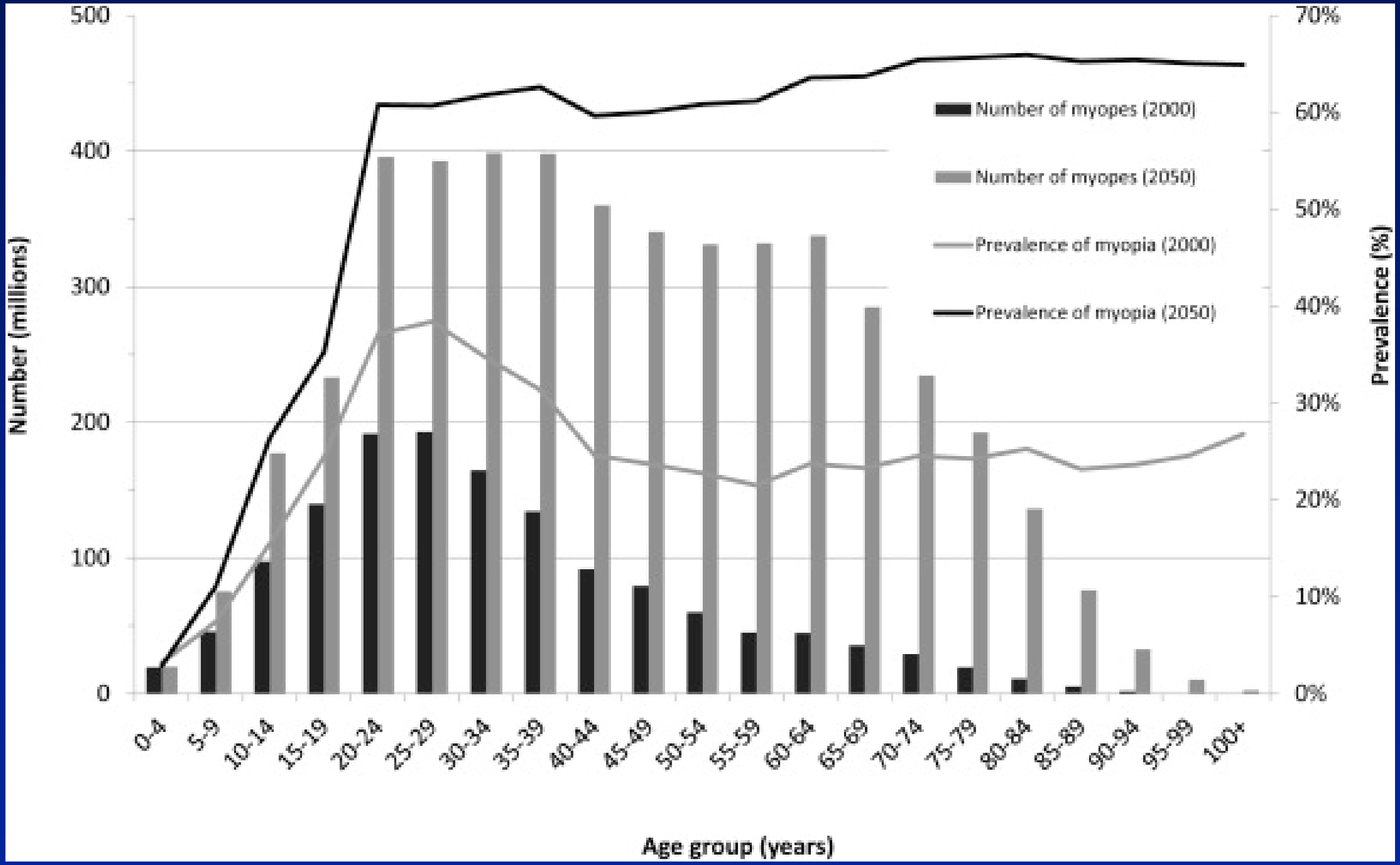
14.5% increase

13.8% increase

30% increase predicted between 2010 and 2050

- https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/nearsightedness-myopia-data-and-statistics/nearsightedness-myopia-tables (website last updated Feb. 7, 2020)

"50% of the world myopic by 2050" Holden BA, 2016



What are risk factors for myopia?

- Race
- Genetics
  - Parental myopia
- Environmental Factors
  - Near work?
  - Level of education
  - Refractive Error
  - Blue light? Circadian rhythm?
- Peripheral Hyperopic Defocus

Myopia Risk Factor: Race

- CLEERE Study 2003
  - Kleinstein et al report myopia in 9.9% of children aged 5-17 years and sig differences depending upon race / ethnicity:
    - Asian, 18.5% (84% by age 18 years in Taiwan)
    - Hispanic, 13.5%
    - African-American, 6.6%
    - Caucasian, 4.4%

Myopia Risk Factor: Race

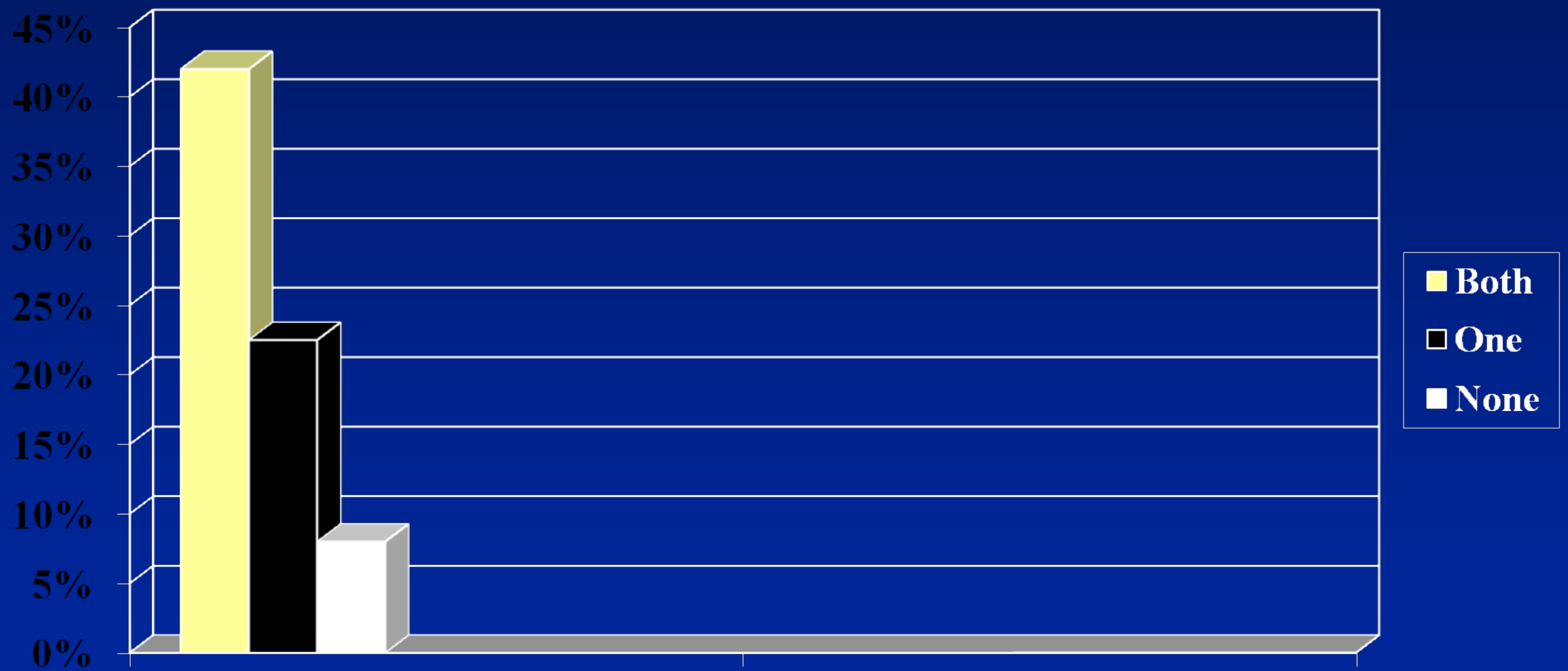
- **“Taiwan To Fine Parents of Kids Who Spend Too Much Time on Mobile”**
- Eric Jou; 1/26/15
- 0-2 years old; no time on iPad
- 3-18 years old: 30-minute sessions max
- $1595 fine

Myopia Risk Factor: Genetics

Myopia Risk Factor: Genetics

(WMT slide)

Gwiazda et al, 1993



Development of myopia depends upon the # of myopic parents.

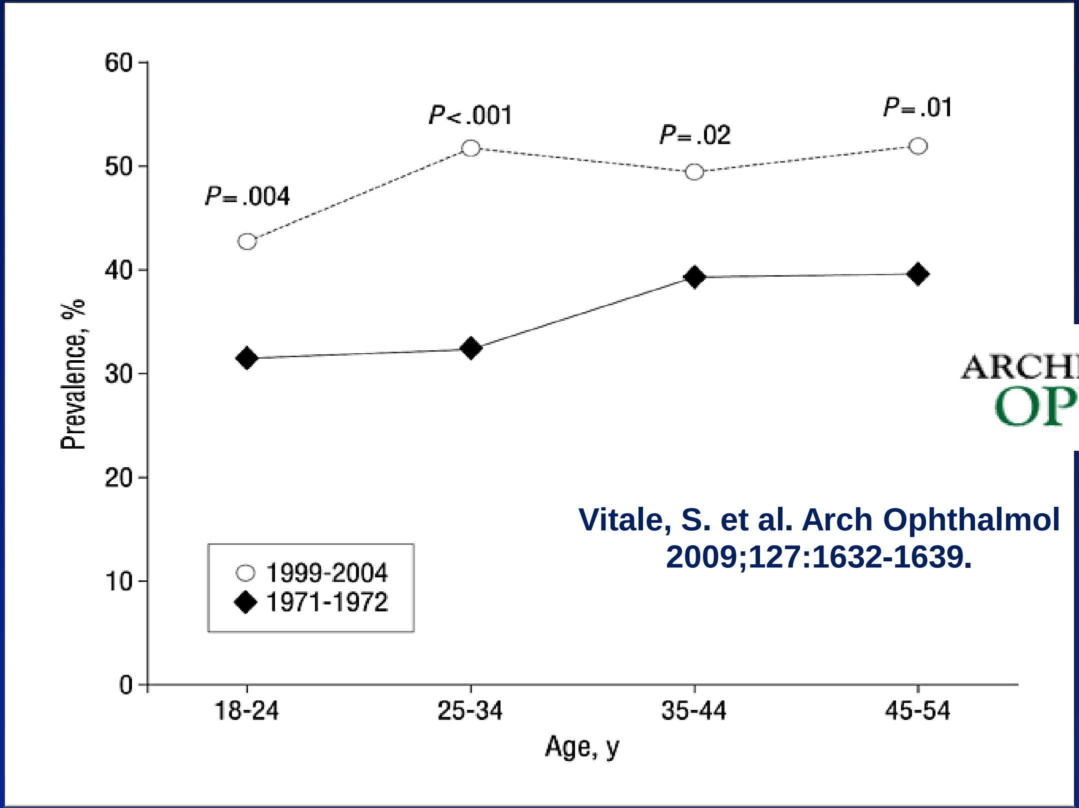
Myopia Risk Factor: Genetics

- Compared to children with no myopic parents,
  - 1 parent: 2 times more likely
  - 2 parents: 5 times more likely to have myopia
    - Jones LA et al. IOVS 2007 (OSU)

  - Odds ratio for two compared with no parents with myopia was 6.40
    - Orinda 1991-1996 (366 8^{th} grade children in US)

Myopia Risk Factor: Education

Prevalence higher among those with > 12 yrs Education



ARCHIVES OF OPHTHALMOLOGY

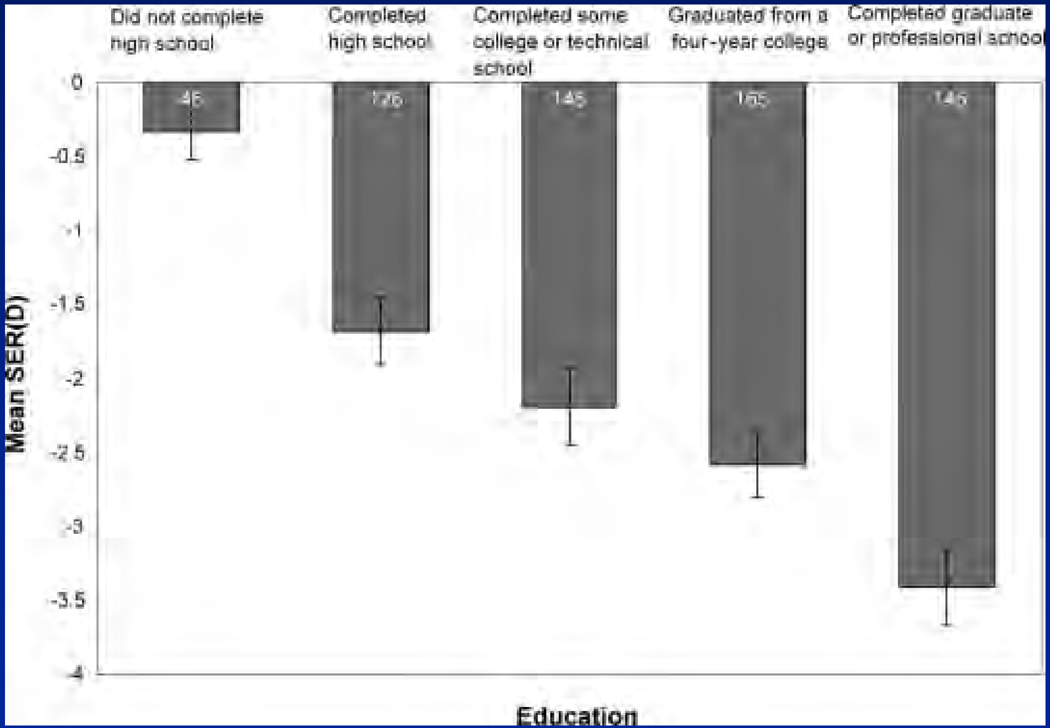
Vitale, S. et al. Arch Ophthalmol 2009;127:1632-1639.

Prevalence of myopia in persons with 12 or more years of formal education, comparing National Health and Nutrition Examination Survey data from 1971-1972 vs 1999-2004

COMET Parents and Education:

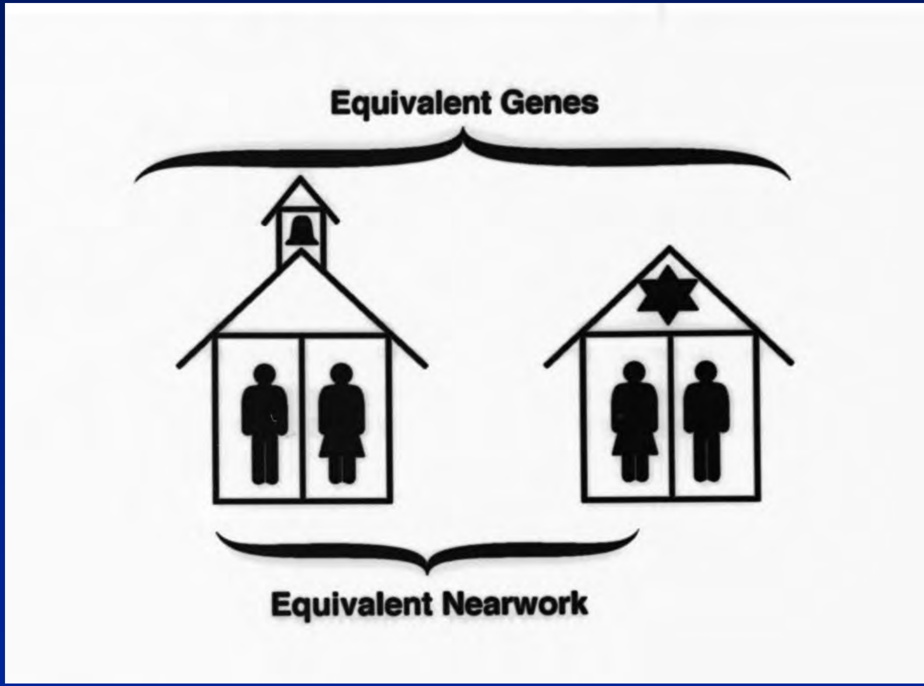
Parental Myopia Study

- More education of parent of a near-sighted COMET kid, the more near-sighted the parent is
  - See also genetics



Myopia Risk Factor: Education?

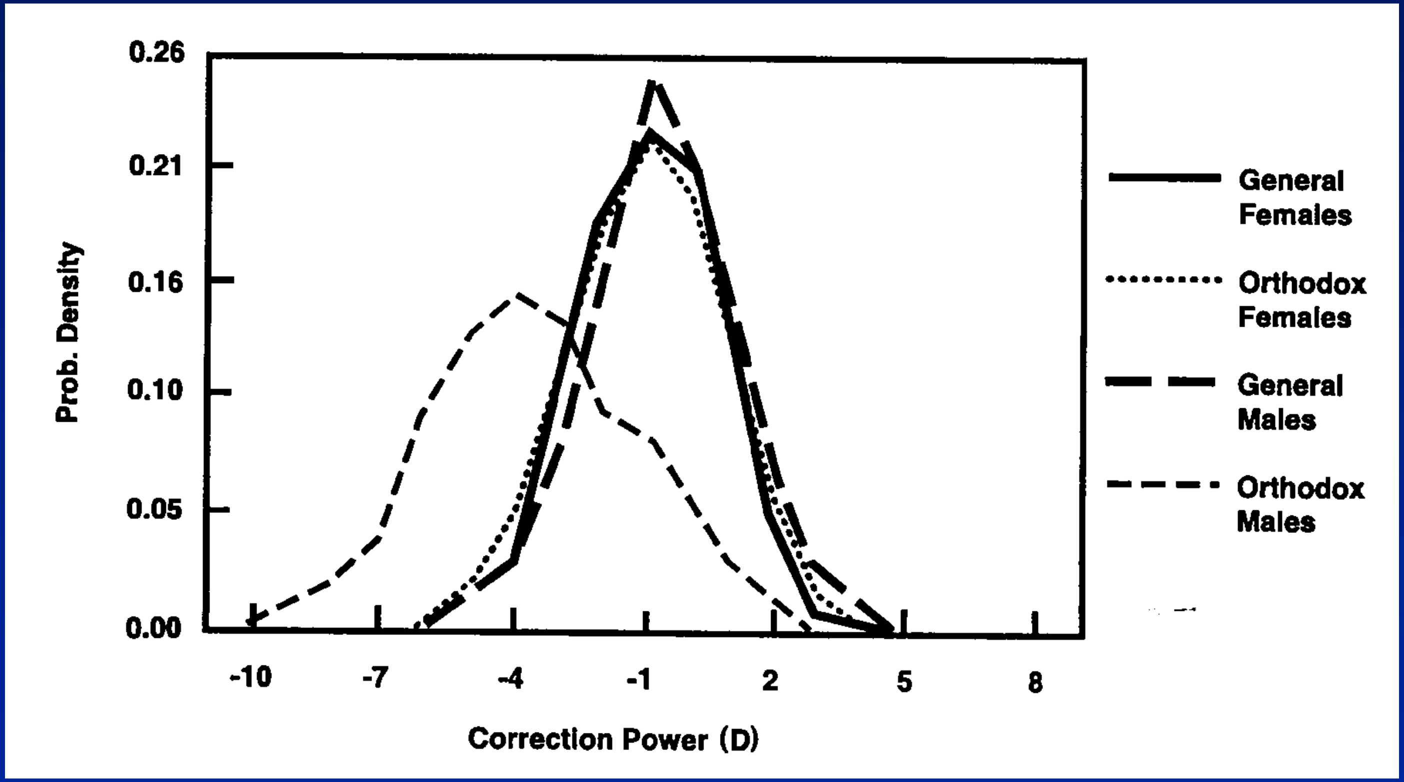
Orthodox girls,
boys and girls in general school:
6 hours/d of class;
1 to 3 hours/d of homework



Orthodox boys:
16 hours/d reading
very small print

Zylbermann R, Landau D, Berson D. 1993. The influence of study habits on myopia in Jewish teenagers. *J Pediatr Ophthalmol Strabis* 30:319.

Myopia Risk Factor: Education



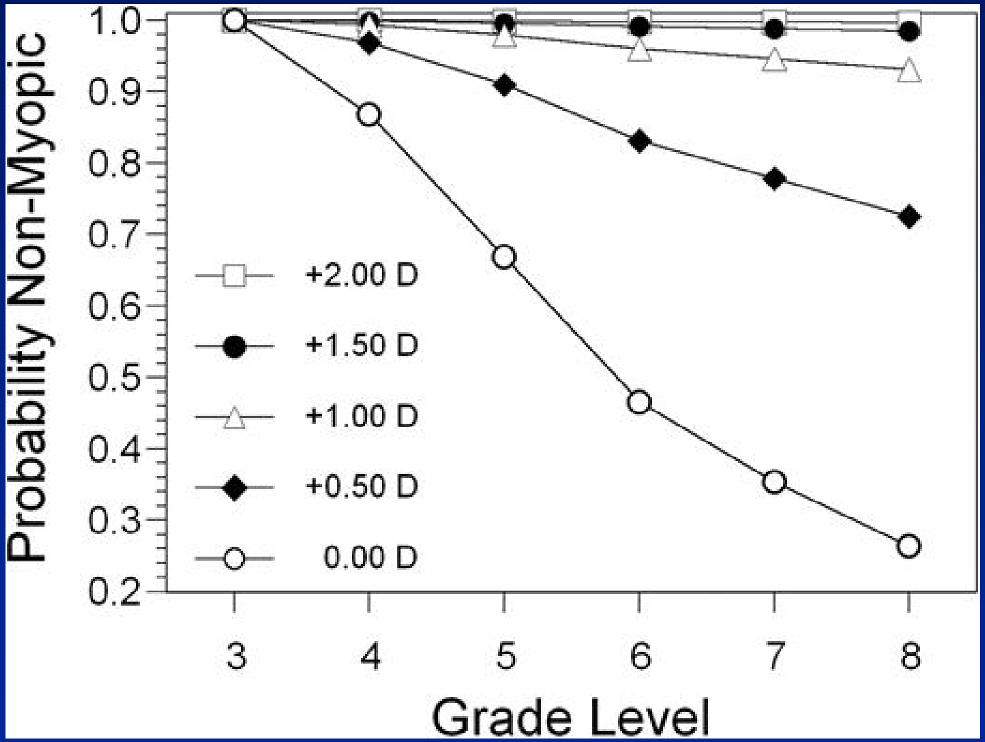
The Orthodox males, who spent 16 hours/day at school, got more nearsighted.

Myopia Risk Factor: Refractive Error

(CLEERE)

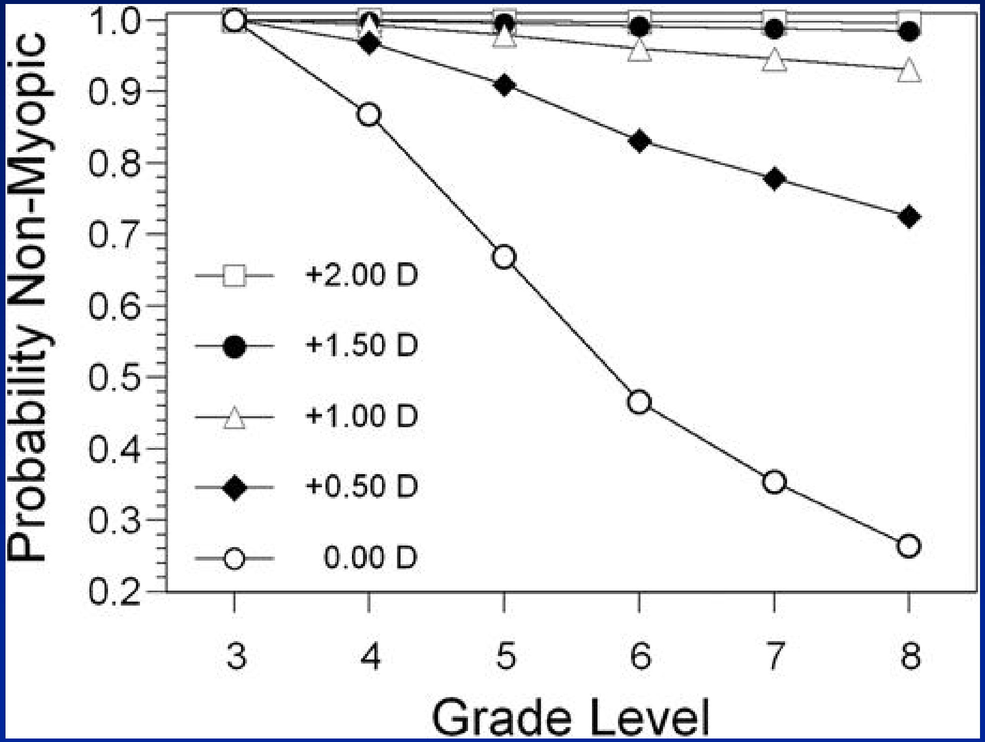
- +0.75 D hyperopia or less in 1st grade (Zadnik K 2007)
  - "High risk" for myopia onset
  - KW Rule of thumb
    - +0.50 D by 5 yo
    - <1.00 by 1st grade

Myopia Risk Factor: Refractive Error
(CLEERE)



- If you are emmetropic in 3rd grade, it is likely that you'll become near-sighted.

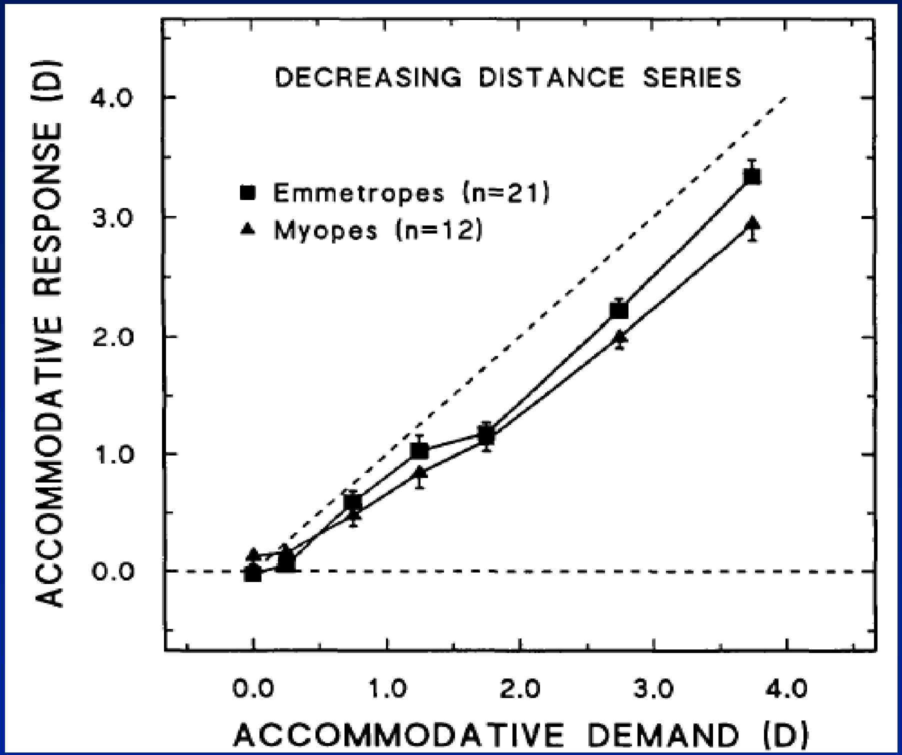
Myopia Risk Factor: Refractive Error
(CLEERE)

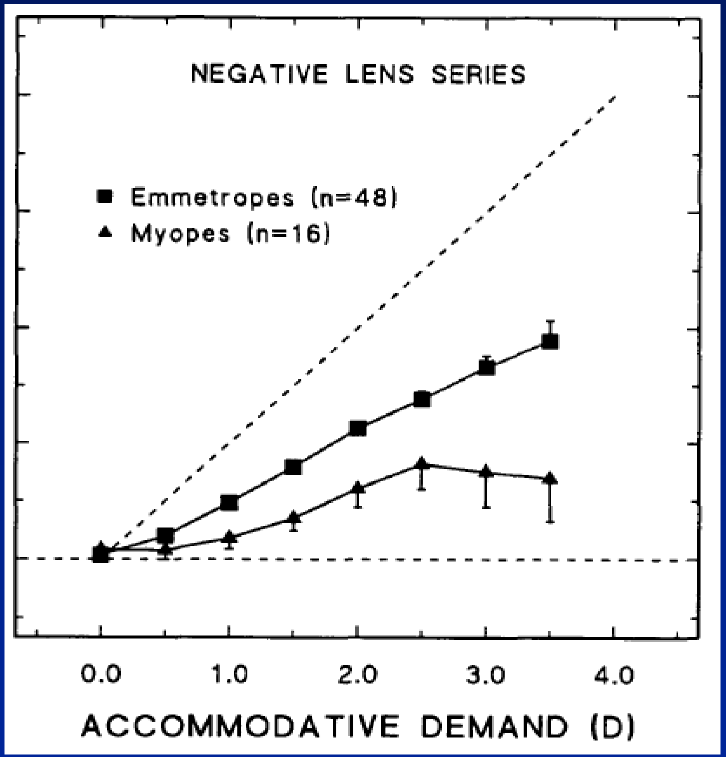


- If you are far-sighted by age 8 or 9 (and have no parents who are near-sighted), you tend to avoid near-sightedness

Myopia Risk Factor: Near Work?

Myopic children have insufficient accommodative response to near blur (high acc. "lag")





Gwiazda J, Thorn F, Bauer J, Held R. Myopic children show insufficient accommodative response to blur. Invest Ophthalmol Vis Sci. 1993 Mar;34(3):690-4.

Inconsistent evidence that accommodative lag is related to myopia onset or progression

- References
  - Gwiazda, Thorn, Held OVS 2005
    - high accommodative lag precedes and continues after myopia onset
  - Mutti, Mitchell, et al. IOVS 2006
    - high acc lag seen only after the onset of myopia
  - Weizhong L, Zhikuan Y, et al, Ophthalmic Physiol Opt. 2008
    - no diff in progression for high vs low acc lag
  - Berntsen, Sinnot et al. CLEERE Vis Res 2011
    - acc lag not associated with progression

Myopia Risk Factor: Near work?

- No measure of near work is consistently found to be linked with myopia onset or progression
  - Time spent reading
  - Books read per week / longer durations;
  - Selective schools;
  - Reduced working distance...
- Is it the Eye's response to near?
  - Relative Peripheral Hyperopia (later);
  - accommodative hysteresis/lag
  - increased contrast adaptation in myopes
- Is it Reduced outdoor activity?

Myopia Risk Factor: Peripheral Hyperopic Defocus

Ocular Components before and after myopia onset
Mutti et al, IOVS 2007 48(6):2510-19

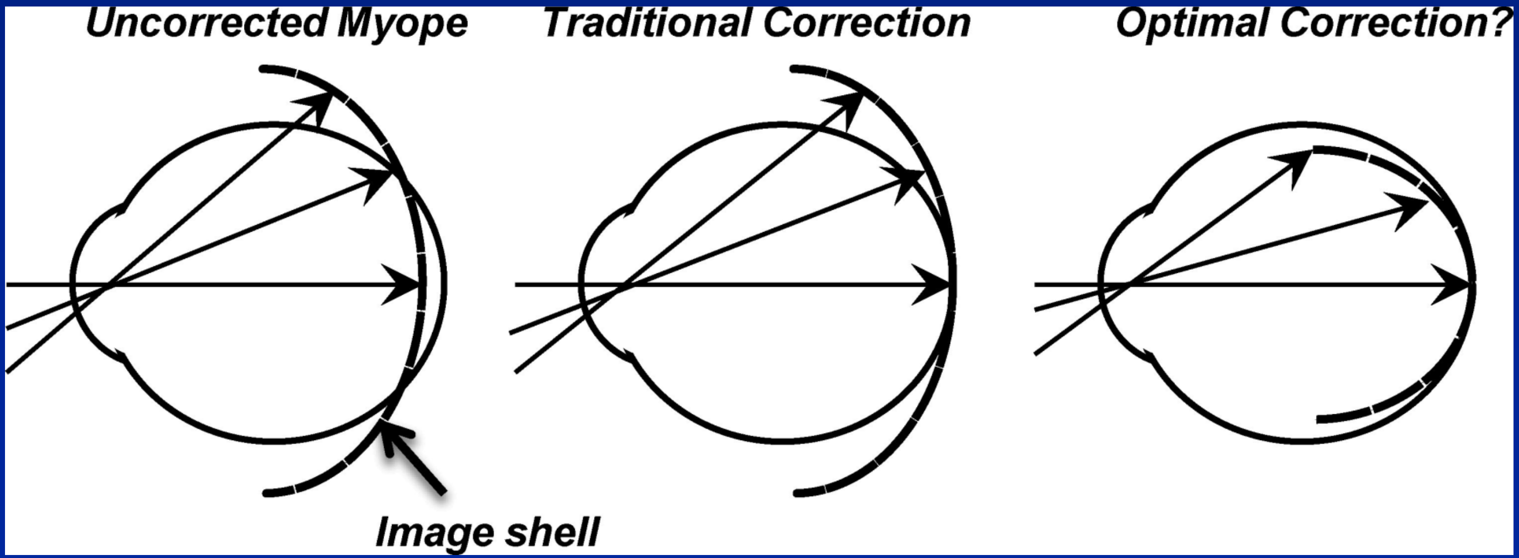
- Compared to matched emmetropes, prior to onset of myopia, myopic children have:
  - Increased rate of “myopisation”
  - Increased rate of axial elongation
  - Relative hyperopic peripheral refraction

Myopia Risk Factor: Peripheral Hyperopic Defocus

- Is Foveal Blur Important?
  - Yes, blur on the retina (macula) causes growth of the eye
  - Yes, but…in monkeys, Smith et al. showed that a minus lens causes myopia even if the fovea is destroyed (laser photocoagulation)
    - Growth from blur not just isolated to fovea
- Blur in the periphery can stimulate the emmetropization mechanism
  - Hyperopic blur in periphery may be a factor in myopic progression
  - Has led to new treatments now in clinical trials

How Peripheral Blur Can Stimulate Elongation

- Prolate shape of myopic eye results in “relative peripheral hyperopic (RPH) blur affecting large areas of the retina
- RPH may be worsened by single vision corrections



Myopia Risk Factor: Environment

- "Environment" might include visual factors that alter retinal activity
  - Near work and lag of accommodation
  - Outdoor activity
    - pupil size, depth of focus, distance view
- "Environment" might include non-visual things that alter biochemical activity in retina or sclera

Myopia Risk Factor: Outdoor Play (vs. Race)

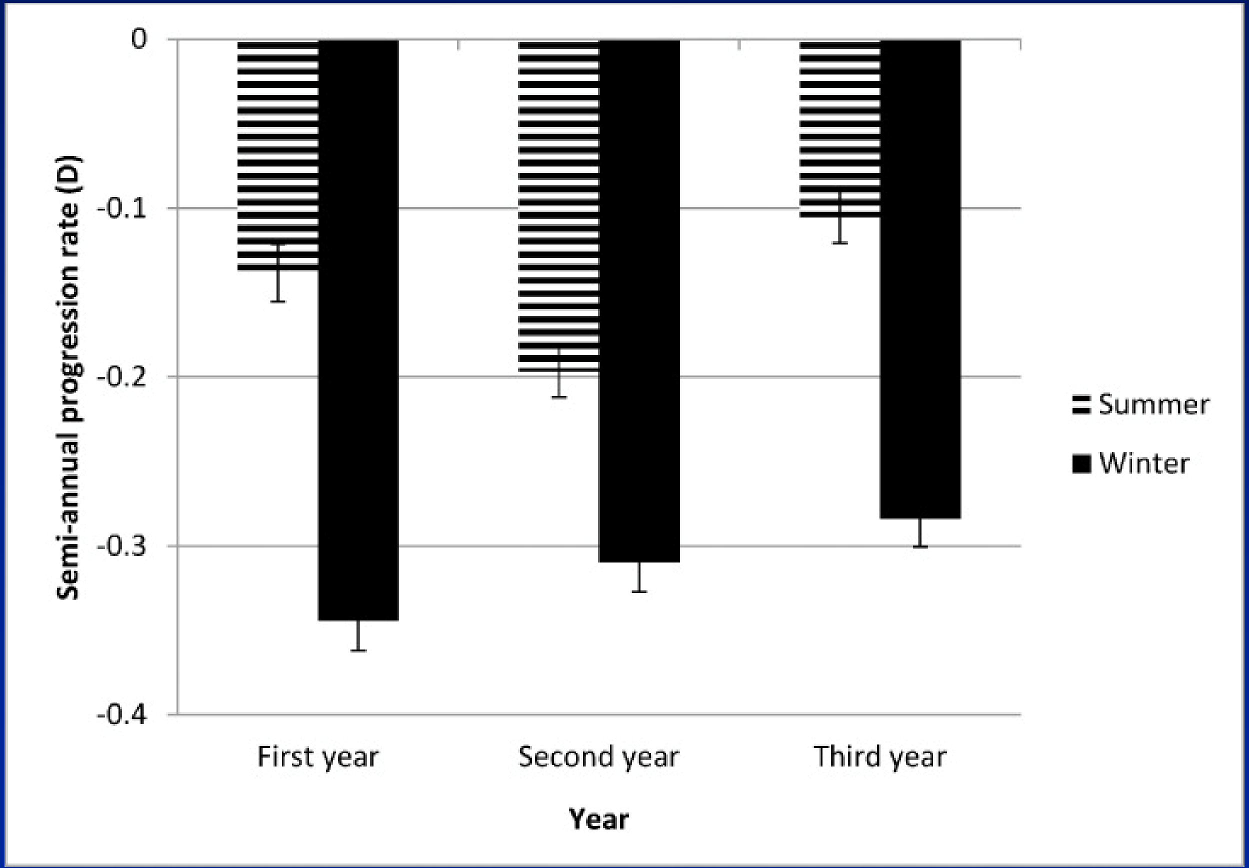
Chinese, aged 6-7 yrs, in Sydney vs. Singapore

	% Myopic	Hrs. Outdoors
Sydney	3.3%	13.75
Singapore	29.1%	3.1

.. Lifestyle in Singapore, with a high population density, most living in high rise apartments, with early educational pressures and reduced outdoor activity.. These may contribute to very high prevalence of myopia ..

* Rose KA, Morgan IG, et al, Myopia, lifestyle and schooling in students of Chinese ethnicity in Singapore and Sydney. Arch Ophthalmol 2008; 126:527

Is Outdoor play protective? COMET (Gwiazda 2014 IOVS)



Modifiable risk factor?
Outdoor activity - small consistent protective effect on myopia (?)

- Orinda Longitudinal Study of Myopia, 2007
- Sydney Myopia Study, 2008
- SCORM: Singapore Cohort study Of Risk factors for Myopia, 2009
- CLEERE, Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error Study, 2011
- Beijing Eye Study Lin Z et al, 2014

Is Outdoor play protective?
2017 Review

- Increased time outdoors is effective in
  - preventing the onset of myopia as well as in
  - slowing the myopic shift in refractive error

- But paradoxically, outdoor time was not effective in slowing progression in eyes that were already myopic.

- Further studies evaluating effect of outdoor in various doses and objective measurements of time outdoors may help improve our understanding of the role played by outdoors in onset and management of myopia.

- Xiong S, Sankaridurg P, Naduvilath T, et al. Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. *Acta Ophthalmol*. 2017;95(6):551–566. doi:10.1111/aos.13403

What’s special about “outdoors”?

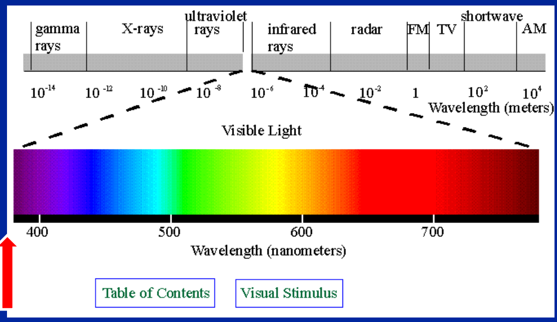
- Vitamin D? (affects collagen synthesis)
    - No relationship to myopia development (Guggenheim et al, 2014 ALSPAC)
    - Lower serum levels related to myopia after adjustment for confounding factors (Yazar et al, 2014 RAINE (Western Australia)

- Light Levels? (Read SA at al, 2014)
  - Children aged 10-14 yrs wearing ACTIWatch 2
    - Myopic children measured lower light levels
    - Similar activity in myopic vs non-myopic children

- Less progression during summer months
    - Fulk 2002, COMET 2014

- Physical activity: a systematic review
  - More physical activity: less myopia was observed.
  - However! No evidence of physical activity as an independent risk factor for myopia
  - May be time spent outdoors.
  - Suhr Thvkiaer A, Dec 2016

- Violet Light?
  - VL suppressed the axial length (AL) elongation in the chick myopia model
  - Torri H. et al. Feb. 2017



What's special about "outdoors"?

- Variety of horizons?
- Depth of focus?
  - As the pupil size becomes very small, about the size of a pinhole, the depth of focus should be very large
    - Schwartz T, 1959, JAMA OMD

Red Light? Blue Light?

- Blue light increase→
- melatonin suppression→
- reduced melatonin→
- reduced circadian rhythm→
- increase myopia??

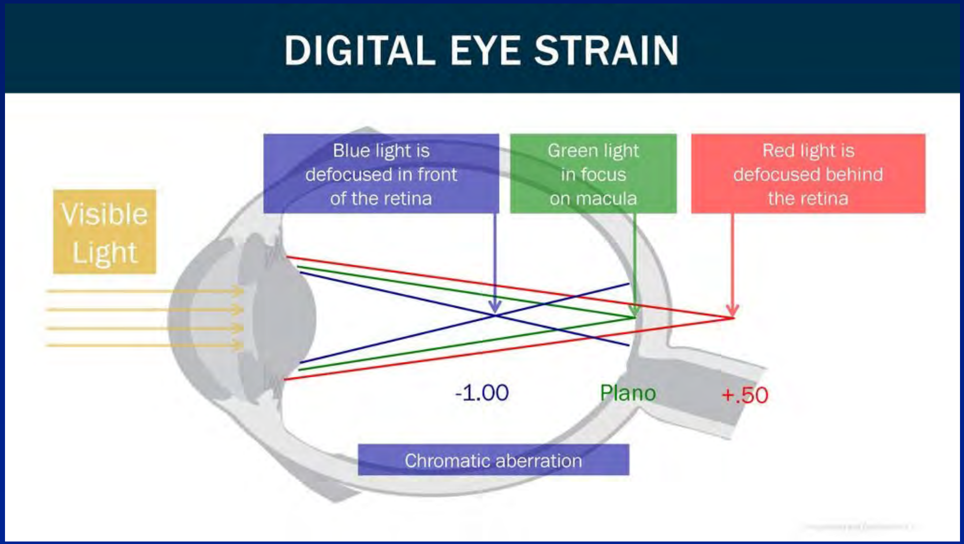
- Drop in the bucket?
- To be determined…

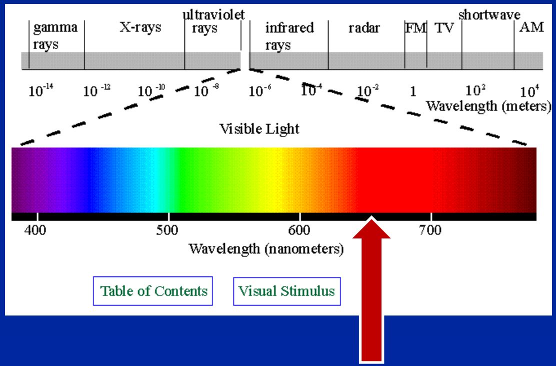
Red Light? Blue Light?

Red Light: good?

- Long wavelength light (N650 nm, red) has been shown to act as a strong inhibitor of eye growth
  - In rhesus monkeys
    - (Smith et al., 2015)
  - In tree shrews
    - (Gawne T. et al 2016).
  - Schaeffel F., Smith E. 2017 commentary

(Blue Light: bad??!)

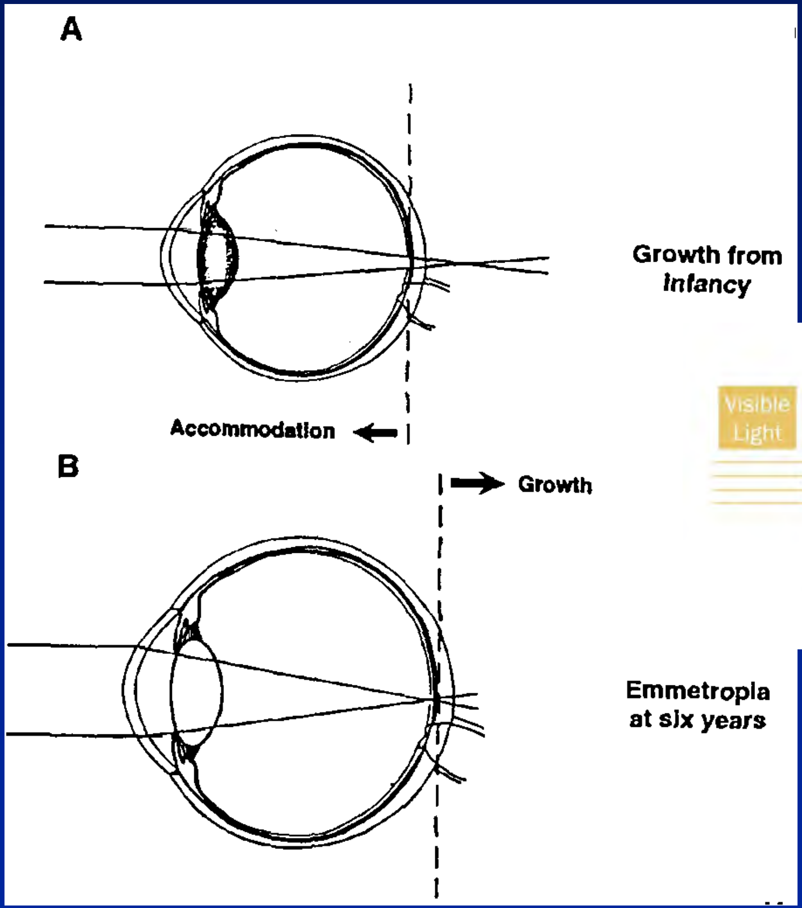


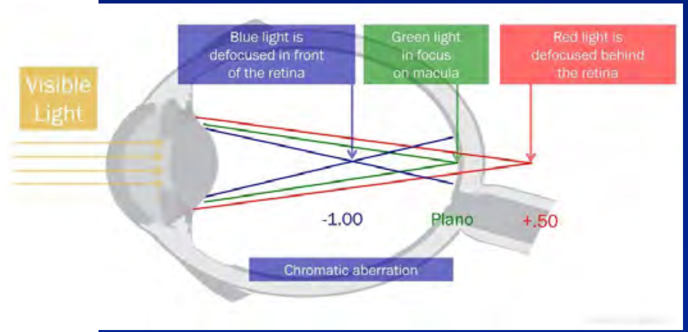


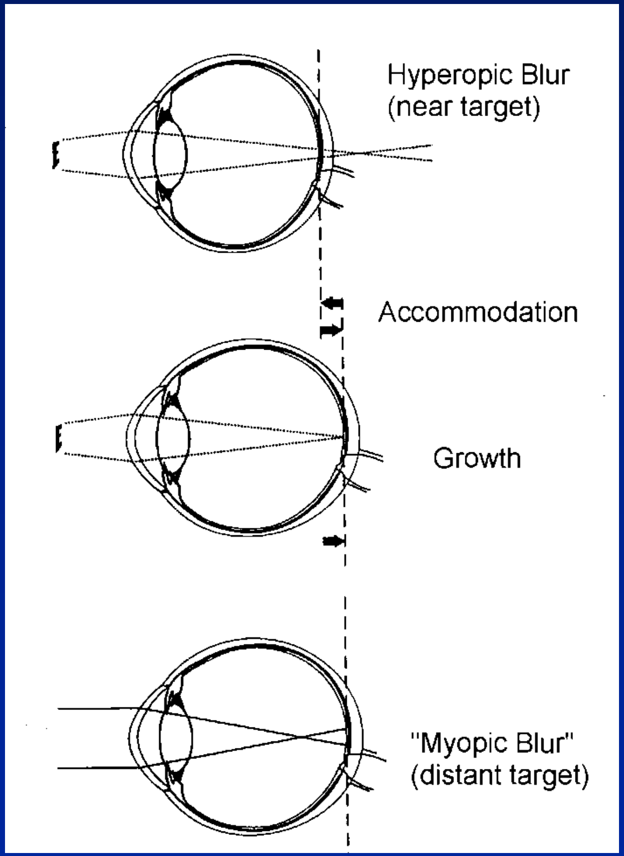
Theory of Myopia Development

Emmetropization

"Myopization"





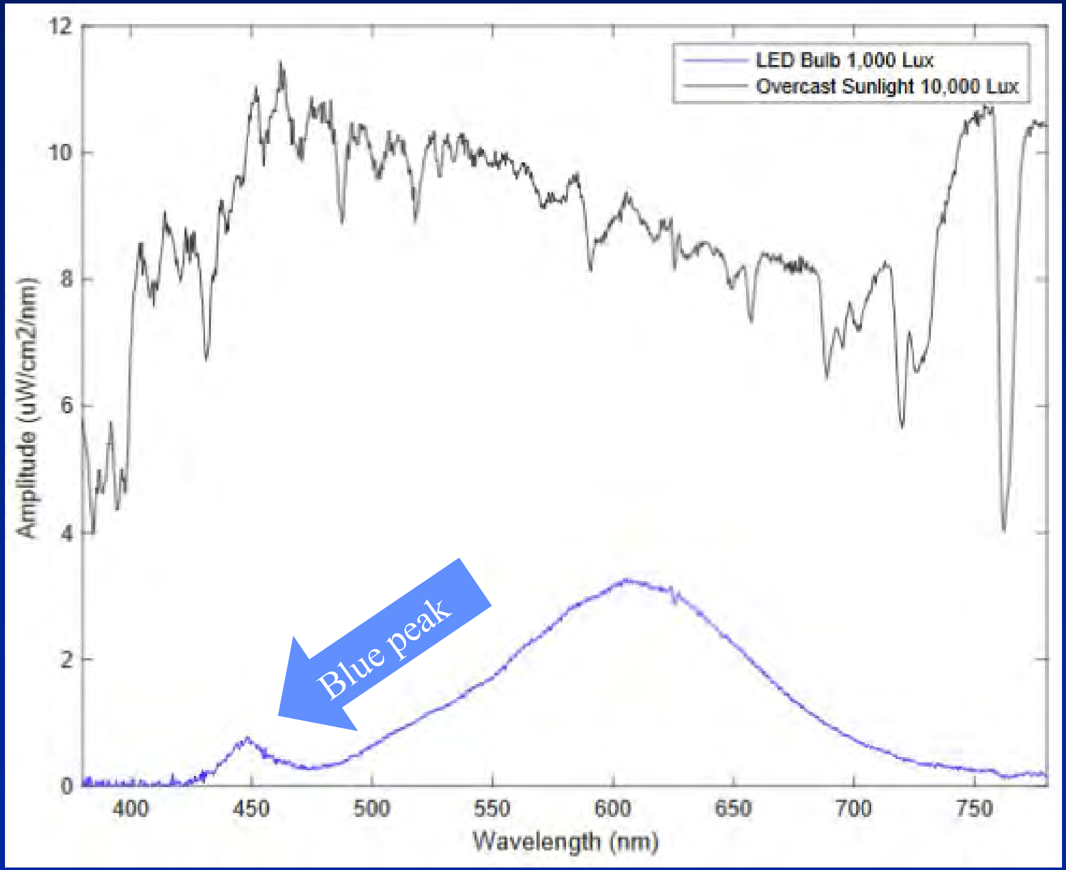


Modifiable Risk Factor?
Screen Time?

- "A pooled OR of 1.02 (95% CI: 0.96–1.08; *p* = 0.48) suggests that screen time is not associated with prevalent and incident myopia in this group of five studies."
- The results for screen time and myopia are mixed. Further studies with objective screen time measurements are necessary to assess evidence of an association between screen time and myopia.
- Lanca C, Saw SM. The association between digital screen time and myopia: A systematic review [published online ahead of print, 2020 Jan 13]. *Ophthalmic Physiol Opt*. 2020;10.1111/opo.12657. doi:10.1111/opo.12657

Tim Gawne, PhD (UAB) 2020: Spectrophotometer on an *overcast* day vs. indoor LED light

- "White" LED has a blue peak at 450 nm (true)
- Size of the blue peak is very small compared to an overcast day



Dr. Gawne's White LED :)

Dr. Gawne's/Oechslin's Handheld device :)

Level 2, 3?

- "Progression of Myopia in School-Aged Children After COVID-19 Home Confinement" by Wang, Li, Musch, et al., JAMA Ophthalmol. Jan 2021.

Level 2, 3?

- Mccrann S, Loughman J, Butler JS, Paudel N, Flitcroft DI. Smartphone use as a possible risk factor for myopia. Clin Exp Optom. 2021 Jan;104(1):35-41.
- Smartphone Use Associated with Refractive Errors in Teenagers: The Myopia App Study," by Enthoven et al., Ophthalmology, 2021.

Interventions

- Optical interventions
  - 1. Atropine
  - 2. MFCL
  - 3. Ortho-K
  - 4. Glasses (SightGlass (DOT), DIMS)
  - 5. Chromatic?
- Environment
  - Working distance?
  - Outdoor play?
    - Vitamin D? Depth of focus? Diversity your working distance?

1. Atropine


Sterile 5 ml Bottle
Atropine Sulfate Solution
0.01%
Ophthalmic Solution
Compounded for a licensed professional
or patient use by
Imprimis Rx
Imprimis RX NJ
1705 Route 46 West, Suite 4
Ledgewood, NJ 07852 (973)328-8756

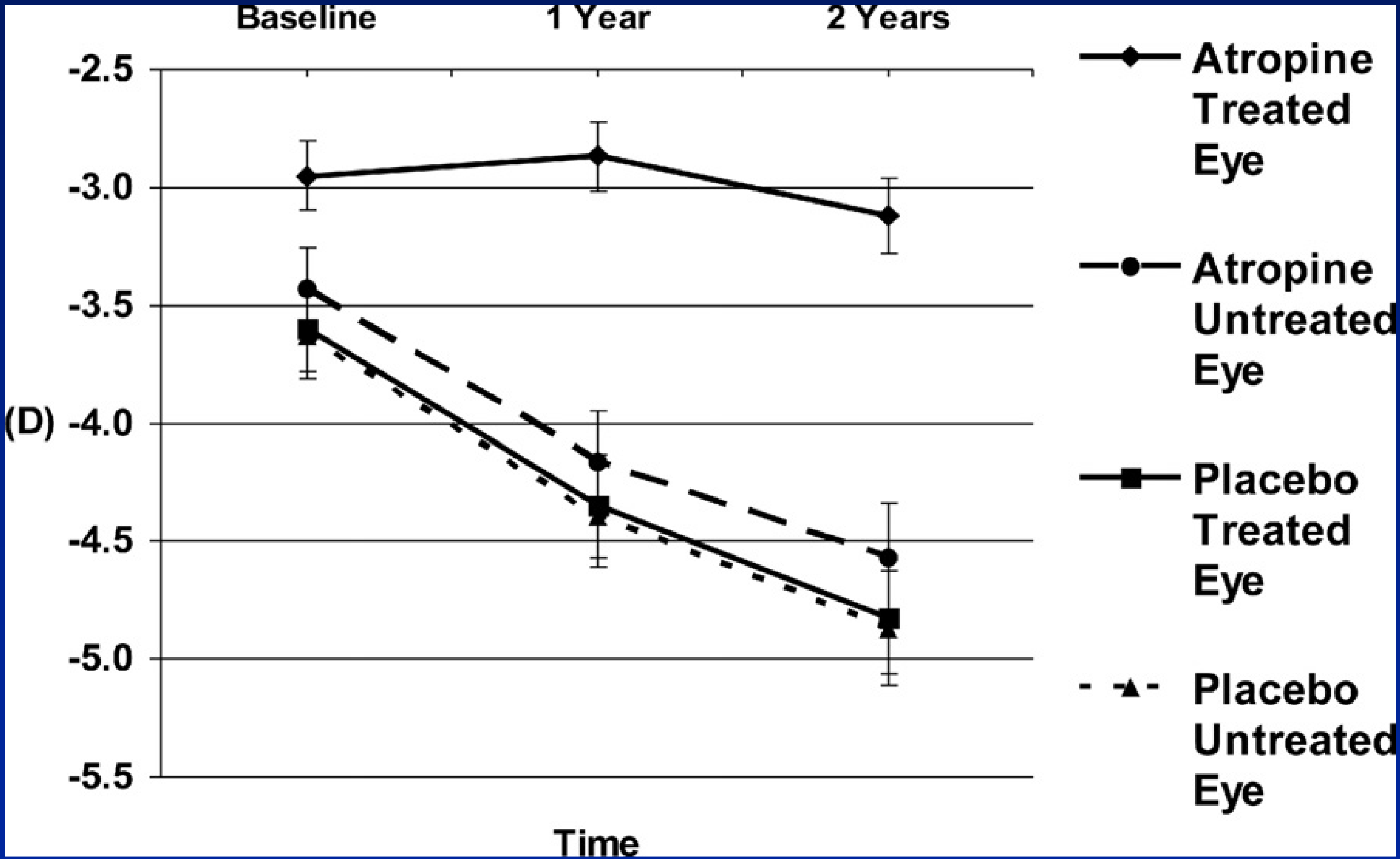

Contains 0.01% atropine
OR placebo ophthalmic solution
Only for use in:
MTS1 Myopia Treatment Study
(IND#137441)
In case of emergency,
call 813-294-1343
to unmask to treatment
CAUTION:
New Drug-Limited by Federal
(or United States) law
to investigational use
[redacted]
Labeled and distributed by:
Tampa Family Pharmacy
2919 W. Swann Ave, Suite 101
Tampa FL 33609
Package Number: M1746
Verification Code: 4252
Participant Name
Store at room temperature (68F to 77F)


Singapore National
Eye Centre
Myopine™
Atropine Sulphate
0.01% w/v Eye Drops
5ml
STERILE


AiM 麥迪森
Atropine
eye drops
0.01%
*不含防腐劑
不交互感染 不含防腐劑 安全衛生 攜帶方便
0.5mL x 30支


Myopil
Myopil
10ml
Atropine Sulphate
USP 0.01% W/v
Eye drops

Atropine 1.0%
Chua W, 2005



Atropine 1.0, 0.5, 0.1, 0.01%?
Chia A, 2016 (ATOM2)

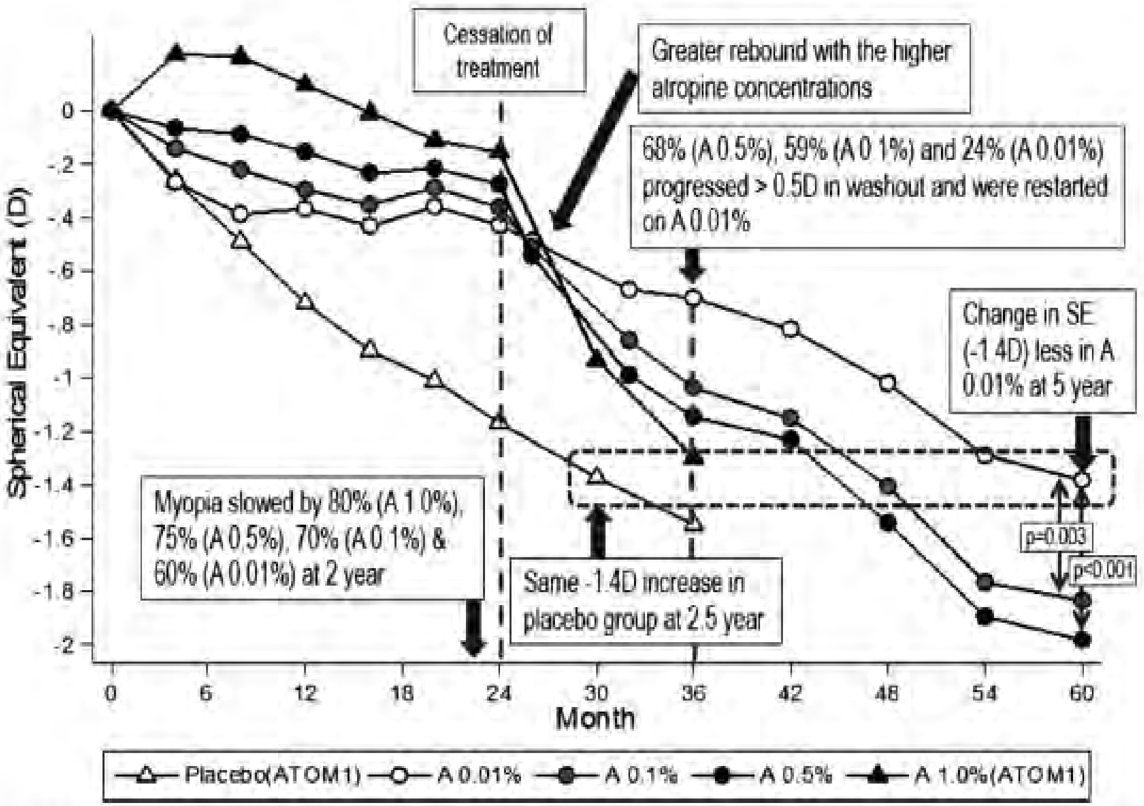


Figure 6. Summary of findings from the ATOM1 and ATOM2 studies: change in spherical equivalent (SE). ATOM = Atropine for the Treatment of Myopia; D = diopter.

Atropine 1.0, 0.5, 0.1, or 0.01%?

ATOM2 (Chia A, 2012)

Characteristics at Baseline and Second Baseline (i.e., 2 Weeks after Starting Trial Medication)

Variable	0.01%	0.1%	0.5%	P-value
Accommodation (D) (baseline)	16.2 (3.4)	16.7 (3.0)	15.8 (3.4)	0.01
Accommodation (D)(on tx)	11.3 (4.3)	3.8 (2.5)	2.2 (1.2)	<0.001
Near VA (LogMAR) (baseline)	0.04 (0.09)	0.04 (0,08)	0.04 (0.07)	0.38
Near VA (LogMAR) (on tx)	0.06 (0.08) **20/20-**	0.29 (0.18) **20/40+**	0.48 (0.16) **20/63+**	<0.001

The higher the concentration, the more side effects.

ATOM2

Chia et al · Atropine Treatment of Childhood Myopia

Table 2. Ophthalmology Parameters at Second Annual Visit

	Atropine (A) Dose, Mean (SD)			
	A 0.01%	A 0.1%	A 0.5%	**P Value**
Accommodation (D)				
-at 1 yr	11.7 (4.3)	6.0 (3.4)	3.6 (3.2)	<0.001*,†,‡
-at 2 yrs	11.8 (3.2)	6.8 (3.4)	4.0 (2.6)	<0.001*,†,‡
-mean change over 1 yr	−4.4 (4.9)	−10.9 (4.0)	−12.4 (3.3)	<0.001*,†,‡
-mean change over 2 yrs	−4.6 (4.2)	−10.1 (4.3)	−11.8 (4.4)	<0.001*,†,‡
Near vision (logMAR)				
-at 1 yr	0.03 (−0.06)	0.15 (0.15)	0.35 (0.18)	<0.001*,†,‡
-at 2 yrs	0.01 (0.07)	0.10 (0.13)	0.29 (0.18)	<0.001*,†,‡
-mean change over 1 yr	−0.01 (0.10)	0.10 (0.16)	0.32 (0.19)	<0.001*,†,‡
-mean change over 2 yrs	−0.02 (0.08)	0.06 (0.13)	0.25 (0.19)	<0.001*,†,‡

Atropine or 0.01, 0.025, 0.05, 01, 1.0%?

- What are factors in choosing myopia concentration?

Atropine 1.0, 0.5, 0.1, or 0.01%?

- Factors
  - Myopia progression
  - Axial elongation
  - Side Effects
    - Near blur
    - Pupil Dilation
  - Rebound Effect
  - Cost?
    - $40-$60 per month

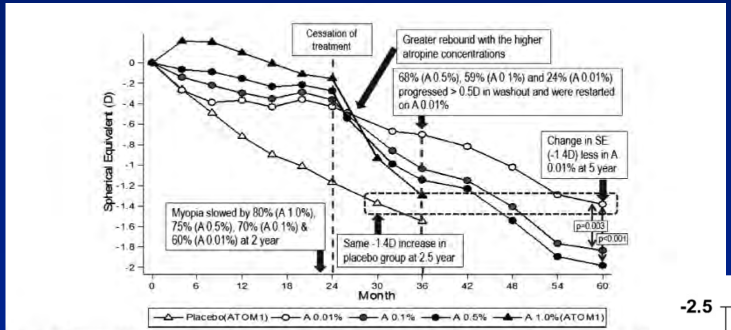
PEDIG: Atropine 0.01%

Meta-analysis?

- Gong Q. May 11, 2017
  - 19 studies
  - 3,137 unique children
  - meta-analysis suggests that the efficacy of atropine is dose independent within this range, whereas the adverse effects are dose dependent.

How does Atropine work?

- Dose-dependent! XOXOX :)



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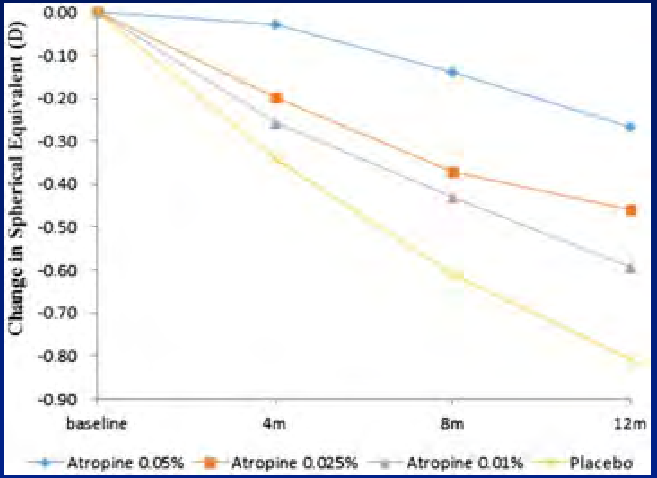
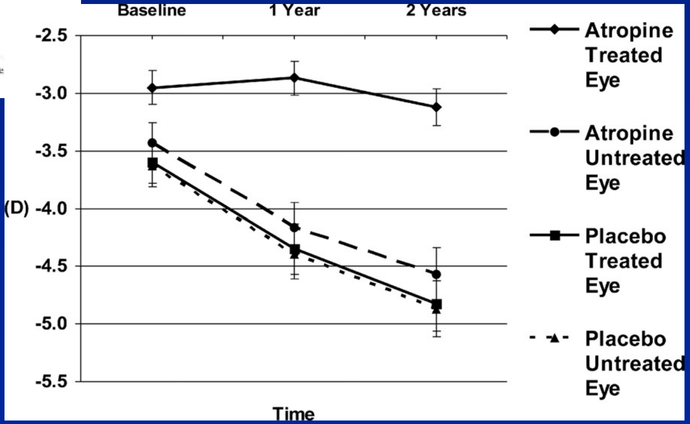




Mechanism of Action 1: Chemical (?)

- Atropine – works throughout the retina level?
  - Small molecule that gets beyond ciliary body to retina
    - Muscarinic receptors are found in CB and retina; and possibly sclera
    - Eye drop soaks through cornea and possibly conjunctiva and gets into retina via the vitreous
  - Broad spectrum but low dose
    - all 5 muscarinic receptors are blocked by atropine
      - Atropine is a muscarinic receptor antagonist
      - Not sure if mechanism is at M2 receptor or a different one, so broad spectrum is good
    - (vs. pirenzepine which was specific to one, M2)
- Atropine “fools the retina into thinking everything is in focus” (Norton)
    - Sends the “stop” signal to the sclera (?)

Mechanism of action 2: Choroid level

- Intravitreal injection of atropine in chicks
  - Results in choroidal thickening and subsequent slowed elongation of axial length
    - Nickla DL 2013

Atropine Studies

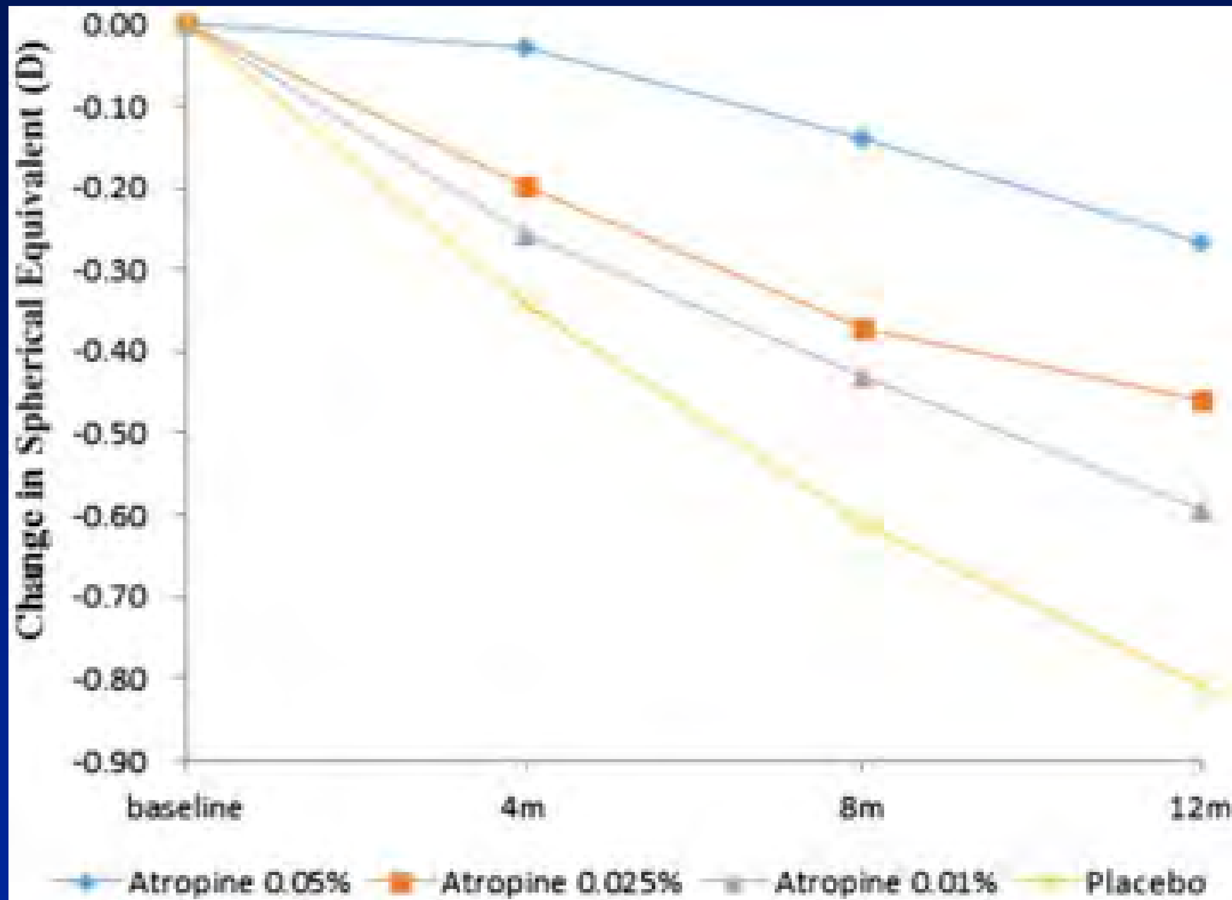
- CHAMP study
  - Vyluma/industry funded
  - Recruitment ended summer 2019
  - Also in Europe
- LAMP study
- MTS1
  - NIH funded (PEDIG), recruitment ended March 2020

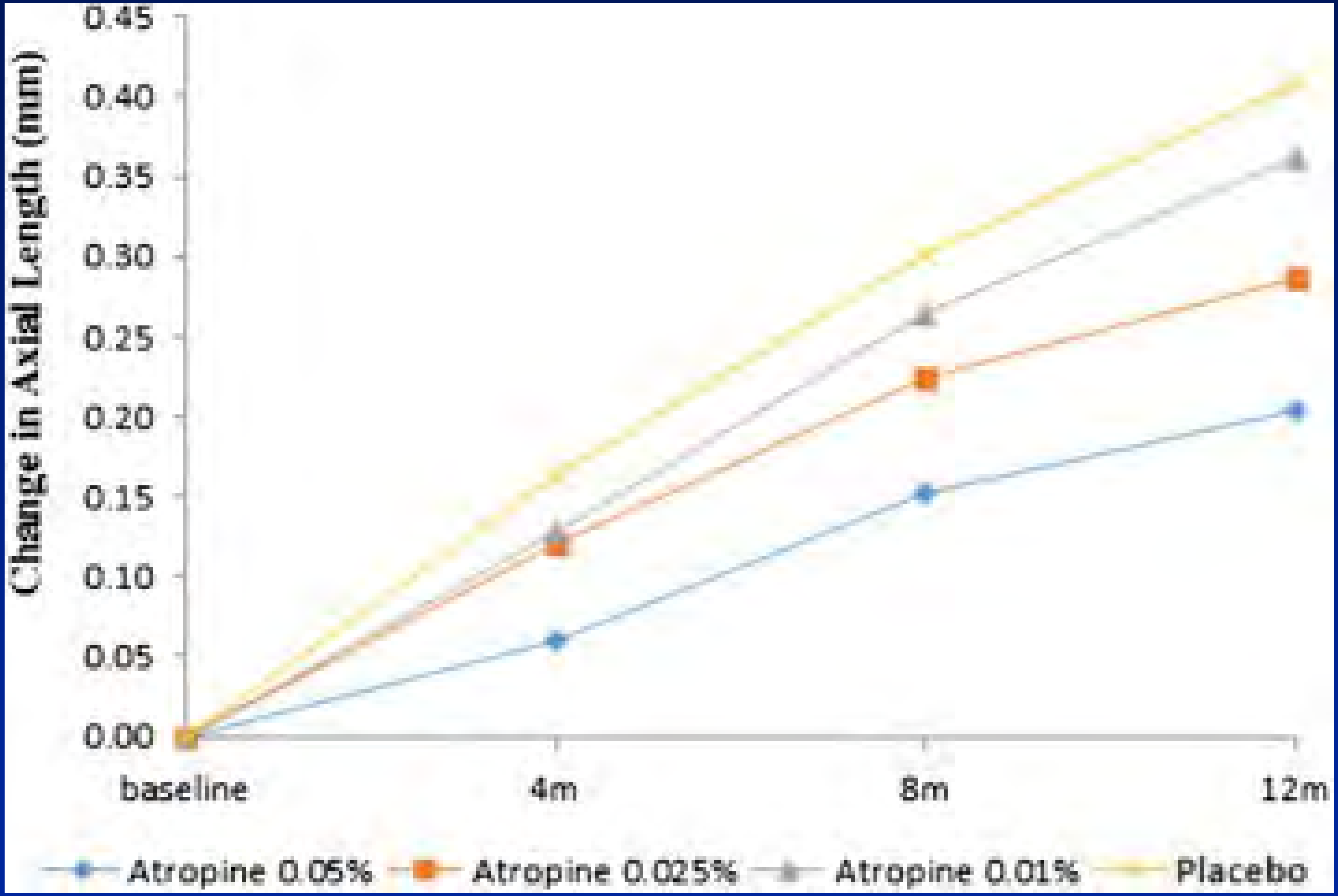
LAMP study

- 5-years
- Single center (Hong Kong)
- 4 to 12 yo with documented myopia progression
- 0.05, 0.025, 0.01% vs. placebo
- Year 1: 0.05 best reduction in progression

- Yam JC, Jiang Y, Tang SM, et al. Low-Concentration Atropine for Myopia Progression (LAMP) Study: A Randomized, Double-Blinded, Placebo-Controlled Trial of 0.05%, 0.025%, and 0.01% Atropine Eye Drops in Myopia Control. *Ophthalmology*.

  2019;126(1):113–124.


Change in Spherical Equivalent (D)
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
-0.70
-0.80
-0.90
baseline
4m
8m
12m
Atropine 0.05%
Atropine 0.025%
Atropine 0.01%
Placebo



Change in Axial Length (mm)
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
baseline
4m
8m
12m
Atropine 0.05%
Atropine 0.025%
Atropine 0.01%
Placebo

LAMP study

- 0.05% may be better overall at slowing progression than 0.01 at 1-year results
- However, look for
  - Side effects
  - Rebound effect
- See also axial length change

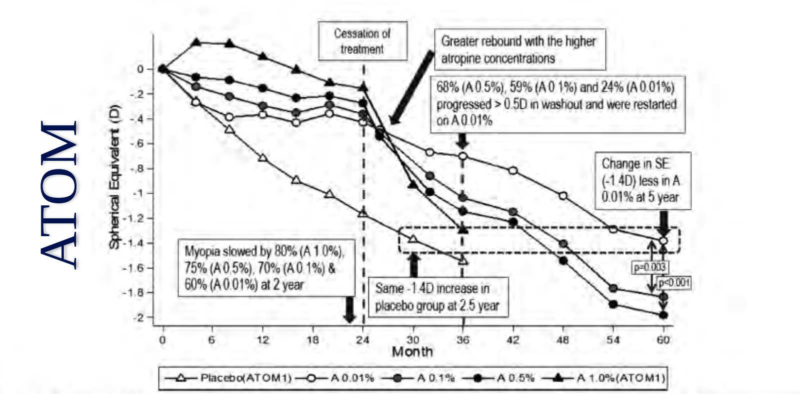


Figure 6. Summary of findings from the ATOM1 and ATOM2 studies: change in spherical equivalent (SE). ATOM = Atropine for the Treatment of Myopia; D = diopter.

- Li FF, Yam JC. Low-Concentration Atropine Eye Drops for Myopia Progression. *Asia Pac J Ophthalmol (Phila)*. 2019;8(5):360–36

FYEye:
LAMP 2019

- "In Phase 2 (1-year period), the placebo group will be crossed over to the optimal group (best treatment to side effect ratio as determined in Phase 1) at the beginning of the second year, because it is unethical to let the children continue placebo treatment once low-concentration atropine is proven effective after 1 year."

LAMP 3-year

Ophthalmology *Volume 129, Number 3, March 2022*

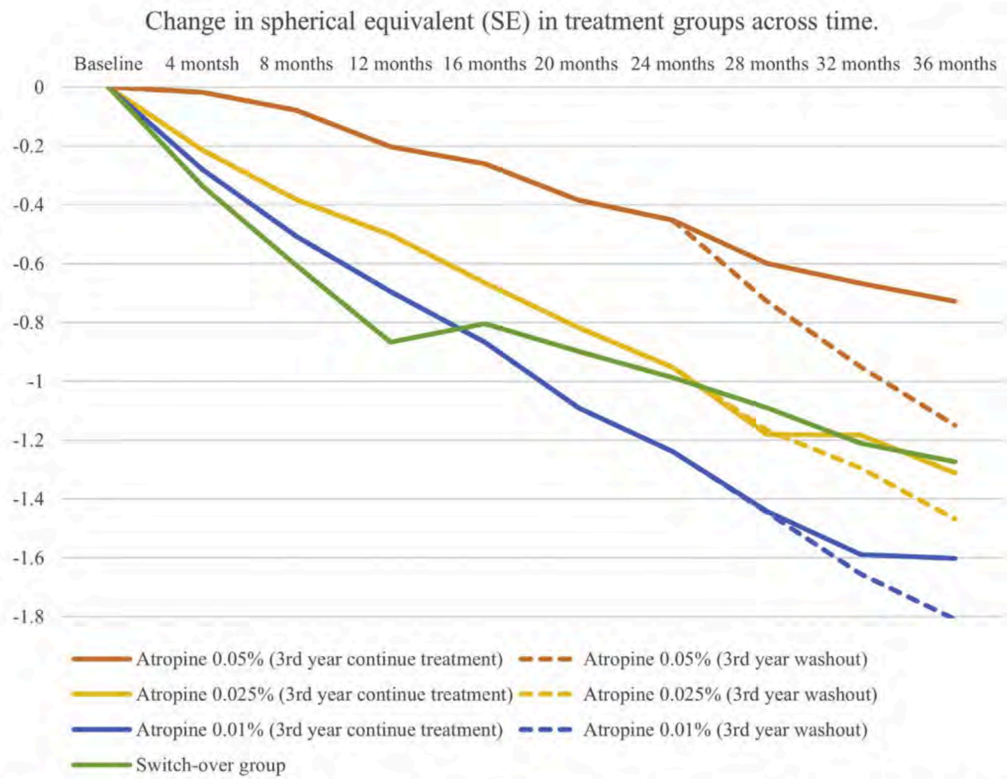


Figure 2. Changes in spherical equivalent (SE) progression for treatment groups over time. The switchover group received placebo during the first year and was then switched over to 0.05% atropine at the beginning of the second year and continued 0.05% treatment at the third year. D = diopters; M = months.

LAMP 3-year

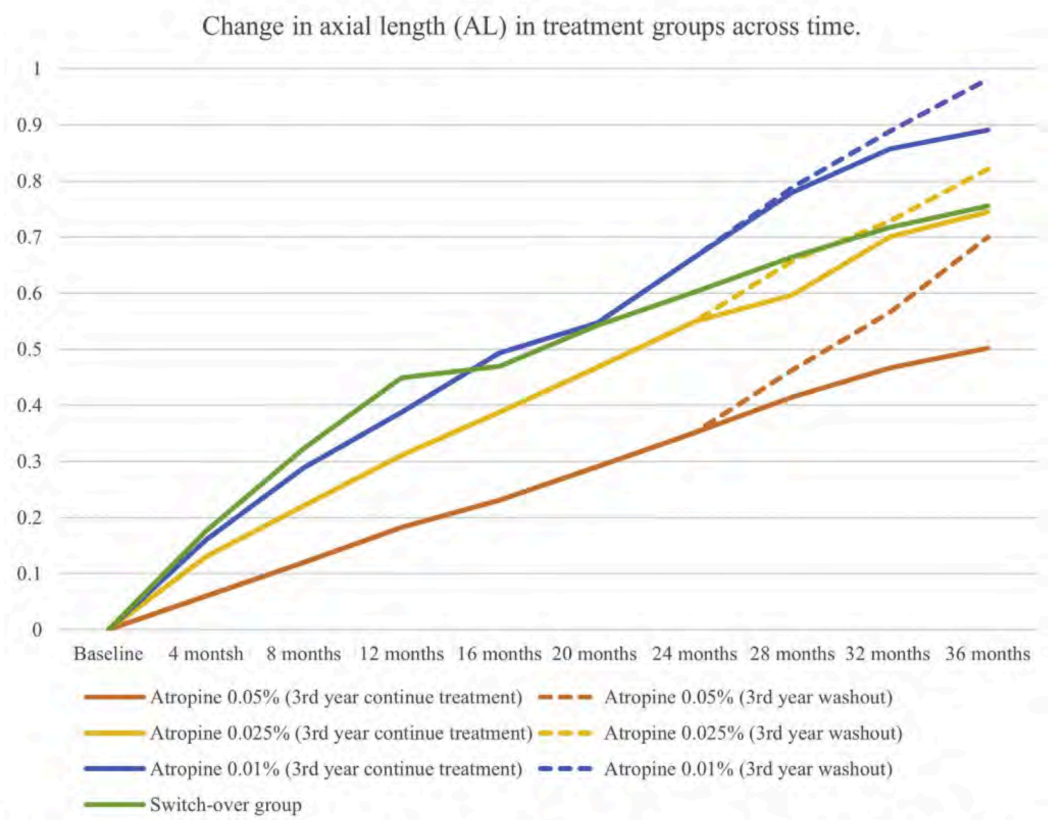


Figure 3. Changes in axial length elongation for treatment groups over time. The switchover group received placebo during the first year and was then switched over to 0.05% atropine at the beginning of the second year and continued 0.05% treatment at the third year. D = diopters; M = months.

What about US Kids?

- CHAMPS (Industry)
- MTS1 (PEDIG/NIH)

Myopia Treatment Study 1 (MTS1): Atropine 0.01% for Treatment of Myopia

Protocol Co-chairs

Kathy Weise & Michael Repka

Lead Statistician

Rui Wu

Jaeb Lead Investigator

Danielle Chandler

Protocol Monitor

Courtney Conner

Pediatric Eye Disease Investigator Group

NIH National Eye Institute

Study Synopsis

1. Run-in Phase
   - Subjects treated with daily artificial tears for 2-4 weeks (>90% required).
   - Glasses updated if needed (paid for by study)

2. Randomization
   - 186 subjects
   - Assigned 2:1 to daily atropine or placebo

Major Eligibility Criteria for Run-In Phase

- Ages 5 to <13 years
- Refractive error meeting the following by cycloplegic *autorefraction*:
  - Myopia -1.00D to -6.00D SE in both eyes
  - Astigmatism <=1.50D in both eyes
  - Anisometropia <1.00D SE
- No prior myopia control treatment

Randomization

- Randomized (2:1) to 1 drop of daily single-use eyedrops (*Vyluma, Inc. Bridgewater, NJ*) for 24 months of:
  - 0.01% atropine (Atropine Group)
  - Placebo vehicle (Placebo Group)

Key Outcomes

- On-treatment primary outcome
  - Change in spherical equivalent refractive error (SER) from baseline to 24-month outcome as measured by a masked examiner using cycloplegic autorefraction
    - Outcome – Baseline
    - Mean of OD and OS
- Off-treatment secondary outcome
  - Change in SER from baseline to 30-month outcome in SER as measured by a masked examiner using cycloplegic autorefraction

Axial Length & Additional Biometry

- Axial length (Lenstar or IOLMaster)
- Flat corneal radius
- Anterior chamber depth
- Lens thickness

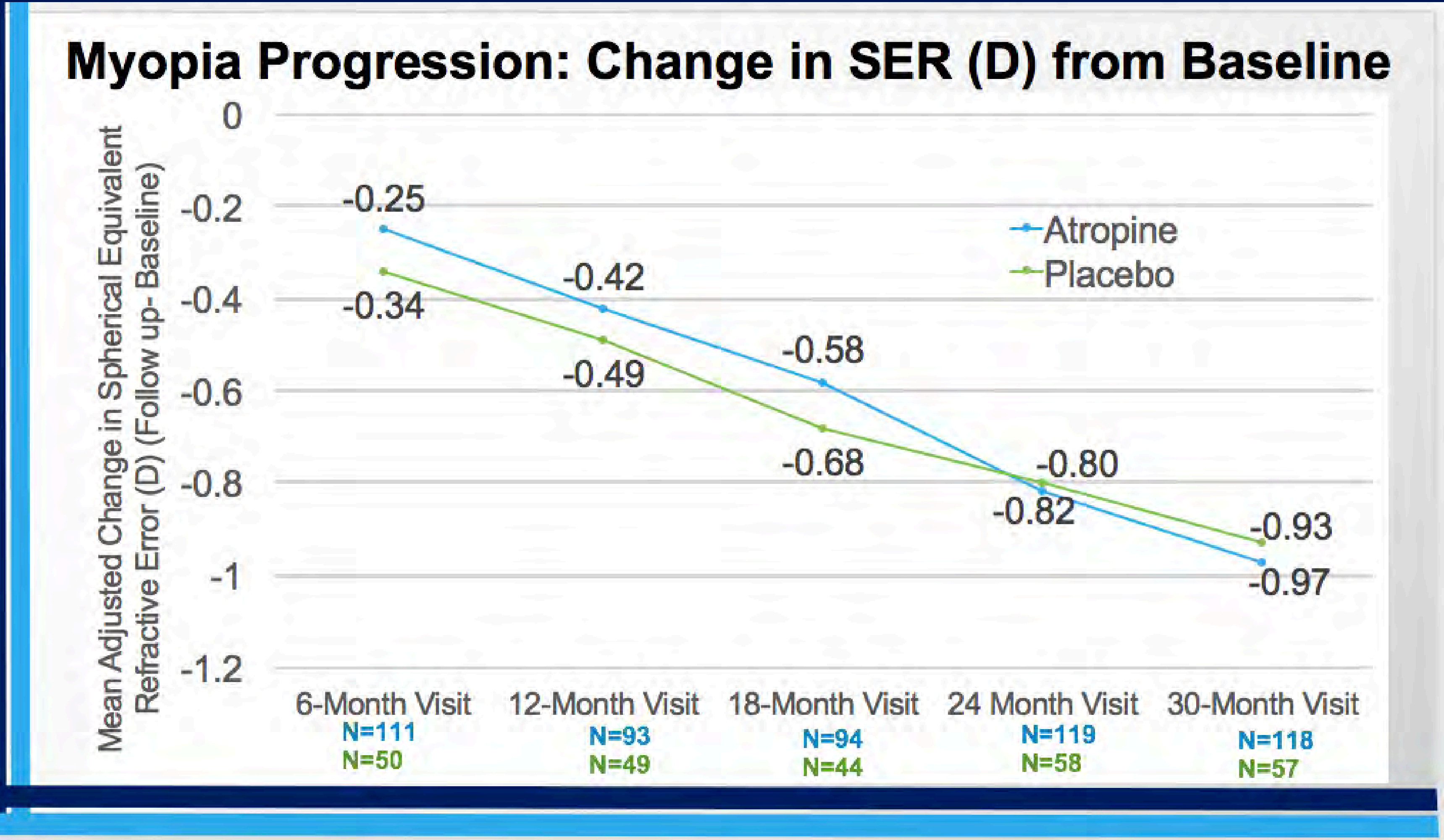
Each value based on the individual instrument’s method of taking and then averaging multiple measures.

MTS1 Retention: 94%

~3-year Myopia Studies	Length of Study	Population	Intervention	Age (Years)	Myopia	n	Retention at Stated Length
BLINK Walline JJ, 2020	3 years	US	BF CL	7-11	-0.75 to -5.00	292/294	**99%**
COMET Gwiazda J, 2003	3 years (14 total)	US	Glasses (SV vs. PAL)	6-11	-1.25 to -4.50	462/469	**99%**
MTS1 2023	2.5 years	US	Atropine 0.01%	5-12	-1.00 to -6.00	175/187	**94%**
LAMP	2 years	Hong Kong	Atropine 0.01%, 0.025%, 0.05%	4-12	>-1.00D	350/383	**91%**
CYPRESS 2022	1 year interim (3 total)	US	SightGlass	6-10	-0.75 to -4.50	234/256	**91%**
ATOM2 Chia, 2016	2 years	Singapore	Atropine 0.01%, 0.1%, 0.5%	6-12	>-2.00 D	355/400	**89%**
MiSight Chamberlin 2019	3 years	Multi	MiSight MFCL	8-12	-0.75 to -4.00	109/144	**76%**

Treatment Adherence

- "Excellent" (76% to 100% of the time) use of Study Medication
  - Atropine Group: > 93% across all visits
  - Placebo Group: > 96% across all visits
- Discontinued Treatment Permanently
  - Atropine Group: 3 (2.4%) patients
  - Placebo Group: 1 (1.6%) patient
- Additional Myopia Control Treatment
  - Atropine: 2 patients
  - Placebo: 0 patients
- Discontinued Treatment Temporarily
  - Atropine: 1 patients
  - Placebo: 5 patients

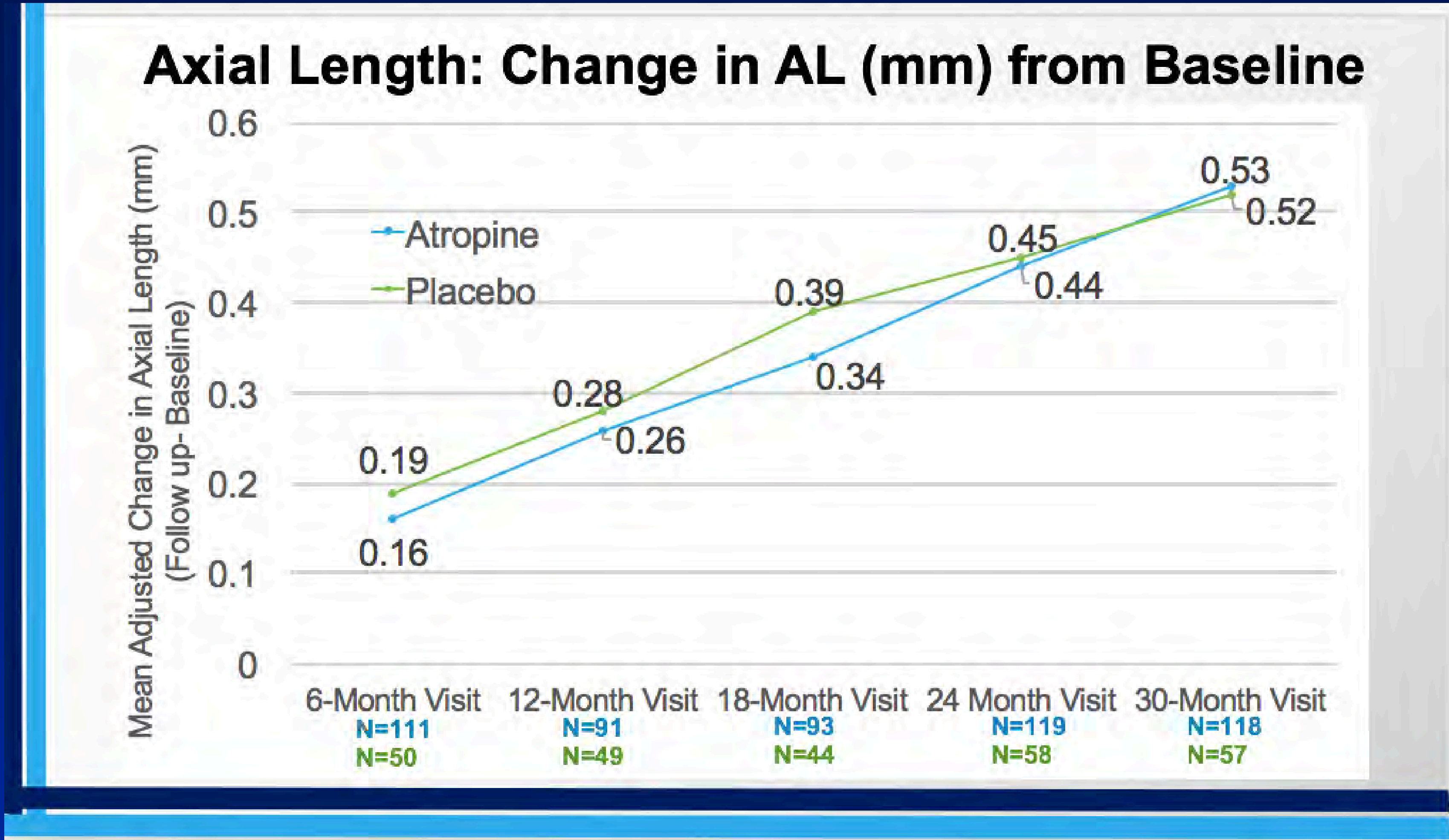


Myopia Progression: Change in SER (D) from Baseline
Mean Adjusted Change in Spherical Equivalent Refractive Error (D) (Follow up- Baseline)
0
-0.2
-0.4
-0.6
-0.8
-1
-1.2
-0.25
-0.34
-0.42
-0.49
-0.58
-0.68
-0.80
-0.82
-0.93
-0.97
Atropine
Placebo
6-Month Visit
12-Month Visit
18-Month Visit
24 Month Visit
30-Month Visit
N=111
N=50
N=93
N=49
N=94
N=44
N=119
N=58
N=118
N=57

Myopia Progression

	24-Month Visit (On Treatment)		30-Month Visit (Off Treatment)	
	Atropine (N=119)	Placebo (N=58)	Atropine (N=118)	Placebo (N=57)
Change of Mean OD and OS SER (D) from Baseline (Outcome – Baseline) [mean (SD)]	-0.78 (0.64)	-0.74 (0.60)	-0.94 (0.77)	-0.88 (0.71)
Treatment Group Difference of Mean Change in SER (D) from Baseline (Atropine – Placebo) (95% CI)[1]	-0.02 (-0.19 to 0.15)		-0.04 (-0.25 to 0.17)	

[1]Adjusted for baseline SER, age, iris color (brown vs. non-brown), and race (East Asian vs. non-East Asian), to account for potential residual confounding.


Axial Length: Change in AL (mm) from Baseline
Mean Adjusted Change in Axial Length (mm)
(Follow up- Baseline)
0.6
0.5
0.4
0.3
0.2
0.1
0
Atropine
Placebo
0.19
0.16
0.28
0.26
0.39
0.34
0.45
0.44
0.53
0.52
6-Month Visit
N=111
N=50
12-Month Visit
N=91
N=49
18-Month Visit
N=93
N=44
24 Month Visit
N=119
N=58
30-Month Visit
N=118
N=57

Axial Length Change

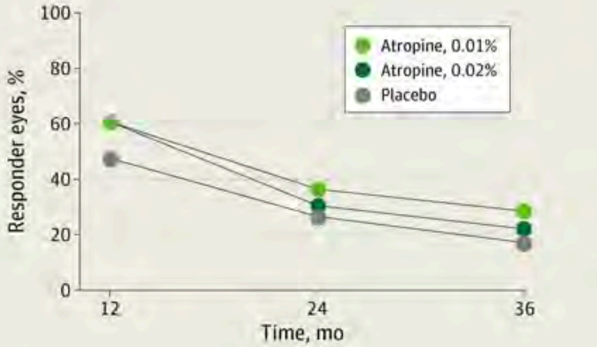
	24-Month Visit		30-Month Visit	
	Atropine (N=119)	Placebo (N=58)	Atropine (N=118)	Placebo (N=57)
Change of Mean OD and OS Axial Length (mm) from Baseline (Outcome – Baseline) [mean (SD)]	0.42 (0.29)	0.41 (0.27)	0.51 (0.35)	0.49 (0.32)
Adjusted Treatment Group Difference of Mean Change in Axial Length (mm) from Baseline (Atropine – Placebo) (Confidence Interval)[1]	-0.002 (-0.106 to 0.102)		0.009 (-0.115 to 0.134)	

[1] The adjusted treatment group difference of mean change in axial length from baseline adjusted for baseline axial length, age, iris color (brown vs. non-brown), and race (East Asian vs. non-East Asian), to account for potential residual confounding. Confidence intervals were adjusted to control the overall false discovery rate for the multiple secondary outcomes at 5%.

CHAMPS

FINDINGS

Compared to placebo, 0.01% atropine significantly increased the proportion of eyes with <0.5 D myopia progression at 36 mo; similar benefit for 0.02% atropine sulfate was not significant



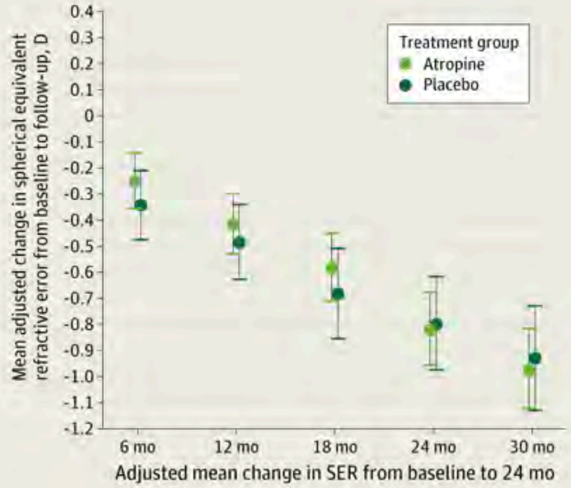
Odds ratios (ORs) for primary outcome at 36 mo:

0.01% Atropine vs placebo: OR, 4.54 (95% CI, 1.15-17.97); *P* =.03
0.02% Atropine vs placebo: OR, 1.77 (95% CI, 0.50-6.26); *P* =.37

MTS1

FINDINGS

There was no significant difference in adjusted mean change in spherical equivalent refractive error from baseline to 24 mo between the atropine and placebo groups



Adjusted mean change in SER
Atropine group: −0.82 D; placebo group: −0.80 D
Adjusted difference, −0.02 D (95% CI, −0.19 to 0.15; *P* = .83)

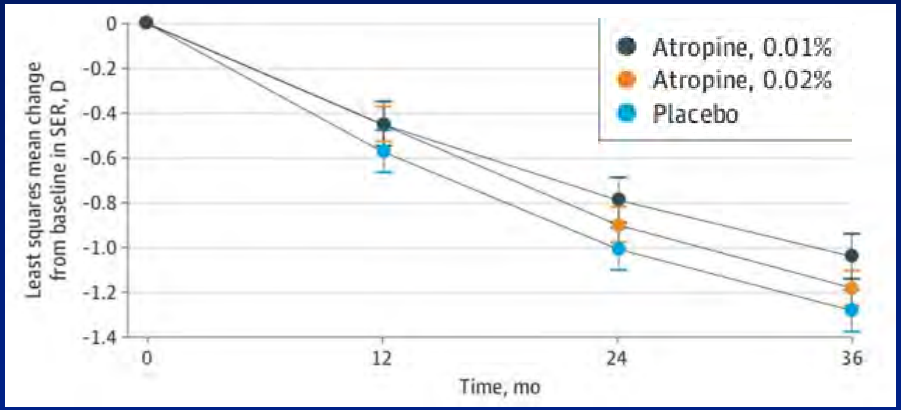
Characteristics of Rigorous Studies

Study Characteristic	CHAMPS, 2023 Placebo/0.01/0.02		MTS1, 2023 Placebo/0.01	
Randomized	2:2:3	●	1:2	●
Placebo Controlled	0.285	●	0.33	●
Clinical Trial		●		●
Drug Manufactured	Vyluma	●	Vyluma	●
Objective Outcome Measure	Cyclo AR	●	Cyclo AR	●
Double Masked (triple?)		●		●
Authorship	Zadnik et al	●	Repka et al	●
Long-term + Longitudinal	3+	●	2+	●
SAP		●		●
Statistically determined high N	489 (144/133/212)	●	187 (62/125)	●
Powered appropriately	95/90	●	97	●

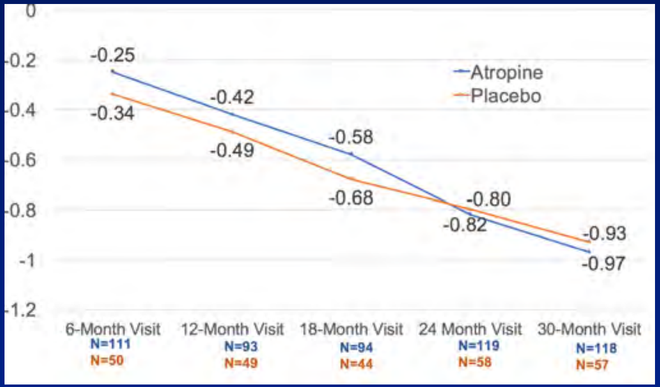
Characteristics of Rigorous Studies

Study Characteristic	CHAMPS, 2023 Placebo/0.01/0.02	MTS1, 2023 Placebo/0.01
Diversity	26 sites, 6 countries	12 sites, US
High Retention	87/75/84	94/95
High Adherence	pupillometer	96/93 calendars/ampules
Low additional treatment	6/5/4	0/2
Statistically Significantly Different <0.50D SER change: 0.01	OR 4.54 P = 0.03*	
Statistically Significantly Different SER: 0.01	1.24 D *P* = /112*	-0.02 D
Statistically Significantly Different AL: 0.01	−0.13 mm *P* < .001*	-0.002 D
Statistically Significantly Different <0.50D SER change: 0.02	OR, 1.77 *P* > /48	
Statistically Significantly Different SER: 0.02	1.10 D *P* > /21	
Statistically Significantly Different AL: 0.02	−0.08 mm *P* = .005*	
Clinically Relevant	?	?

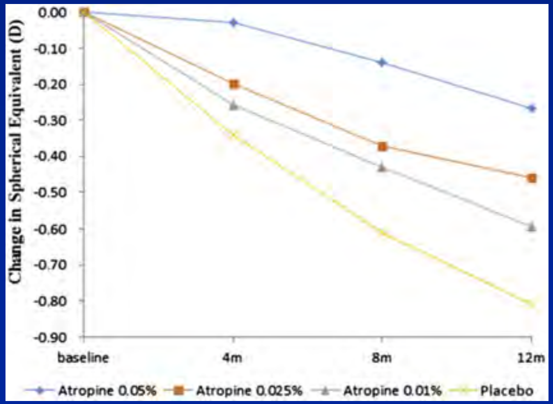
US+ vs. US vs. Asia



CHAMPS



MTS1

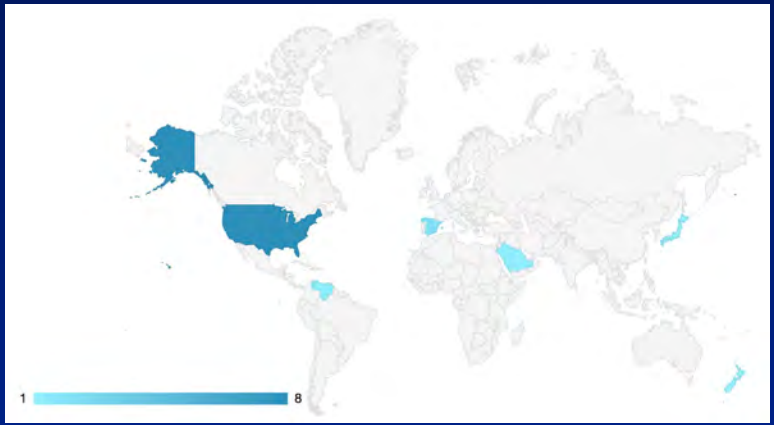


LAMP

MTS1 Dissemination

? About this Attention Score

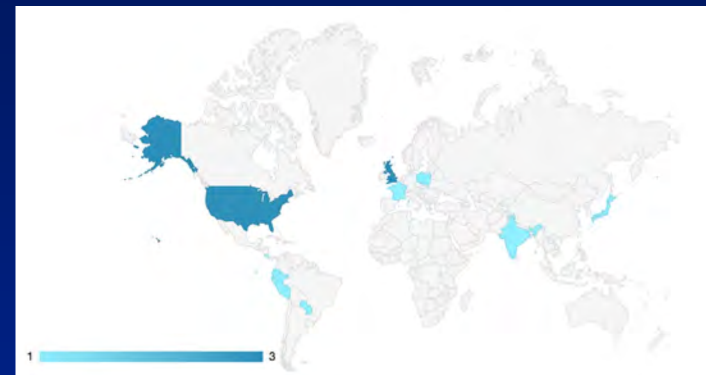
In the top 5% of all research outputs scored by Altmetric



ALL RESEARCH OUTPUTS	OUTPUTS FROM JAMA OPHTHALMOLOGY	OUTPUTS OF SIMILAR AGE	OUTPUTS OF SIMILAR AGE FROM JAMA OPHTHALMOLOGY
#119,858	#77	#1,412	#6
of 24,135,931 outputs	of 3,678 outputs	of 214,990 outputs	of 58 outputs

Altmetric has tracked 24,135,931 research outputs across all sources so far. Compared to these this one has done particularly well and is in the 99th percentile: it's **in the top 5% of all research outputs ever tracked** by Altmetric.

CHAMPS Dissemination



ALL RESEARCH OUTPUTS	OUTPUTS FROM JAMA OPHTHALMOLOGY	OUTPUTS OF SIMILAR AGE	OUTPUTS OF SIMILAR AGE FROM JAMA OPHTHALMOLOGY
#30,933	#28	#757	#2
of 24,135,931 outputs	of 3,678 outputs	of 352,245 outputs	of 85 outputs

Altmetric has tracked 24,135,931 research outputs across all sources so far. Compared to these this one has done particularly well and is in the 99th percentile: it's **in the top 5% of all research outputs ever tracked** by Altmetric.

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JAMA

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John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; et al

Research
Accelerometer-Derived "Weekend Warrior" Physical Activity and Incident Cardiovascular Disease
Shaan Khurshid, MD, MPH; Mostafa A. Al-Alusi, MD; Timothy W. Churchill, MD; et al
Earn CME credit

Medical News & Perspectives
Study: Overweight BMI Not Associated With Increased All-Cause Mortality
Kate Ruder, MSJ

Opinion
Ushering in a New Era of Alzheimer Disease Therapy
Eric W. Widera, MD; Sharon A. Brangman, MD; Nathaniel A. Chin, MD

Opinion
Physical Activity for Health—Every Minute Counts
Peter T. Katzmarzyk, PhD; John M. Jakicic, PhD

JAMA CARDIOLOGY

Research
Syncope Trigger Type and Risk of Subsequent Life-Threatening Events in Patients With Long QT Syndrome
Arwa Younis, MD; J. Martijn Bos, MD, PhD; Wojciech Zareba, MD, PhD; et al

Research
Tracking Treatment Response in Cardiac Light-Chain

Research
Corticosteroids and Survival Outcomes in Patients With Metastatic Renal Cell Carcinoma
Félix Lefort, MD; Cécile Dalban; Marine Gross-Goupil, PhD; et al

JAMA OPHTHALMOLOGY

Research
Low-Dose 0.01% Atropine Eye Drops vs Placebo for Myopia Control
Michael X. Repka, MD, MBA; Katherine K. Weise, OD, MBA; Danielle L. Chandler, MSPH; et al

Research
Objectively Measured Visual Impairment and Dementia Prevalence in Older Adults in the US
Olivia J. Killeen, MD, MS; Yunshu Zhou, MS; Joshua R. Ehrlich, MD, MPH

Opinion
Atropine, 0.01%, for Myopia Control
Jeffrey J. Walline, OD, PhD; David A. Berntsen, OD, PhD

JAMA OTOLARYNGOLOGY - HEAD & NECK SURGERY

Research

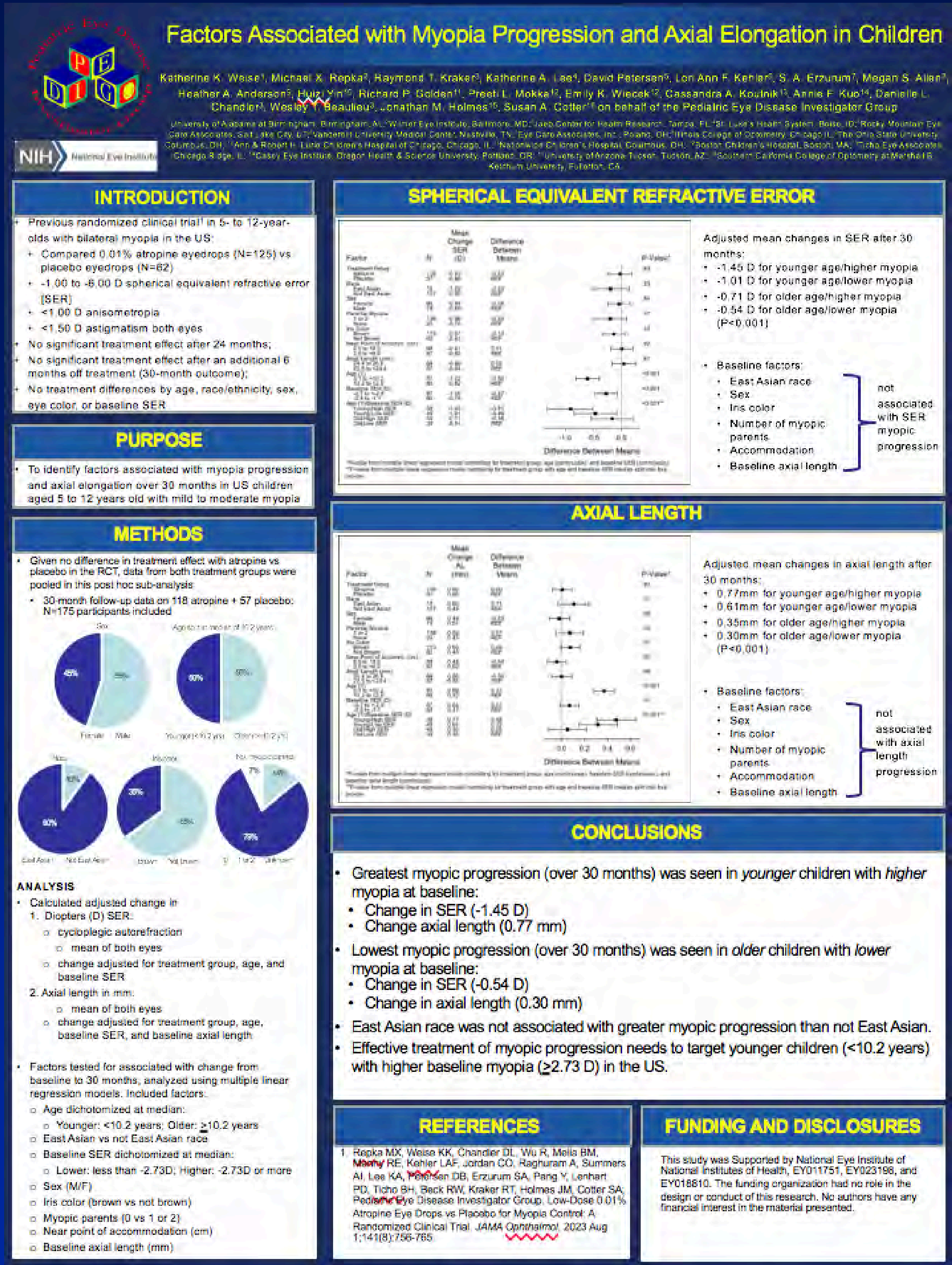
Practical Atropine Nuggets

- Use 0.01? 0.02? 0.05?
- ~$40-60/month
- Must use compounding pharmacy (and even then…Richdale K, 2023)
- Big box pharmacies don’t have it yet

- Questions???
  - What is best dose? (concentration, frequency)
  - When do we stop it?!
  - How do we stop?
  - How young can we go?

The younger/more myopic,
the faster it grows.

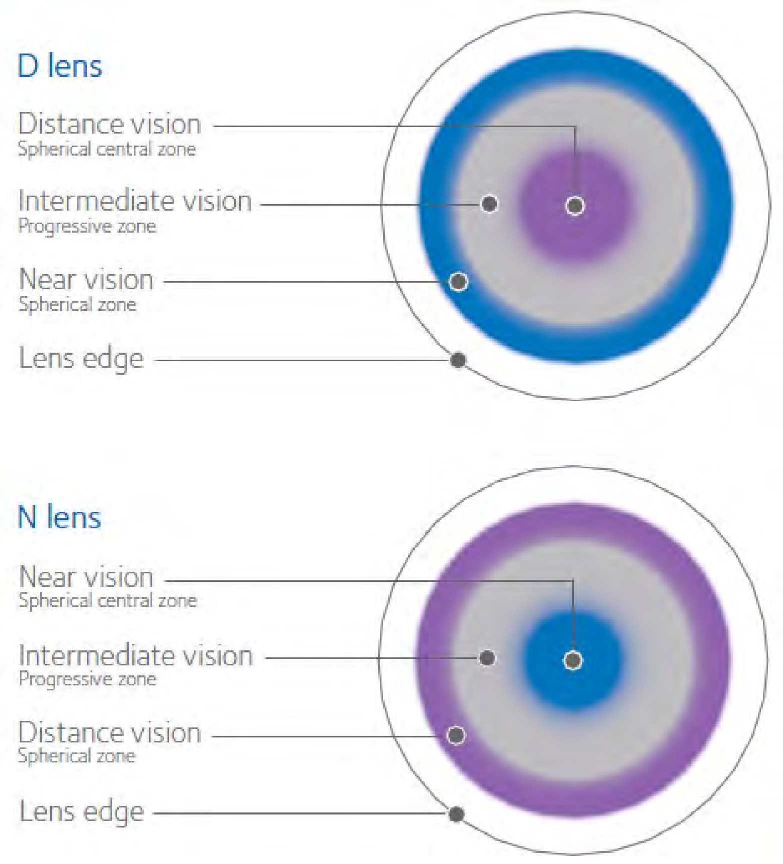
Older/less myopic doesn’t grow too fast.



ATOM kids grown up

- Li Y, Yip M, Ning Y, Chung J, Toh A, Leow C, Liu N, Ting D, Schmetterer L, Saw SM, Jonas JB, Chia A, Ang M. Topical Atropine for Childhood Myopia Control: The Atropine Treatment Long-Term Assessment Study. JAMA Ophthalmol. 2023 Nov 30. doi: 10.1001/jamaophthalmol.2023.5467. Epub ahead of print. PMID: 38019503.
- ATOM1 (2006) and ATOM2 (2012)
  - 1% vs. Placebo
  - 0.01% vs. 0.1% vs. 0.5% (no placebo)
  - E. Asia/Chinese
  - Low-dose atropine had treatment effect while on treatment; had smaller rebound effect in the immediate post-treatment phase
  - 25% of original cohorts studied
  - No treatment benefit in adulthood
  - Increased risk of MMD not seen in atropine 1% , but seen in 0.5% vs. 0.1% (2.60X risk: 38% vs. 17%
- Future Research
  - RCT/Short-term trials
  - Long-term follow-up
  - Precision medicine
    - Younger
    - Higher baseline data
    - Duration of treatment
  - Taper?

2. MFCL


D lens
Distance vision
Spherical central zone
Intermediate vision
Progressive zone
Near vision
Spherical zone
Lens edge
N lens
Near vision
Spherical central zone
Intermediate vision
Progressive zone
Distance vision
Spherical zone
Lens edge

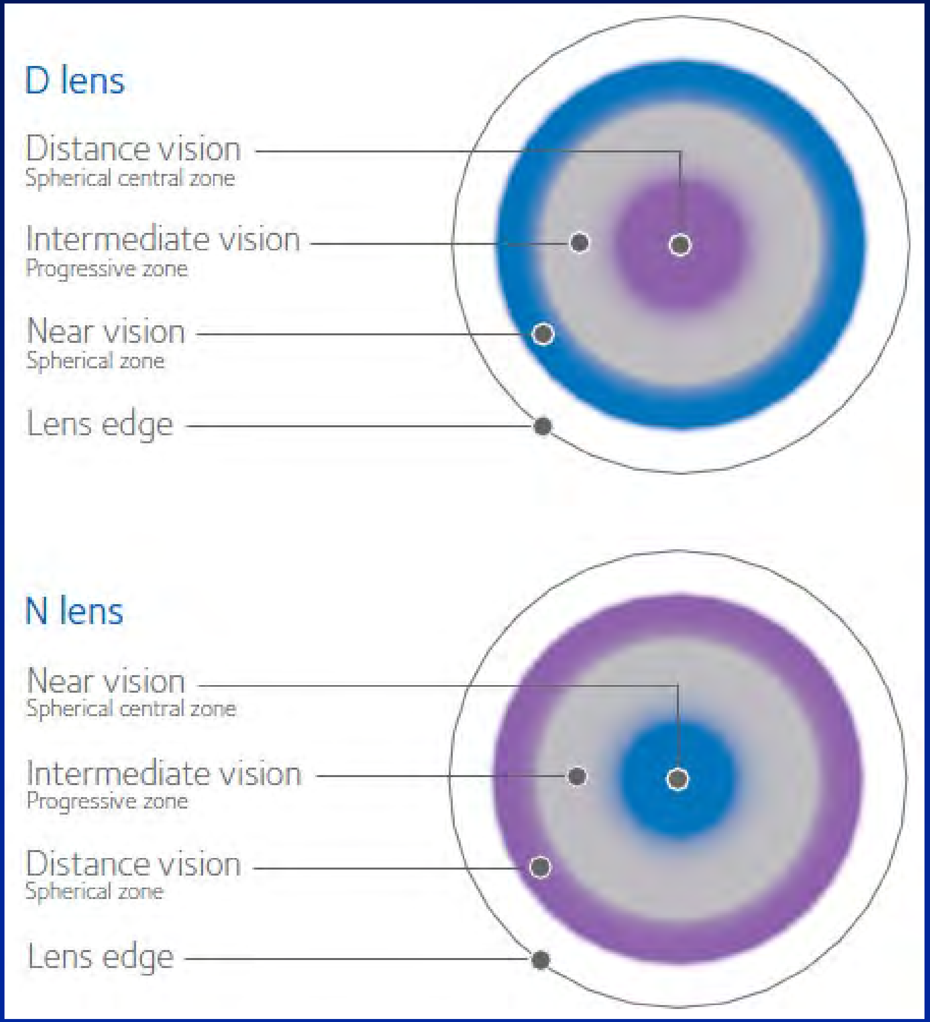
How do we slow myopia 1995: PAL?

- Correction of Myopia Evaluation Trial (Gwiazda J)
  - 469 kids aged 6 to 11 years old
  - -1.25 to -4.50
    - Monitored for 14 years (1997 to 2011) (!)
    - UAB: 118/133
  - PAL's vs. SV
    - PAL's "won" by ~0.20 D and mainly in first year (Gwiazda J 2003)
    - Showed proof of concept for peripheral hyperopic defocus
  - November 20, 1995-November 30, 2015
    - Gwiazda, Marsh-Tootle, Norton

How do we slow myopia 2016-2021: MF CL?

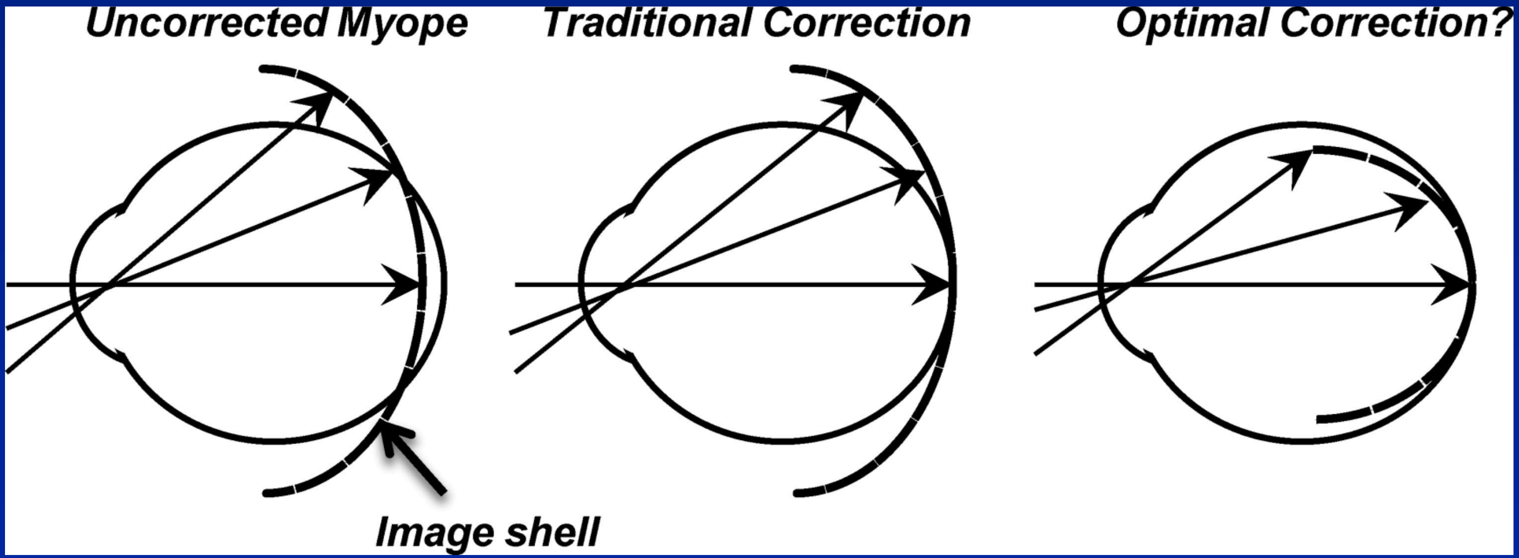
Multi-focal Contact Lens

- BLINK study (Bifocal Contact Lenses in Near-sighted Kids)
  - Walline J (OSU)
  - N = 294
  - 7 to 11 years
  - $7.5 M over 5 years
  - Multifocal contact lenses with distance center, near surround
- Biofinity MF (D center)



How Peripheral Blur Can Stimulate Elongation

- Prolate shape of myopic eye results in “relative peripheral hyperopic (RPH) blur affecting large areas of the retina
- RPH may be worsened by single vision corrections



BLINK

BLINK Study (Walline JJ, 2020)

- Walline JJ, Walker MK, Mutti DO, Jones-Jordan LA, Sinnott LT, Giannoni AG, Bickle KM, Schulle KL, Nixon A, Pierce GE, Berntsen DA; BLINK Study Group. Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial. JAMA. 2020 Aug 11;324(6):571-580.
- CooperVision Biofinity MF
  - Off the shelf
- 3 years
- 292/294 (99%) included in analyses

Results

- Mid level add (+1.50) no better than single vision
  - 0.16 D progression difference at year 3
  - -0.07 mm AL difference
- High add (+2.50) showed promise compared to single vision
  - 0.46 D progression difference at year 3
  - -0.23 mm AL difference

From: **Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial**

JAMA. 2020;324(6):571-580. doi:10.1001/jama.2020.10834

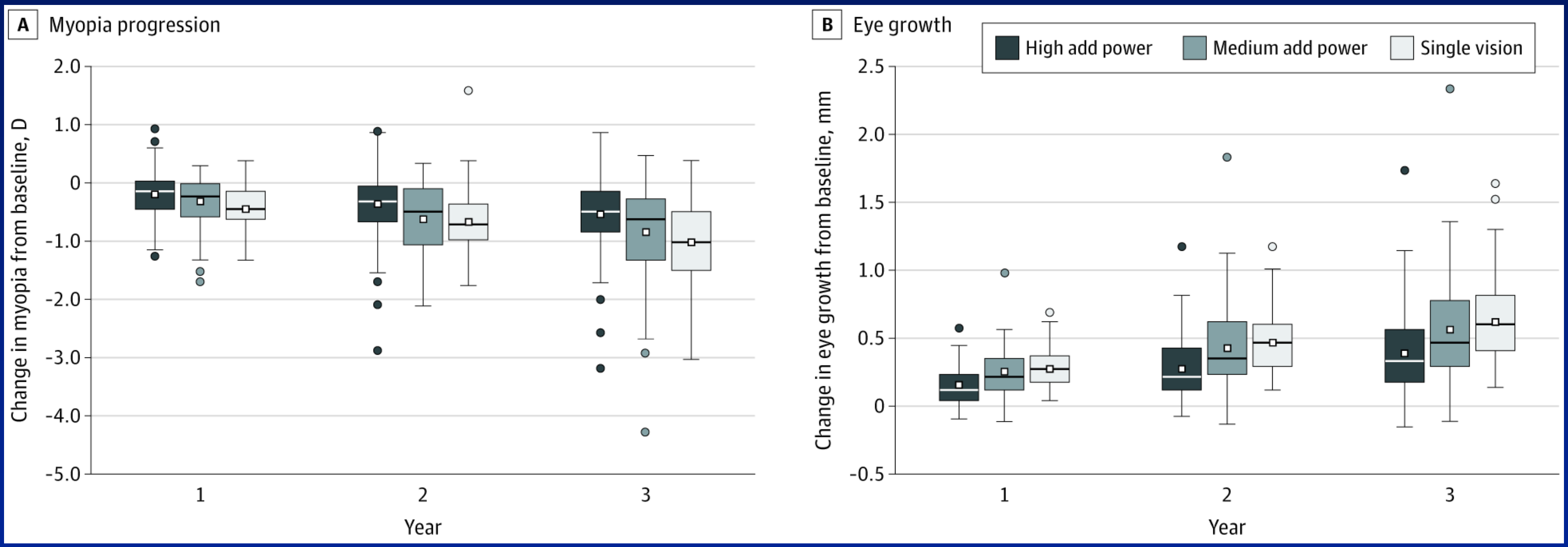


Figure Legend:

Myopia Progression and Eye Growth in a Study of the Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in ChildrenBox plots are shown in which the middle line represents the median change from baseline, boxes represent the interquartile range, whiskers extend to the most extreme observed values withing 1.5 × the interquartile range of the nearer quartile, and dots represent observed values outside that range. The data represent the mean change of the 2 eyes. A, More negative values indicate myopia progression. B, More positive values indicate eye growth.

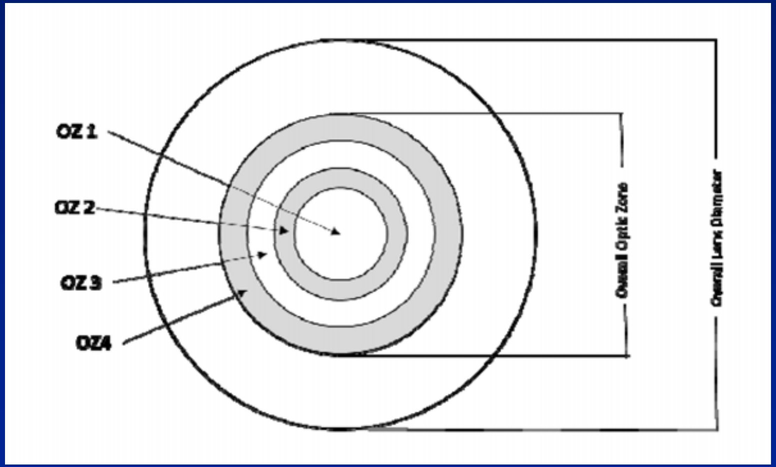
What else is new in MFCL?

MiSight Assessment Study Spain (MASS, Jan. 2018)

- MiSight CL's vs. SV Glasses
- Age: 8 to 12 years old
- Myopia: -0.75 to -4.00 D
- 24 months
- N = 74 completed
- Less progression: 0.45 D vs 0.74 D, $p < 0.001$
  - 39.32% less progression
- Less axial elongation: 0.28 mm vs 0.44 mm, $p < 0.001$
  - 36.04%

MiSight: FDA Approved for Myopia Control (1st)

- MiSight FDA approved for myopia control: November 2019
- 1-day lens
- Note Dk: not a SiHi
- Chamberlin P, 2019
  - 59% reduction in SE refractive error
  - 52% reduction in axial elongation
  - Compared to 1-day single vision lenses



MiSight (Chamberlin, 2019)

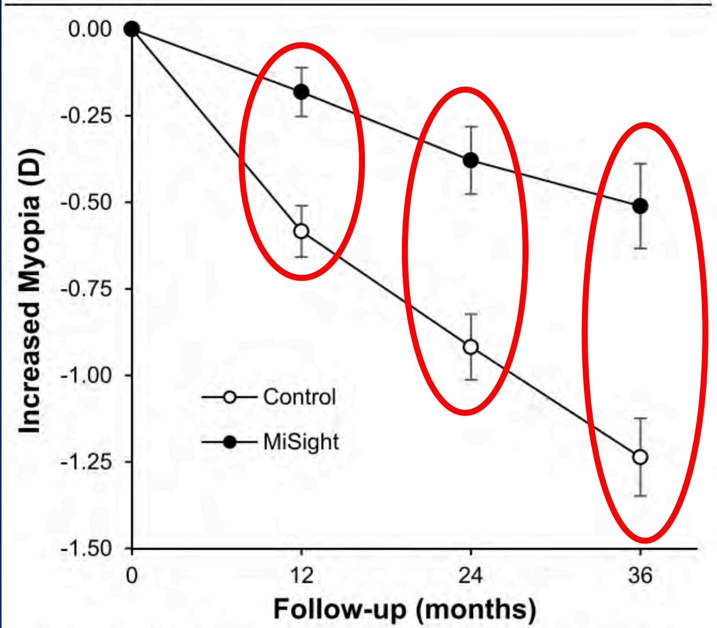


FIGURE 2. Mean unadjusted changes in spherical equivalent refractive error (D) for the test (MiSight) and control (Proclear 1-day) study groups. The filled and open symbols represent the MiSight and control groups, respectively, for the 36-month study period. The error bars denote the 95% CI of the mean changes. The mean unadjusted differences were 0.40 D less with MiSight at 12 months, 0.54 D less at 24 months, and 0.73 D less at 36 months. CI = confidence interval.

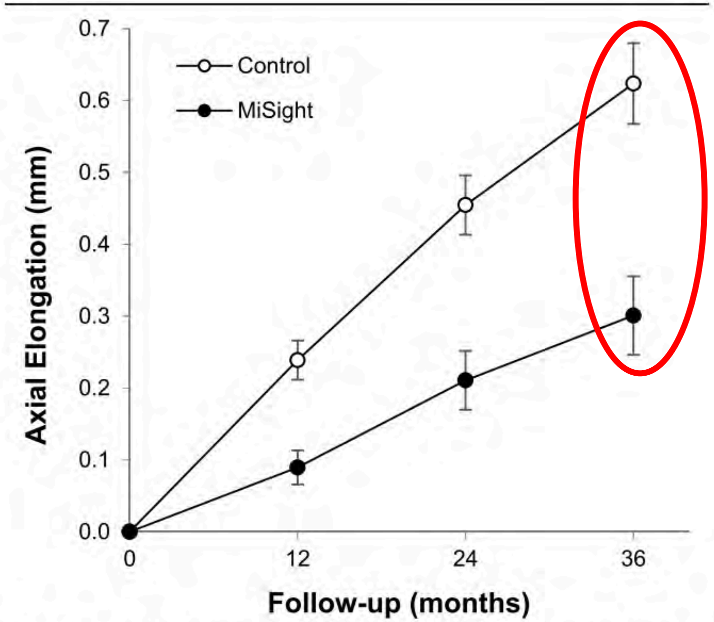


FIGURE 4. Mean unadjusted changes in axial length (in millimeters) for the test (MiSight) and control (Proclear 1-day) study groups. The filled and open symbols represent the MiSight and control groups, respectively, for the 36-month study period. The error bars denote the 95% CI of the mean changes. The mean unadjusted differences were 0.15 mm less with MiSight at 12 months, 0.24 mm less at 24 months, and 0.32 mm less at 36 months. CI = confidence interval.

MiSight® 1 day clinical study outcomes

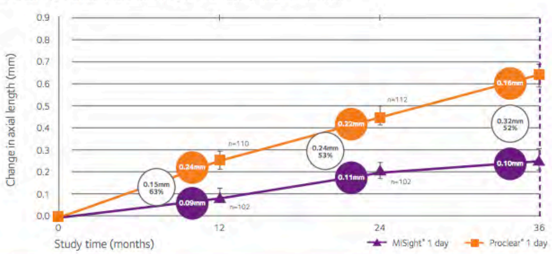
Part 1 (Years 1-3)

Objective: Quantify the effectiveness of MiSight® 1 day in **slowing the rate of myopia progression** compared to a single vision 1-day lens over a 3-year period

Result: 52% average reduction in axial elongation with **MiSight® 1 day**[1*]

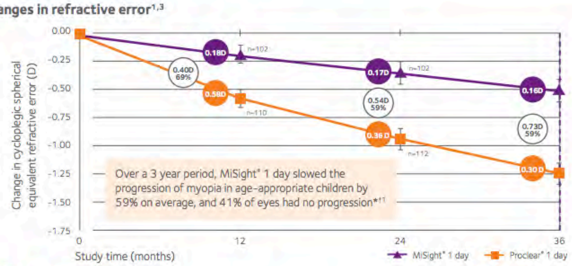
Changes in axial length[1,3]

• Increased axial length is associated with a higher likelihood of visual impairment[4]



Result: 59% on average reduction in myopia progression with **MiSight® 1 day**[1*]

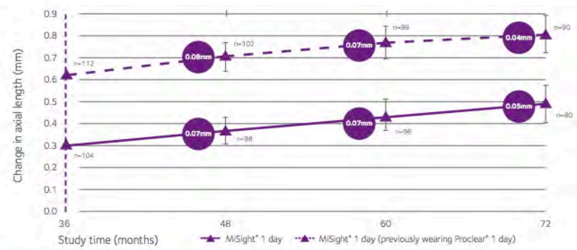
Changes in refractive error[1,3]



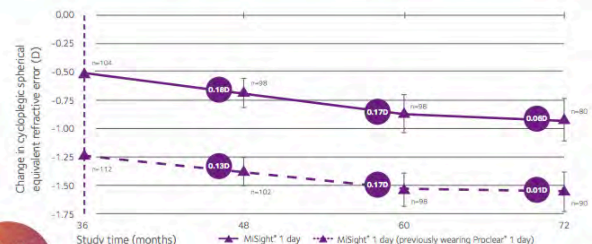
Part 2 (Years 4-6)

Objective: Compare **the rate of myopia progression** between children new to MiSight® 1 day and those who had worn MiSight® 1 day for the previous 3 years

Result: New and established **MiSight® 1 day** wearers had comparable rates of axial length growth[5]



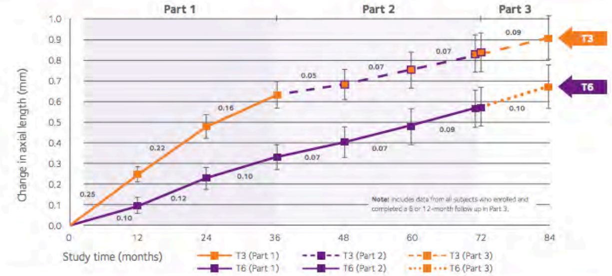
Result: New and established **MiSight® 1 day** wearers had comparable rates of myopic progression[5]



Part 3 (Year 7)

Objective: Assess **the impact of cessation on the prior accumulated treatment effect** following 3 or 6 years of treatment with MiSight® 1 day (T3 and T6, respectively)

Result: Evidence indicates that there is no rebound effect with **MiSight® 1 day** contact lenses[5,6*]



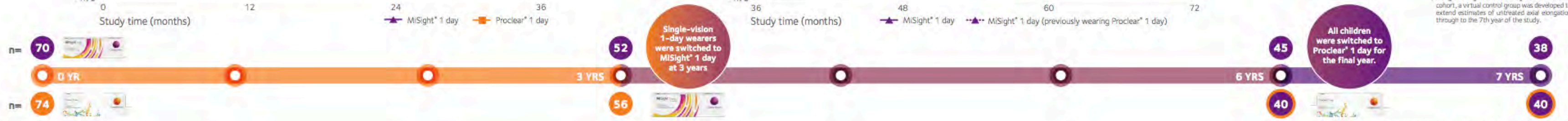
Result: After MiSight 1 day treatment ceased, myopia control treatment gains were retained over 12 months[5,6*]

Axial length growth control modeling and measured values (mm)

Year	Control group model†	T3 group (measured)	T6 group (measured)
1	0.247	0.253	0.103
2	0.207	0.216	0.115
3	0.178	0.159	0.109
4	0.153	0.049	0.074
5	0.131	0.065	0.074
6	0.115	0.072	0.089
7	0.100	0.091	0.109

† Using the age and ethnicity of the control cohort, a virtual control group was developed to extend estimates of untreated axial elongation through to the 7th year of the study.

■ Proclear® 1 day ■ MiSight® 1 day



CooperVision®

* Compared to a single vision 1-day lens over a 3 year period.
† -0.25D or less of change. Fitted at 8-12 years of age at initiation of treatment

* Preliminary international study data shows that, on average, for children that discontinued treatment at age 14-19 following 3 or 6 years of MiSight® 1 day wear, the eye growth reverted to age-expected average myopic progression rates. Disclaimer: The stability of the myopia reduction effect 1-year post-treatment is being further evaluated in a post-approval study in the U.S. as a condition of FDA approval for MiSight® 1 day.

Table 1 Interventions with efficacy in controlling myopia progression in children

Efficacy	Interventions
High	Atropine 1%, 0.5%, 0.1%, 0.05%, 0.025% and 0.01%
> − 0.50 D/year	Pirenzepine 2%
Moderate	Orthokeratology
− 0.25 to − 0.50 D/year	Peripheral defocus contact lens
	Peripheral defocus ophthalmic lens
Low	Bifocal or progressive addition spectacles
0 to − 0.25 D/year	Increased outdoor activities

Efficacy compared with single vision spectacles as control. Own table calculated via a network meta-analysis of 30 randomised controlled trials [14]

D diopters

Ruiz-Pomeda A, 2020; Sankaridurg P, 2018

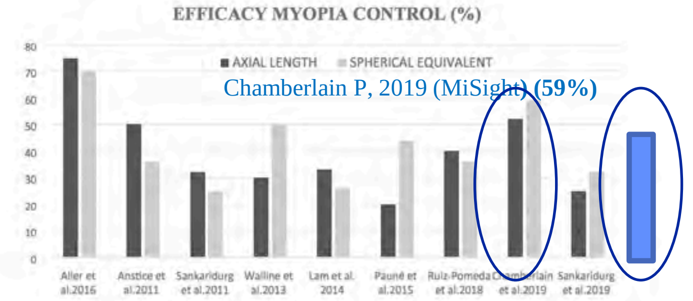


Fig. 1 Efficacy of soft contact lenses for myopia control (own figure based on data of published articles)

Walline J, 2020 (BLINK) (43%)

Adis

Multifocal Contact Lenses

- Clinical note:
  - Increased Accommodative lag
  - Increased Exophoria?
  - Gong CR, March 2017
- Clinical Note
  - “If you can’t get 20/25 on MF, choose another design”
  - High adds (+2.50 D or more)

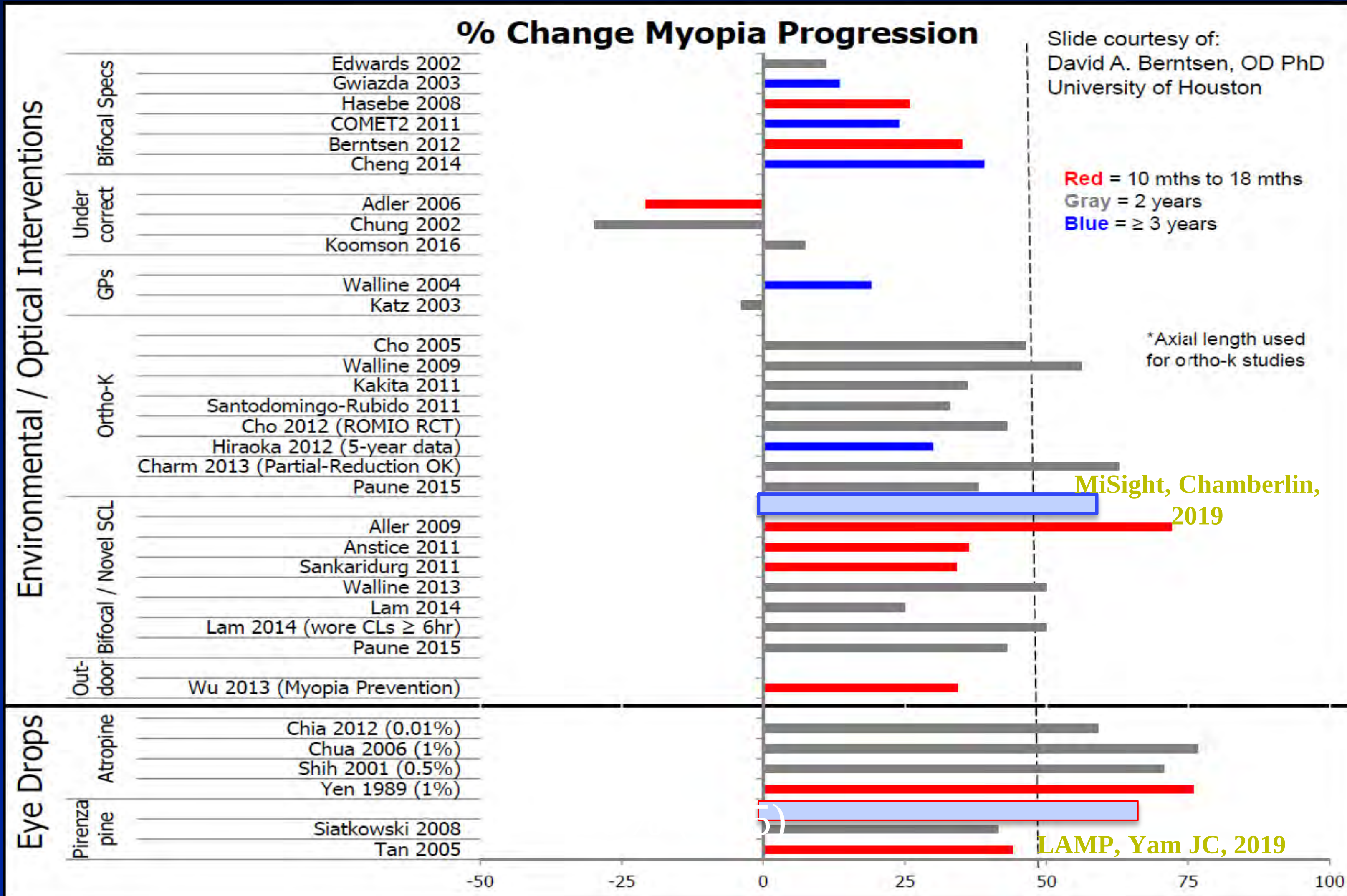
What are treatment options for myopia?

- 1. Side effect of blur
- 2. Progression

Treatment Options 2022:

- 1) Treat the Side Effect of Blur
  - Glasses
  - Contacts
  - Transition Lenses
  - AR Coating
  - Polycarb
  - Rec Specs
  - Swim goggles
  - Hi-index
    - Trivex

What are treatment options for myopia progression?


% Change Myopia Progression
Slide courtesy of:
David A. Berntsen, OD PhD
University of Houston
Red = 10 mths to 18 mths
Gray = 2 years
Blue = ≥ 3 years
*Axial length used for ortho-k studies
Environmental / Optical Interventions
Bifocal Specs
Edwards 2002
Gwiazda 2003
Hasebe 2008
COMET2 2011
Berntsen 2012
Cheng 2014
Under correct
Adler 2006
Chung 2002
Koomson 2016
GPs
Walline 2004
Katz 2003
Ortho-K
Cho 2005
Walline 2009
Kakita 2011
Santodomingo-Rubido 2011
Cho 2012 (ROMIO RCT)
Hiraoka 2012 (5-year data)
Charm 2013 (Partial-Reduction OK)
Paune 2015
Bifocal / Novel SCL
MiSight, Chamberlin, 2019
Aller 2009
Anstice 2011
Sankaridurg 2011
Walline 2013
Lam 2014
Lam 2014 (wore CLs ≥ 6hr)
Paune 2015
Out-door
Wu 2013 (Myopia Prevention)
Eye Drops
Atropine
Chia 2012 (0.01%)
Chua 2006 (1%)
Shih 2001 (0.5%)
Yen 1989 (1%)
Pirenza pine
LAMP, Yam JC, 2019
Siatkowski 2008
Tan 2005
-50
-25
0
25
50
75
100

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings 1: change in refractive error at 1 year

Interventions for myopia control in children: a living systematic review and network meta-analysis

Population: children with progressive myopia (38 studies, 6525 participants in analyses)

Interventions: optical and pharmacological

Comparator: control (36 studies, 2846 participants). Control arms for optical interventions are either single vision spectacles or contact lenses. Placebo eyedrops were the usual comparator for pharmacological interventions

Outcome: progression of myopia (difference in change in spherical equivalent refraction (SER)) at 1 year (dioptres)

Setting: primary eye care

Assumed control risk: median change in SER in control arms at 1 year −0.65D

Equivalence criterion: difference in change in spherical equivalent less than 0.25 D

Treatment (vs control)	Number of studies in the treatment arm (participants)	Corresponding intervention risk MD (95%CI). Direct estimates from pairwise MA	Corresponding intervention risk MD (95%CI). Estimates from NMA	Certainty of evidence
High-dose atropine (≥ 0.5%)	3 (512)	0.90 (0.62 to 1.18)	0.89 (0.65 to 1.12)	Moderate[a]
Moderate-dose atropine (0.1% to < 0.5%)	2 (254)	-	0.65 (0.27 to 1.03)	Moderate[a]
Low-dose atropine (< 0.1%)	4 (497)	0.38 (0.10 to 0.66)	0.43 (0.24 to 0.61)	Very low[b]
Pirenzepine	2 (210)	0.32 (0.15 to 0.49)	0.27 (−0.13 to 0.67)	Very low[b]
7-methyxanthine	1 (77)	0.07 (−0.09 to 0.24)	0.07 (−0.33 to 0.48)	Low[c]
Multifocal soft contact lenses	8 (712)	0.26 (0.17 to 0.35)	0.23 (0.09 to 0.37)	Very low[b]
Rigid gas-permeable contact lenses	2 (178)	0.02 (−0.05 to 0.10)	0.17 (−0.12 to 0.46)	Very low[b]
Peripheral plus spectacle lenses	5 (480)	0.51 (0.19 to 0.82)	0.28 (0.05 to 0.51)	Very low[b]
Multifocal spectacle lenses	9 (729)	0.14 (0.08 to 0.21)	0.14 (−0.04 to 0.32)	Low[c]
Undercorrected single vision spectacles	2 (72)	−0.15 (−0.29 to 0.00)	−0.15 (−0.45 to 0.15)	Low[c]

GRADE Working Group grades of evidence

High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate-certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.

Low-certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

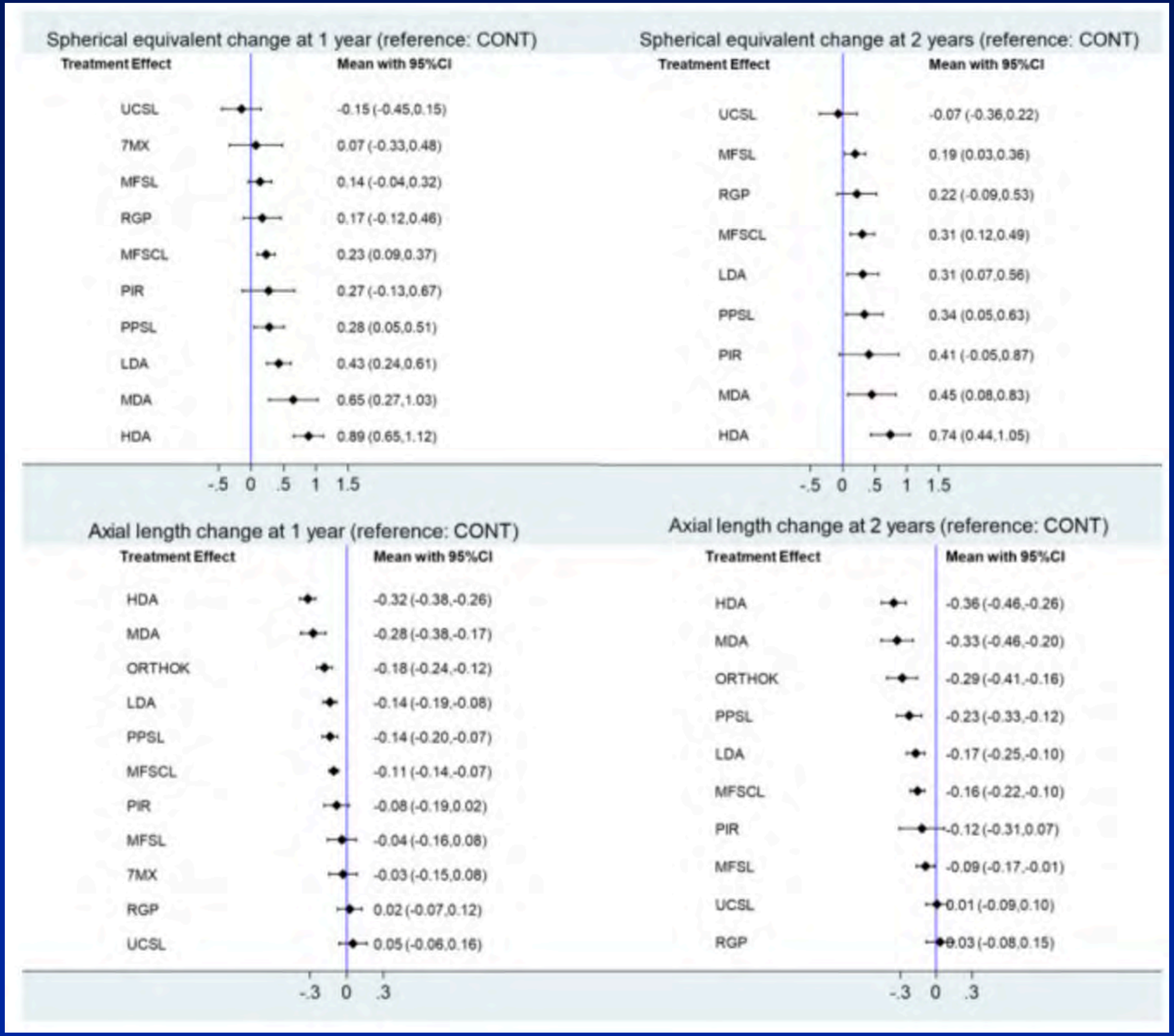
Treatment (vs control)	Number of studies in the treatment arm (participants)	Corresponding intervention risk MD (95%CI) Direct estimates from pairwise MA	Corresponding intervention risk MD (95%CI) Estimates from NMA	Certainty of evidence
High-dose atropine (≥ 0.5%)	2 (428)	1.26 (1.17 to 1.36)	0.74 (0.44 to 1.05)	Moderate[a]
Moderate-dose atropine (0.1% to < 0.5%)	2 (247)	-	0.45 (0.08 to 0.83)	Low[b]
Low-dose atropine (< 0.1%)	2 (249)	0.24 (0.17 to 0.31)	0.31 (0.07 to 0.56)	Low[b]
Pirenzepine	1 (53)	0.41 (0.13 to 0.69)	0.41 (−0.05 to 0.87)	Low[b]
Multifocal soft contact lenses	5 (540)	0.30 (0.19 to 0.41)	0.31 (0.12 to 0.49)	Low[b]

Year 2

Cochrane Library
Trusted evidence. Informed decisions. Better health.
Cochrane Database of Systematic Reviews

Rigid gas-permeable contact lenses	2 (154)	One study showed no difference and the other a beneficial effect	0.22 (−0.09 to 0.53)	Very low[c]
Peripheral plus spectacle lenses	2 (188)	0.34 (−0.08 to 0.76)	0.34 (0.05 to 0.63)	Very low[c]
Multifocal spectacle lenses	8 (696)	0.19 (0.08 to 0.30)	0.19 (0.03 to 0.36)	Low[b]
Undercorrected single vision spectacles	2 (122)	0.02 (−0.05 to 0.09)	−0.07 (−0.36 to 0.22)	Very low[c]

Walline J et al:
Cochrane Review 2023



Bullimore M:
Myopia Control: Why Each Diopter Matters

- **Abstract**
- Reducing the incidence or prevalence of any disease by 40% is of huge public health significance. Slowing myopia by 1 diopter may do just that for myopic maculopathy-the most common and serious sight-threatening complication of myopia. There is a growing interest in slowing the progression of myopia due to its increasing prevalence around the world, the sight-threatening consequences of higher levels of myopia, and the growing evidence-based literature supporting a variety of therapies for its control. We apply data from five large population-based studies of the prevalence of myopic maculopathy on 21,000 patients. We show that a 1-diopter increase in myopia is associated with a 67% increase in the prevalence of myopic maculopathy. Restated, slowing myopia by 1 diopter should reduce the likelihood of a patient developing myopic maculopathy by 40%. Furthermore, this treatment benefit accrues regardless of the level of myopia. Thus, while the overall risk of myopic maculopathy is higher in a -6-diopter myope than in a -3-diopter myope, slowing their myopic progression by 1 diopter during childhood should lower the risk by 40% in both.

What's new?

Special Specs

Special Specs

- DIMS (HOYA): MiyoSmart

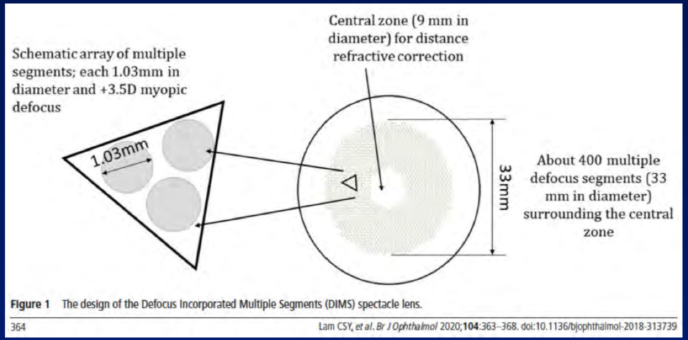
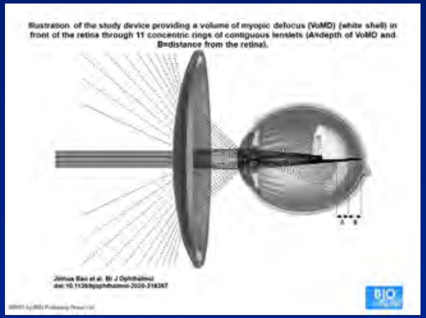


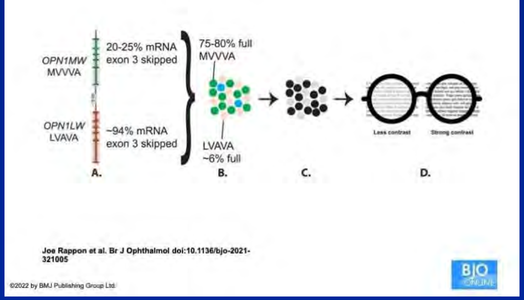
Figure 1 The design of the Defocus Incorporated Multiple Segments (DIMS) spectacle lens.

364 Lam CSY, *et al*. *Br J Ophthalmol* 2020;**104**:363–368. doi:10.1136/bjophthalmol-2018-313739

- HALT (Essilor): Stellest



- DOT (Essilor/CooperVision): SightGlass



DIMS (Hoya): MiYOSMART

- **Defocus Incorporated Multiple Segments (DIMS) - Hoya MiYOSMART**
- Defocus Incorporated Multiple Segments (DIMS) technology was designed by Hong Kong Polytechnic University. It is described in the clinical trial paper as "compris[ing] a central optical zone (9 mm in diameter) for correcting distance refractive errors, and an annular multiple focal zone with multiple segments (33 mm in diameter) having a relative positive power (+3.50 D). The diameter of each segment is 1.03 mm. This design simultaneously introduces myopic defocus and provides clear vision for the wearer at all viewing distances. There are multiple foci from myopic defocus at a plane in front of the retina, which would be received as blur images on the retina."[1]

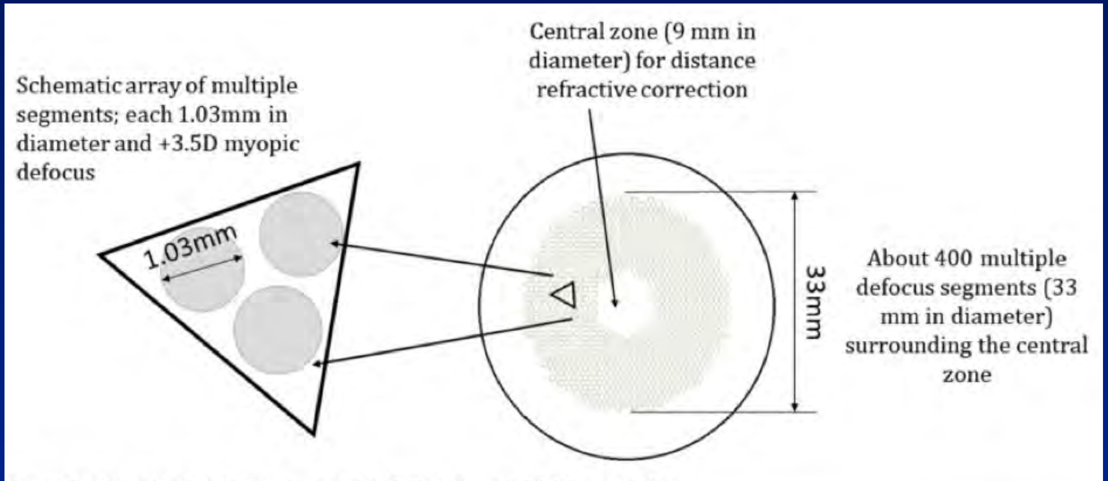


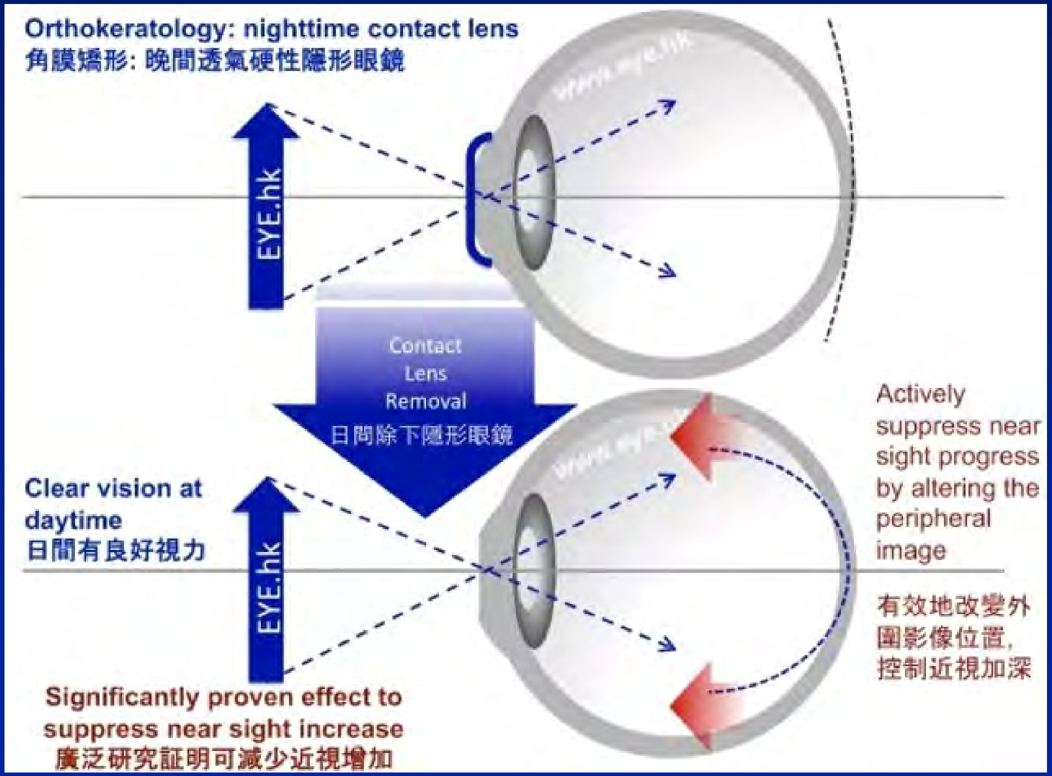
Figure 1 The design of the Defocus Incorporated Multiple Segments (DIMS) spectacle lens.

364 Lam CSY, *et al. Br J Ophthalmol* 2020;**104**:363–368. doi:10.1136/bjophthalmol-2018-313739

DIMS

- **Defocus incorporated multiple segments (DIMS) lens**
- Slows myopia progression by 52%
- Slows AL by 62%
- Lam C 2019 BJO

DIMS 6 year



- Defocus Incorporated Multifocal Segment (DIMS)
  - N = 90 (6 year)
  - DIMS lens maintained the effect on slowing myopia progression and axial growth in myopic children over a period of 6 years. When children stopped DIMS lens wear and wore single vision lenses, their myopia progression was faster than the children who continued with DIMS lens wear.
  -

HALT (Essilor): Stellest

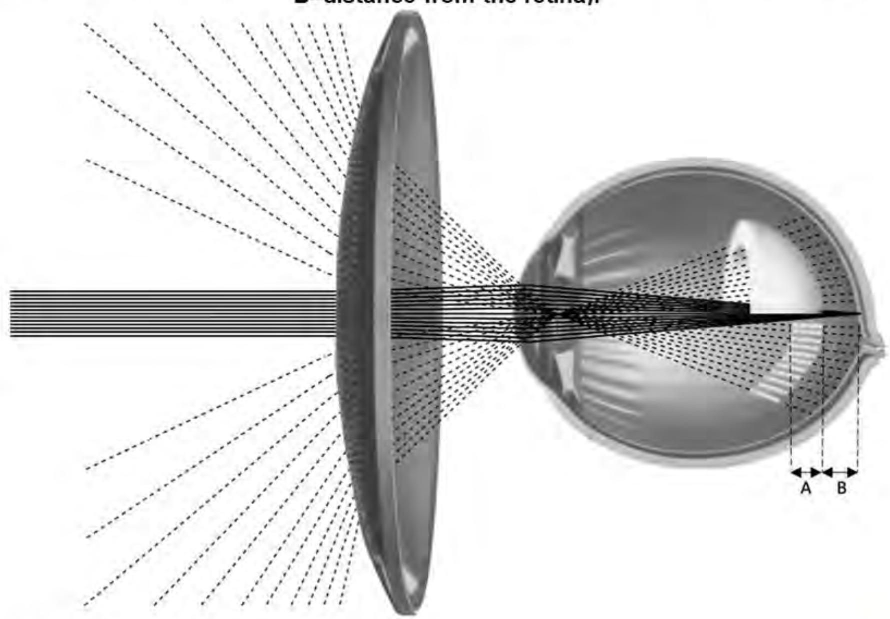
- **Highly Aspherical Lenslet Target (H.A.L.T.) technology - Essilor Stellest™**

- Essilor Stellest™ is described as comprising Highly Aspherical Lenslet Target or H.A.L.T. technology in this **Press Release**. The recent publication of the **one year clinical trial paper**[2] describes these spectacle lenses as having "a spherical front surface with 11 concentric rings formed by contiguous aspherical lenslets (diameter of 1.1 mm). The area of the lens without lenslets provides distance correction. The geometry of aspherical lenslets has been calculated to generate a VoMD in front of the retina at any eccentricity, serving as a myopia control signal (figure 1)." The image below is Figure 1 from the open access paper.

- The clinical trial paper[2] describes the use of aspherical lenses with a power gradient in animal studies as a basis for use of the highly aspherical lenslets. It states that "Instead of focusing light on two distinct surfaces, as in the case of competing defocus lenses, these aspherical lenses deviate rays of light continuously in a nonlinear manner that creates a three-dimensional quantity of light in front of the retina, which we call volume of myopic defocus (VoMD) in this paper. Greater asphericity, that is, a larger VoMD, reduces lens-induced myopia in chicks."

HALT (Essilor): Stellest

Illustration of the study device providing a volume of myopic defocus (VoMD) (white shell) in front of the retina through 11 concentric rings of contiguous lenslets (A=depth of VoMD and B=distance from the retina).



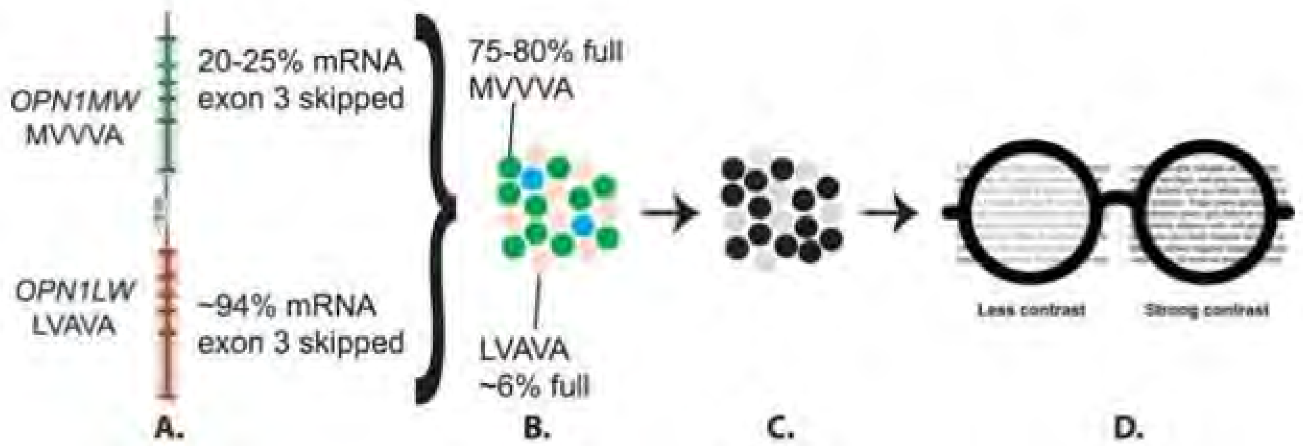
Jinhua Bao et al. Br J Ophthalmol
doi:10.1136/bjophthalmol-2020-318367

BJO ONLINE

DOT (Essilor/CooperVision): SightGlass

- **Diffusion Optics Technology (DOT) – SightGlass Vision**
- Diffusion optics technology (DOT) lenses are a little bit different from DIMS and H.A.L.T. in that they do not use lenslets, but diffusers. What are these diffusers? They are thousands of small elements across the lens, shaped as dots that scatter light onto the retina. The small (around 5mm) central section of the lens does not incorporate these dots, providing clear vision and facilitating lens power verification.
- This entirely different approach is based on studies of genetic forms of myopia, which show cellular defects in cone photoreceptors linked to high myopia. These defects are characterized by some cones having dramatically reduced function, while adjacent cones function more normally. As stated in the randomized controlled trial paper, "This observation suggests that abnormal contrast signalling between neighbouring full and empty cones may stimulate axial elongation."[3]

DOT (Essilor/CooperVision): SightGlass



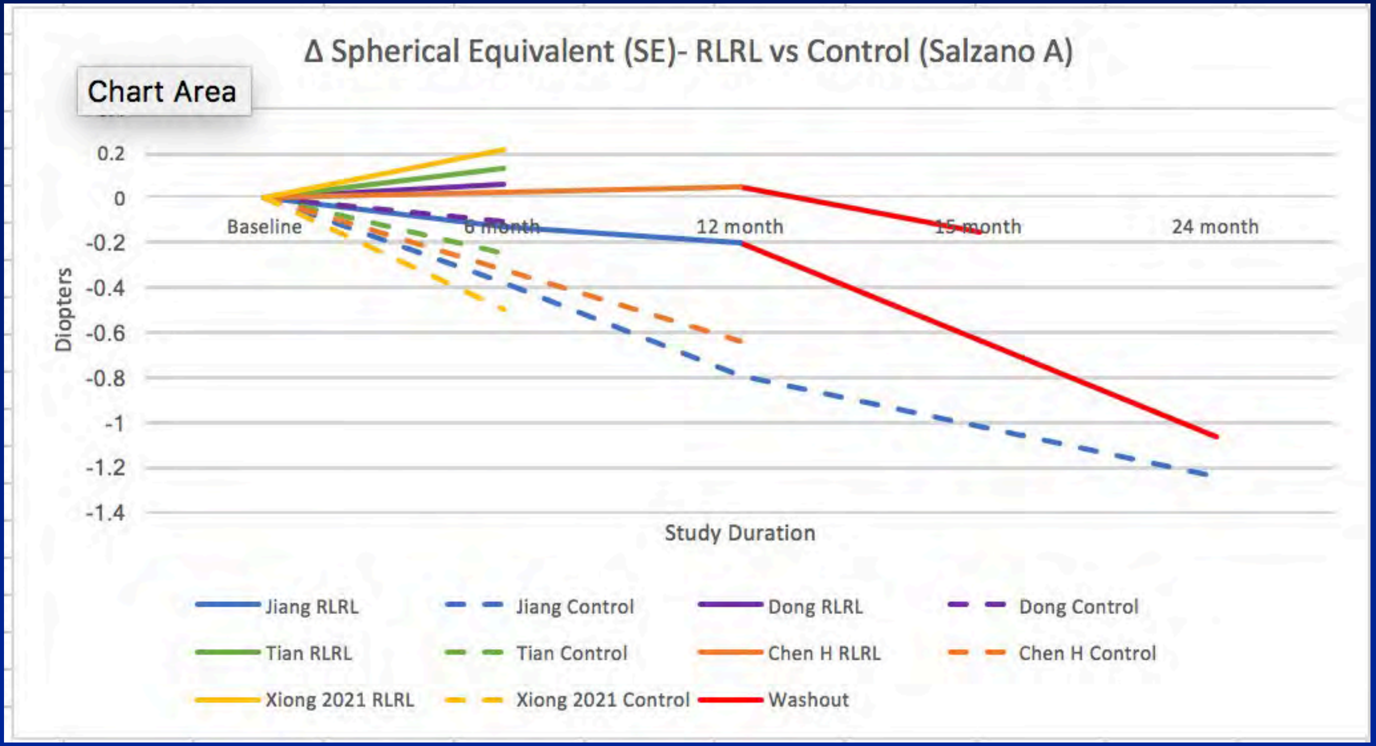
Joe Rappon et al. Br J Ophthalmol doi:10.1136/bjo-2021-321005

DOT (Essilor/CooperVision): SightGlass

- Diffusion Optics Technology (DOT)
  - 6-7 yo
  - N = 256
  - 14 sites (US and Canada)
  - Mean absolute reduction (2 years)
    - 0.27 mm AL
    - 0.77 D

Red Light (RLRL): Good or Bad?

Red light looks Great!
BIG rebound effect!
Safe?
Mechanism?

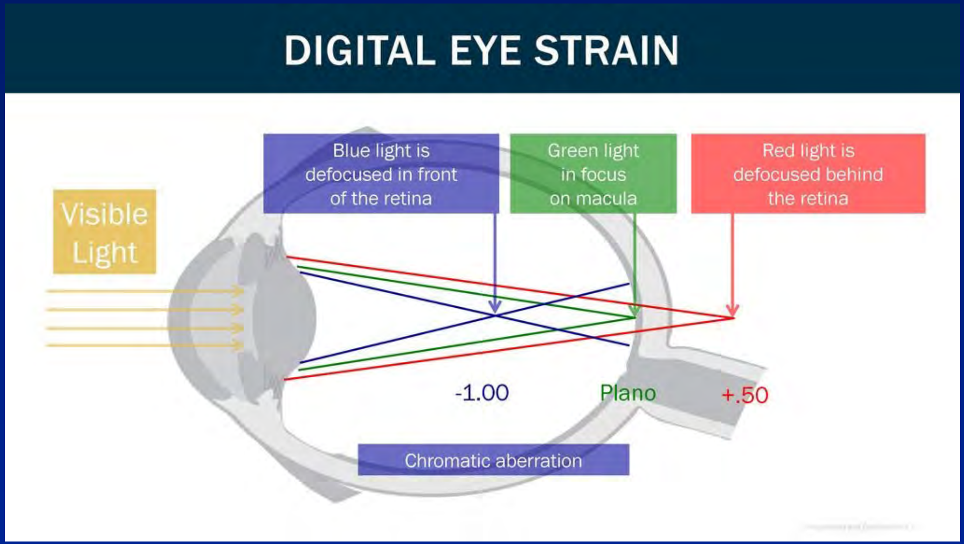


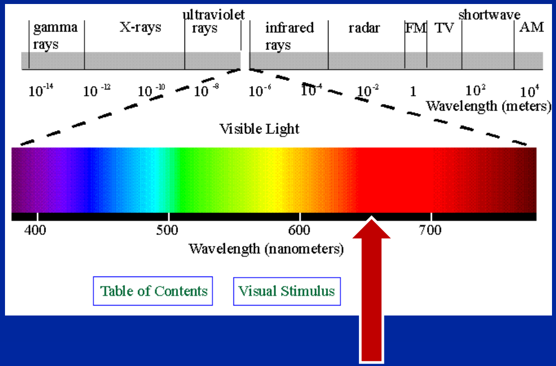
Red Light? Blue Light?

Red Light: good?

- Long wavelength light (N650 nm, red) has been shown to act as a strong inhibitor of eye growth
  - In rhesus monkeys
    - (Smith et al., 2015)
  - In tree shrews
    - (Gawne T. et al 2016).
  - Schaeffel F., Smith E. 2017 commentary

(Blue Light: bad??!)





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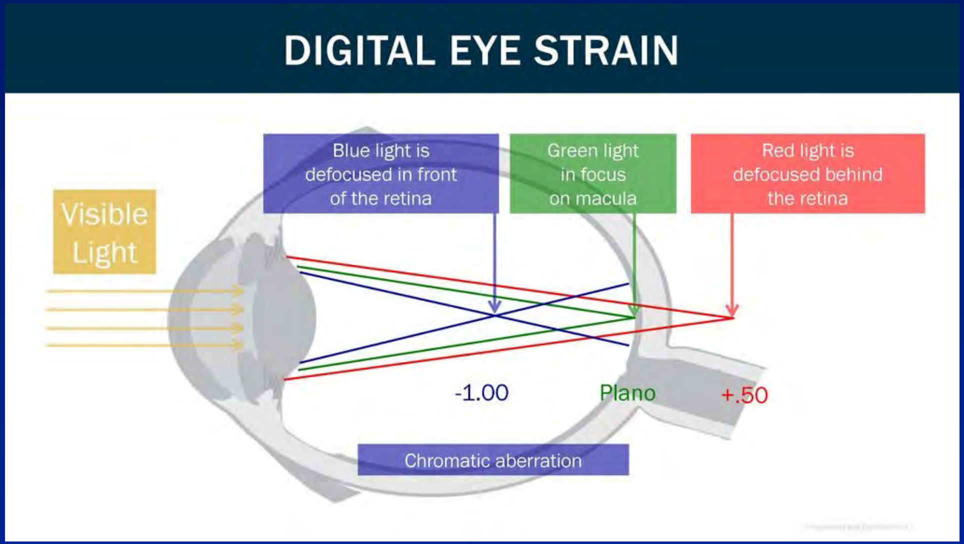
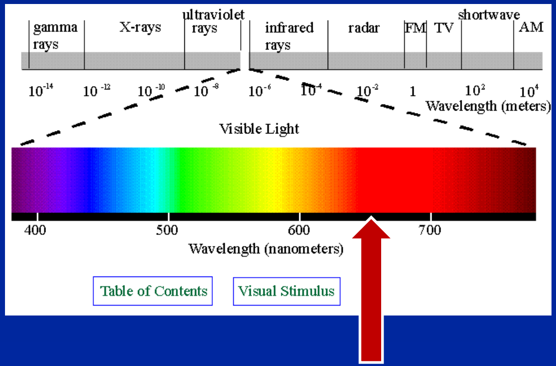
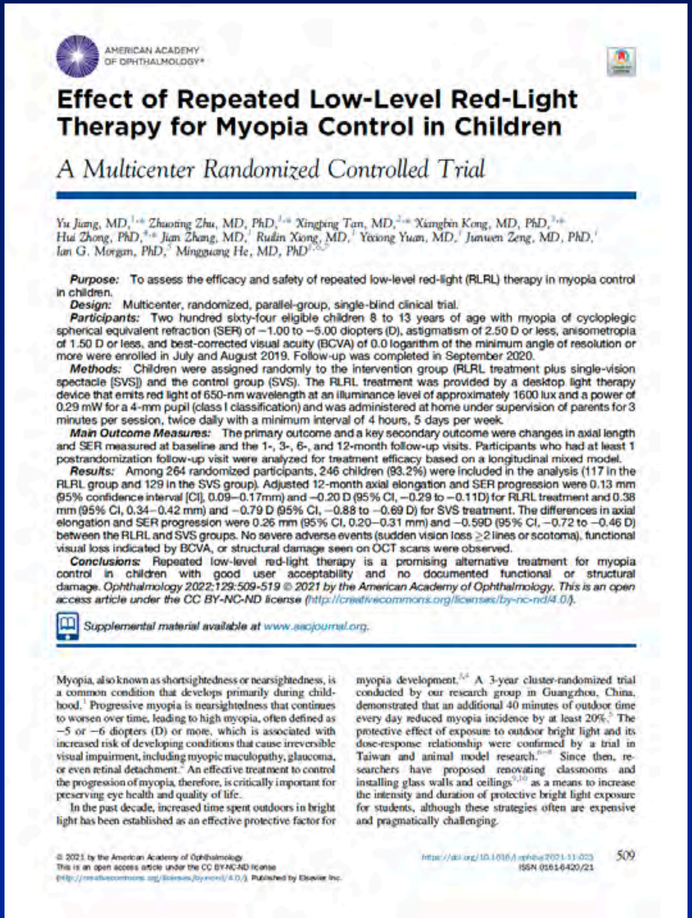




Repeated Low-Level Red-Light Therapy



AMERICAN ACADEMY OF OPHTHALMOLOGY

Effect of Repeated Low-Level Red-Light Therapy for Myopia Control in Children

A Multicenter Randomized Controlled Trial

Yu Jiang, MD,[1,*] Zhuoting Zhu, MD, PhD,[1,*] Xingping Tan, MD,[2,*] Xiangbin Kong, MD, PhD,[3,*] Hui Zhong, PhD,[4,*] Jian Zhang, MD,[1] Rulin Xiong, MD,[1] Yixiong Yuan, MD,[1] Junwen Zeng, MD, PhD,[1] Ian G. Morgan, PhD,[5] Mingguang He, MD, PhD[1,6,7]

Purpose: To assess the efficacy and safety of repeated low-level red-light (RLRL) therapy in myopia control in children.

Design: Multicenter, randomized, parallel-group, single-blind clinical trial.

Participants: Two hundred sixty-four eligible children 8 to 13 years of age with myopia of cycloplegic spherical equivalent refraction (SER) of −1.00 to −5.00 diopters (D), astigmatism of 2.50 D or less, anisometropia of 1.50 D or less, and best-corrected visual acuity (BCVA) of 0.0 logarithm of the minimum angle of resolution or more were enrolled in July and August 2019. Follow-up was completed in September 2020.

Methods: Children were assigned randomly to the intervention group (RLRL treatment plus single-vision spectacle [SVS]) and the control group (SVS). The RLRL treatment was provided by a desktop light therapy device that emits red light of 650-nm wavelength at an illuminance level of approximately 1600 lux and a power of 0.29 mW for a 4-mm pupil (class I classification) and was administered at home under supervision of parents for 3 minutes per session, twice daily with a minimum interval of 4 hours, 5 days per week.

Main Outcome Measures: The primary outcome and a key secondary outcome were changes in axial length and SER measured at baseline and the 1-, 3-, 6-, and 12-month follow-up visits. Participants who had at least 1 postrandomization follow-up visit were analyzed for treatment efficacy based on a longitudinal mixed model.

Results: Among 264 randomized participants, 246 children (93.2%) were included in the analysis (117 in the RLRL group and 129 in the SVS group). Adjusted 12-month axial elongation and SER progression were 0.13 mm (95% confidence interval [CI], 0.09–0.17mm) and −0.20 D (95% CI, −0.29 to −0.11D) for RLRL treatment and 0.38 mm (95% CI, 0.34–0.42 mm) and −0.79 D (95% CI, −0.88 to −0.69 D) for SVS treatment. The differences in axial elongation and SER progression were 0.26 mm (95% CI, 0.20–0.31 mm) and −0.59D (95% CI, −0.72 to −0.46 D) between the RLRL and SVS groups. No severe adverse events (sudden vision loss ≥2 lines or scotoma), functional visual loss indicated by BCVA, or structural damage seen on OCT scans were observed.

Conclusions: Repeated low-level red-light therapy is a promising alternative treatment for myopia control in children with good user acceptability and no documented functional or structural damage. *Ophthalmology 2022;129:509-519 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Supplemental material available at www.aaojournal.org.

Myopia, also known as shortsightedness or nearsightedness, is a common condition that develops primarily during childhood.[1] Progressive myopia is nearsightedness that continues to worsen over time, leading to high myopia, often defined as −5 or −6 diopters (D) or more, which is associated with increased risk of developing conditions that cause irreversible visual impairment, including myopic maculopathy, glaucoma, or even retinal detachment.[2] An effective treatment to control the progression of myopia, therefore, is critically important for preserving eye health and quality of life.

In the past decade, increased time spent outdoors in bright light has been established as an effective protective factor for myopia development.[3,4] A 3-year cluster-randomized trial conducted by our research group in Guangzhou, China, demonstrated that an additional 40 minutes of outdoor time every day reduced myopia incidence by at least 20%.[5] The protective effect of exposure to outdoor bright light and its dose-response relationship were confirmed by a trial in Taiwan and animal model research.[6–8] Since then, researchers have proposed renovating classrooms and installing glass walls and ceilings[9,10] as a means to increase the intensity and duration of protective bright light exposure for students, although these strategies often are expensive and pragmatically challenging.

https://doi.org/10.1016/j.ophtha.2021.11.023
ISSN 0161-6420/21

- Multicenter, randomized, single-masked clinical trial
- 264 children
  - 8 to 13 years
  - –1.00 to –5.00 D
- Randomly assigned to
  - intervention group (RLRL)
  - or control

Jiang Y et al. *Ophthalmology*. 2022;129(5):509-519.

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Repeated Low-Level Red-Light Therapy

- RLRL treatment provided by desktop light therapy device:
  - 650 nm
  - Illuminance ~1600 lux
  - 0.29 mW for 4-mm pupil
- Administered at home under parental supervision,
  - 3 minutes per session
  - twice per day (interval ≥ 4 hours)
  - 5 days per week

Jiang Y et al. *Ophthalmology*. 2022;129(5):509-519.

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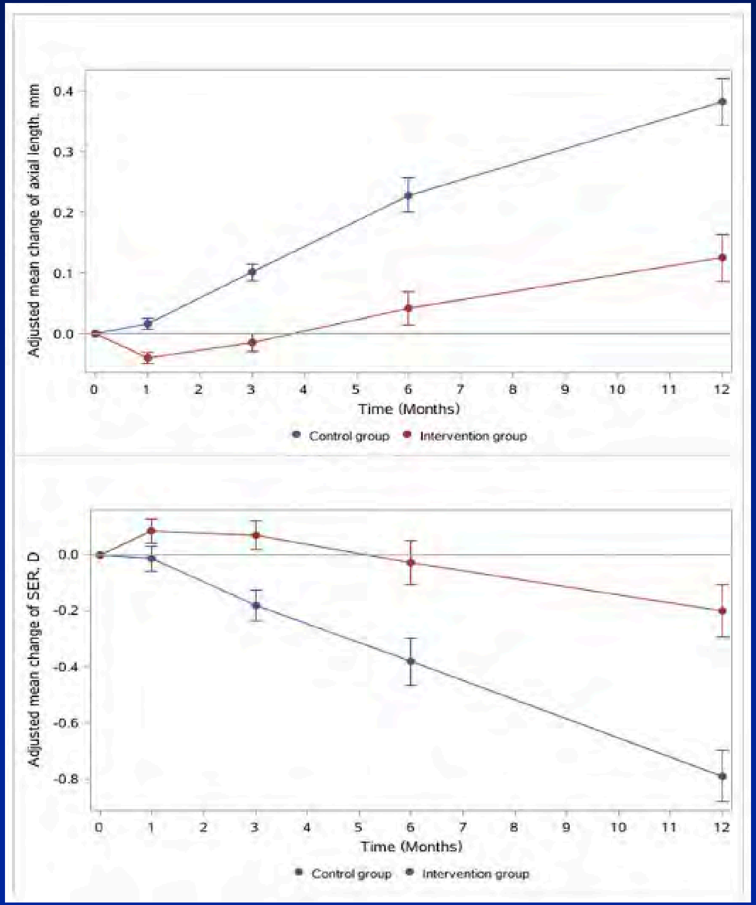
Repeated Low-Level Red-Light Therapy

- Among 264 randomized, 246 (93.2%) included in analysis
- Adjusted 12-month axial elongation
  - RLRL: 0.13 mm Δ = 0.26 mm
  - Control: 0.38 mm
- Adjusted 12-month progression
  - RLRL: –0.20 D Δ = 0.59 D
  - Control: –0.79 D
- No adverse events



Jiang Y et al. *Ophthalmology*. 2022;129(5):509-519.

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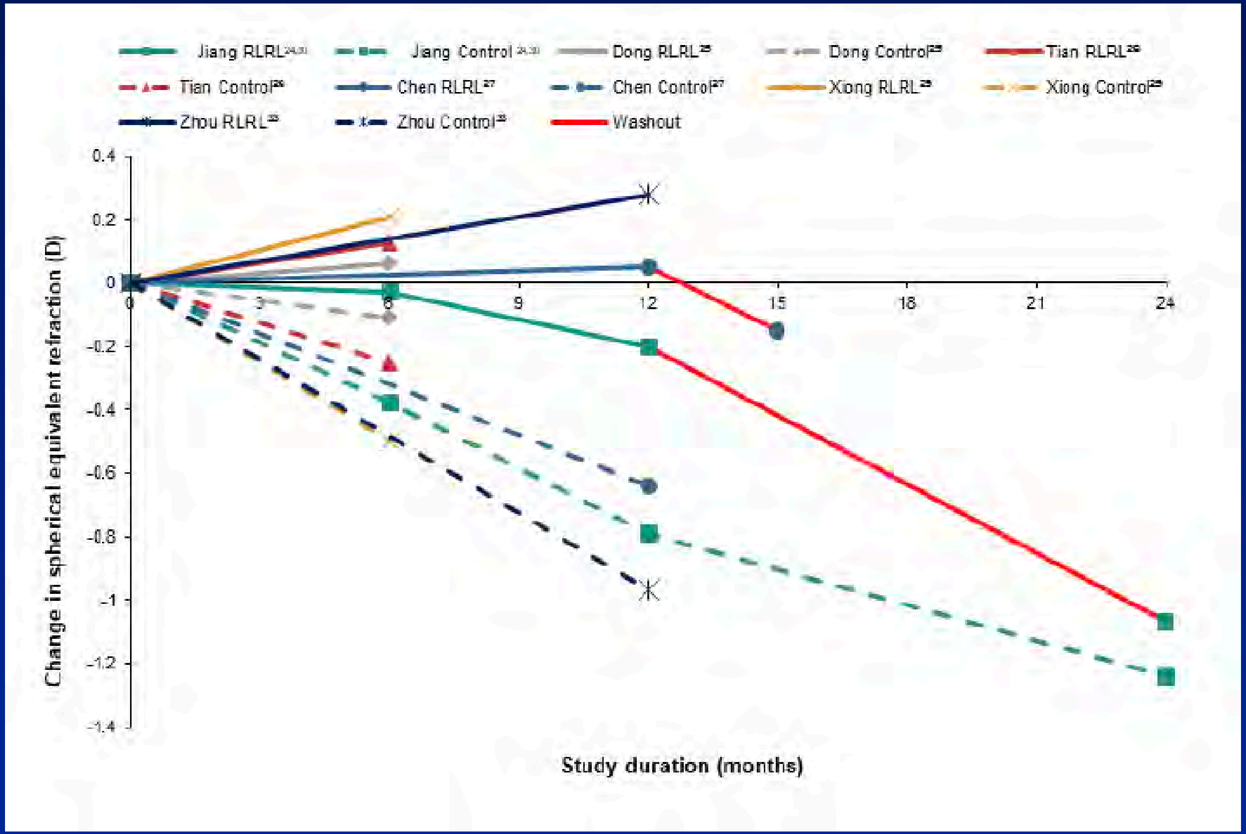
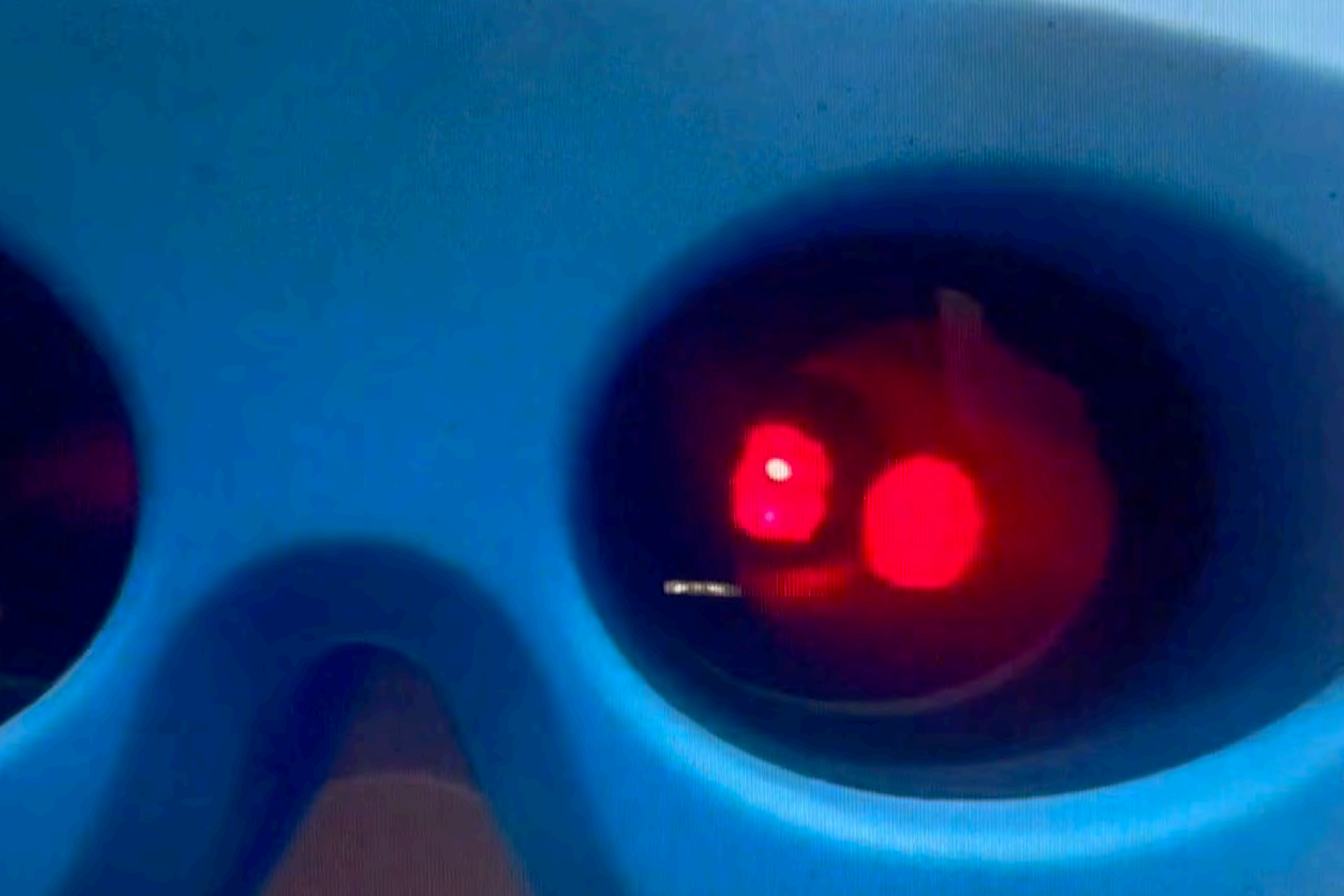
Repeated Low-Level Red-Light Therapy



Salzano AD et al. *Optom Vis Sci*. 2023 Oct 25.

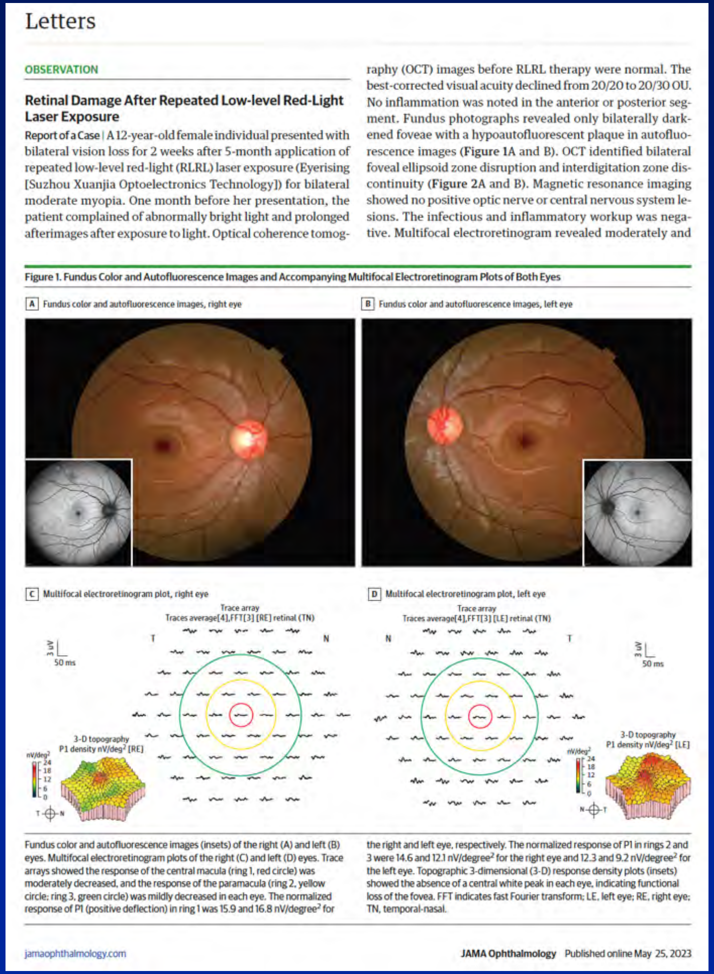
Treatment effect is impressive;
rebound effect is significant

K



Safety Concerns

- 12-year-old female presented with reduced vision after
  5 months of RLRL therapy
- Visual acuity reduced from 20/20 to 20/30 OU
- Bilaterally darkened foveae
- Hypoautofluorescent plaque



Letters

OBSERVATION

Retinal Damage After Repeated Low-level Red-Light Laser Exposure

Report of a Case | A 12-year-old female individual presented with bilateral vision loss for 2 weeks after 5-month application of repeated low-level red-light (RLRL) laser exposure (Eyerising [Suzhou Xuanjia Optoelectronics Technology]) for bilateral moderate myopia. One month before her presentation, the patient complained of abnormally bright light and prolonged afterimages after exposure to light. Optical coherence tomography (OCT) images before RLRL therapy were normal. The best-corrected visual acuity declined from 20/20 to 20/30 OU. No inflammation was noted in the anterior or posterior segment. Fundus photographs revealed only bilaterally darkened foveae with a hypoautofluorescent plaque in autofluorescence images (**Figure 1**A and B). OCT identified bilateral foveal ellipsoid zone disruption and interdigitation zone discontinuity (**Figure 2**A and B). Magnetic resonance imaging showed no positive optic nerve or central nervous system lesions. The infectious and inflammatory workup was negative. Multifocal electroretinogram revealed moderately and

Figure 1. Fundus Color and Autofluorescence Images and Accompanying Multifocal Electroretinogram Plots of Both Eyes

A Fundus color and autofluorescence images, right eye

B Fundus color and autofluorescence images, left eye

C Multifocal electroretinogram plot, right eye

D Multifocal electroretinogram plot, left eye

Fundus color and autofluorescence images (insets) of the right (A) and left (B) eyes. Multifocal electroretinogram plots of the right (C) and left (D) eyes. Trace arrays showed the response of the central macula (ring 1, red circle) was moderately decreased, and the response of the paramacula (ring 2, yellow circle; ring 3, green circle) was mildly decreased in each eye. The normalized response of P1 (positive deflection) in ring 1 was 15.9 and 16.8 nV/degree^2 for the right and left eye, respectively. The normalized response of P1 in rings 2 and 3 were 14.6 and 12.1 nV/degree^2 for the right eye and 12.3 and 9.2 nV/degree^2 for the left eye. Topographic 3-dimensional (3-D) response density plots (insets) showed the absence of a central white peak in each eye, indicating functional loss of the fovea. FFT indicates fast Fourier transform; LE, left eye; RE, right eye; TN, temporal-nasal.

jamaophthalmology.com JAMA Ophthalmology Published online May 25, 2023

Liu H. *JAMA Ophthalmol.* 2023;141(7):693-695.

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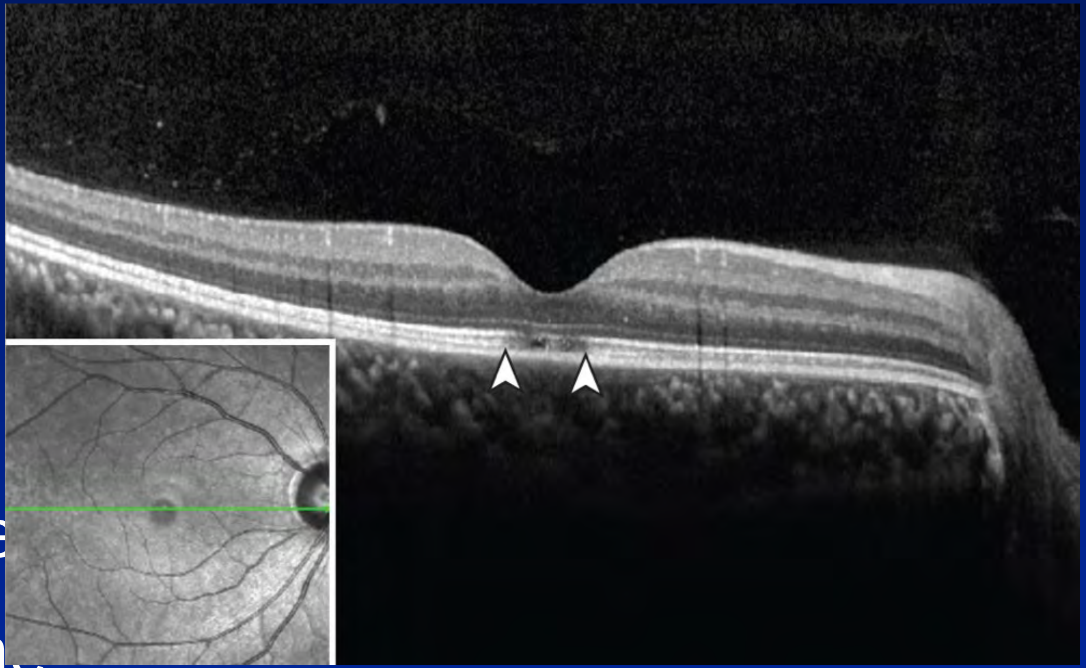
Safety Concerns

- 12-year-old female presented with reduced vision after 5-months of RLRL therapy
- Visual acuity reduced from 20/20 to 20/30 OU
- Bilaterally darkened foveae
- Hypoautofluorescent plaque
- Bilateral foveal ellipsoid zone disruption and interdigitation zone discontinuity



Liu H. *JAMA Ophthalmol.* 2023;141(7):693-695.

Treatment Options 2023:

- Atropine
  - ~~0.01%~~ qhs X 2? 3? More? Years
  - 0.05%? 0.025%?
- MF CL
  - D center, N surround
    - +2.00? +3.00?
    - Biofinity MFCL
    - NaturalView
  - Daily Disp MFCL
    - MiSight (FDA)
- Ortho K
- Chromatic
  - RLRL
  - Special filters in classroom? On eye?
- MF SRx
  - DIMS
  - HALT
  - DOT
- Dual modality?
  - MFCL + atropine
  - Ortho K + atropine

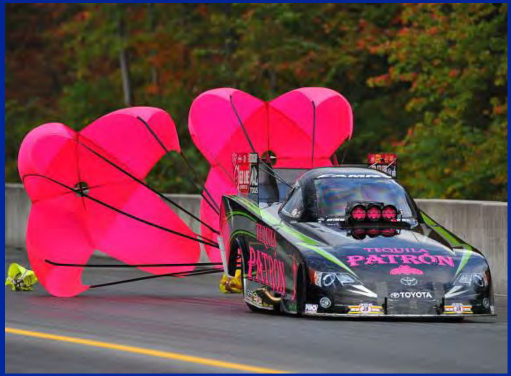
Treatment Options 2023+:

- Quint modality????
  - 1) Optical
    - Contacts
    - Special glasses
  - 2) Pharm
    - Atropine
  - 3) Chromatic
  - 4) Surgical
    - Collagen linking
  - 5) environment
    - More time outdoors
    - Red light classrooms?

Myopia:
AAO 2016 – New Standard of Care?

- 1. Minus lenses
  – Contacts
  – Glasses
  – (Refractive surgery)

2. Myopia control
  – Atropine (low dose)
  – MF CL
  – Ortho-K
  – Defocus Spectacles



- Standard of Care

Myopia 2020: Walline J et al

- Walline JJ, Lindsley KB, Vedula SS, et al. Interventions to slow progression of myopia in children. *Cochrane Database Syst Rev*. 2020;1(1):CD004916. Published 2020 Jan 13. doi:10.1002/14651858.CD004916.pub4

The End?

Infant Myopia?

- Is she myopic?
- Case 2
  - Wet ret: -8.00 DS OD, OS
  - Wet AR: -8.00 DS OD, OS
  - What do you prescribe?

  - What else do we need to know?

Infant Myopia

- Don’t over minus a baby
- Don’t intentionally underplus a baby
- Aim for Clear Image

Infant Myopia

- May be transient
  - Watch for it in school years
- May uncover a more complicated picture
  - Developmental Delay
    - Genetic (Marfan)
    - Environment (FAS, rubella, CP)
  - Systemic
    - Ehlers-Danlos, albinism, homocystinuria
  - Ocular
    - CSNB, RP, coloboma, cone-rod dystrophies, Starguardt, microcornea, glaucoma

Summary:
What are some things you can tell parents about myopia?

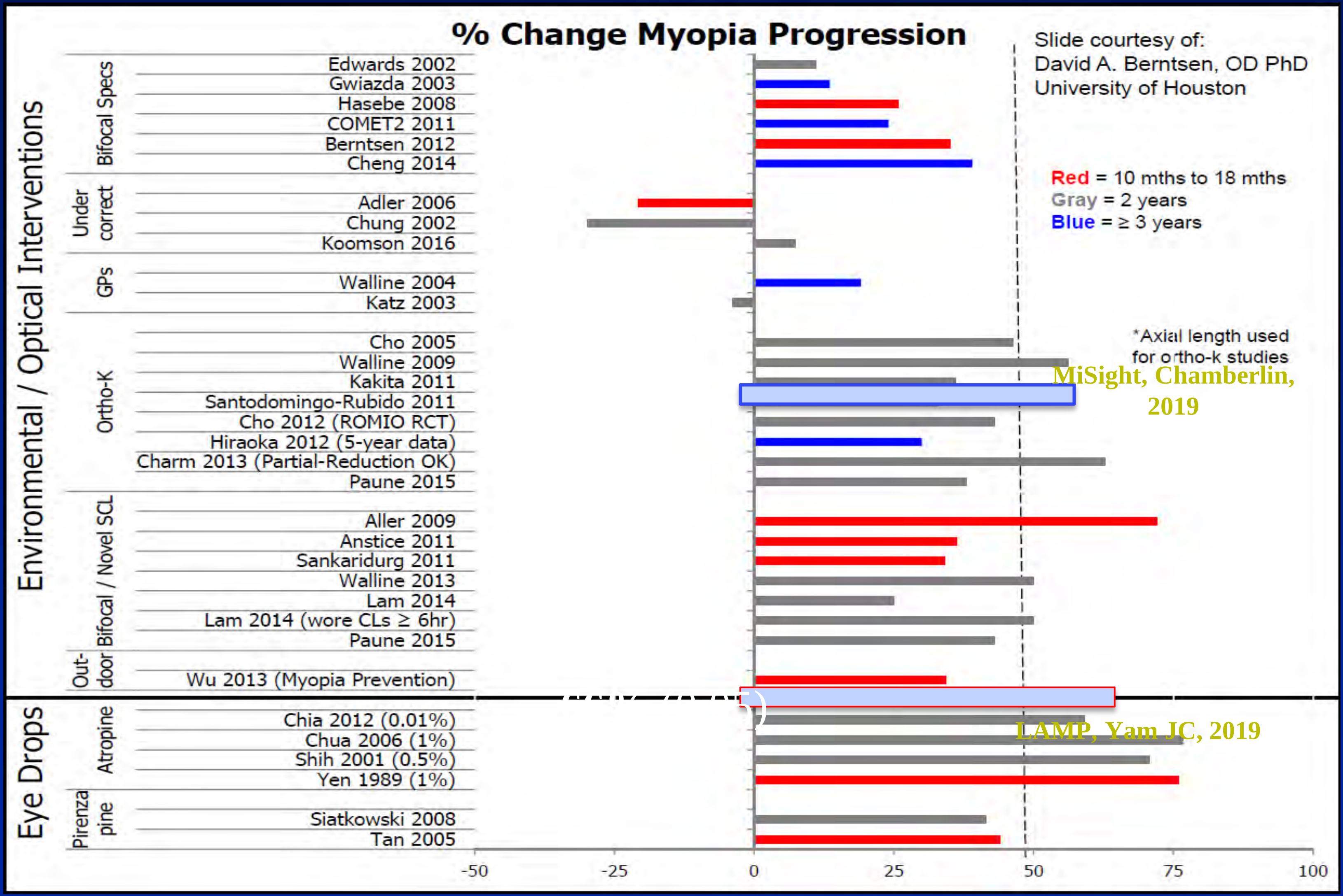
Patient/Parent Education

- Near-sighted eyes are too long, far-sighted eyes are too short. Once you are near-sighted, it's very rare to become less near-sighted. You'll likely wear glasses your whole life.
- Average change per year is 0.50 D (6-12y, 1-4D) and tends to grow for about 9 years
  - Earlier onset, faster progression
- 75% of kids done growing around age 18,
  - 4% still growing at age 24
- Near-sighted eyes are a risk for RD, annual eye exams
  - -5.00 D annual dilations
  - -6.00 D more at risk myopia

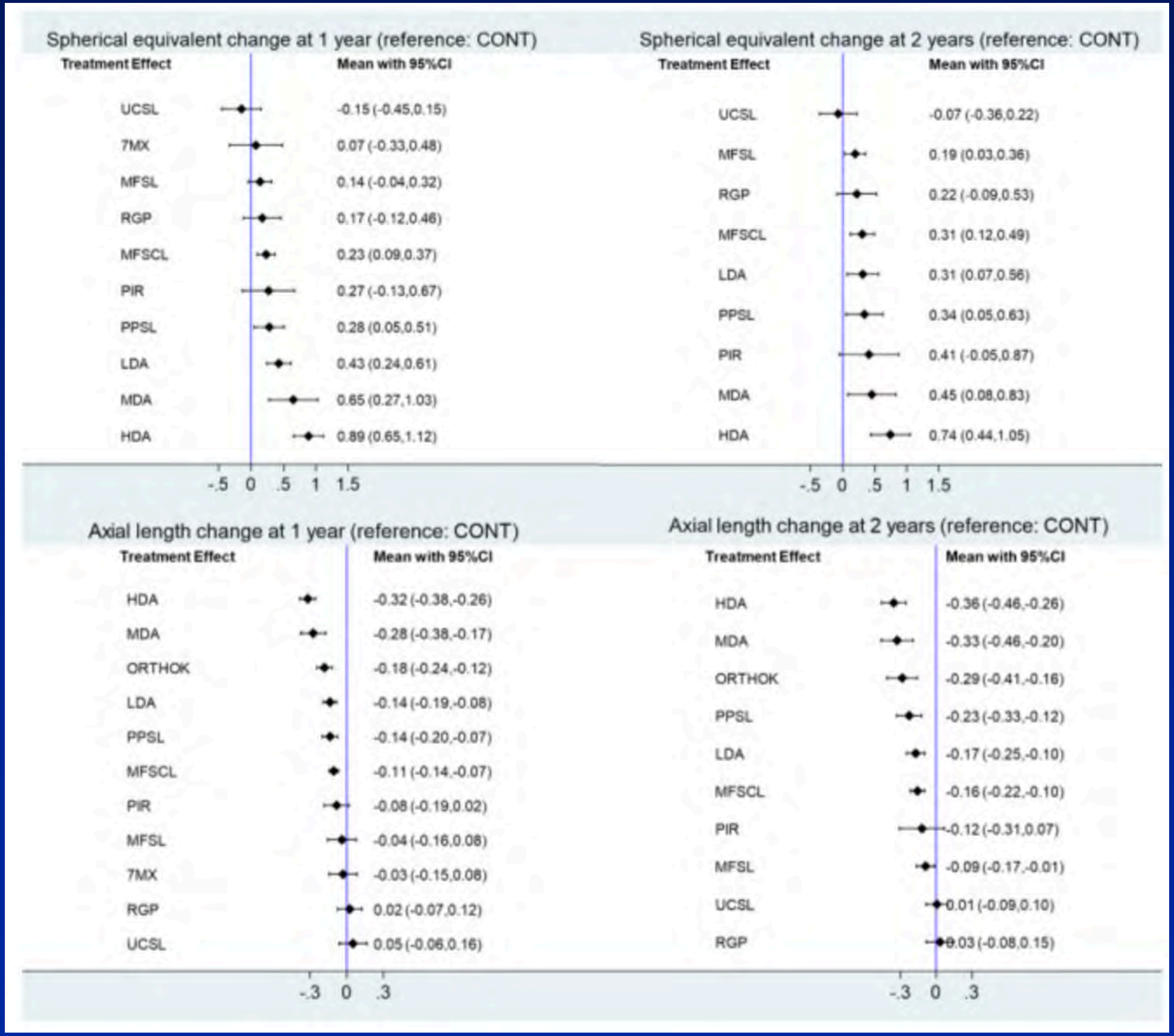
Parent/Patient Education

- 1. Outdoor play 1 hour a day??
- 2. AAP
  - No screen use prior to the age of 18 months of age
  - Between ages 2-5 years, no more than 1 hour per day of high-quality media (ie, Sesame Workshop) with parents re-teaching concepts and helping children understand what they are seeing.
  - Keep mealtimes and bedtimes screen free;
    - no screens 1 hour before bedtime to improve sleep quality.
- 3. Obtuse angle elbow for near??
- 4. Wear sunglasses (Transitions?)
- 5. Wear AR??

Are we curing myopia?



Silver bullet????? Or So What???



Future: You!

- Can we slow myopia down more?
- Can we prevent it?!?!?!
  - Glasses vs. no glasses!
    - (Pretty please? Go figure it out!)

The End.