

WHAT DO WE KNOW ABOUT MYOPIA

LIONEL KOWAL

ACBO 2009

It's good to be a myope!

□ 1: [Ann Acad Med Stetin](#). 2008;54(1):13-6; discussion 16.

Are children with myopia more intelligent? A literature review.

[Czepita D](#), [Lodygowska E](#), [Czepita M](#).

Katedra i Klinika Okulistyki Pomorskiej Akademii Medycznej w Szczecinie al. Powstańców Wlkp. 72, 70-111 Szczecin.

PURPOSE: Refractive errors are a serious worldwide problem. So far a few papers have described the relationship between refractive errors and intelligence. However, based on the growing interest into the relationship between refractive errors and intelligence quotient (IQ) we decided to present and discuss the latest results of the clinical studies on that subject. **MATERIAL AND METHODS:** A review of the literature concerning the relationship between refractive errors and IQ was done. **RESULTS:** In 1958 Nadell and Hirsch found that children in America with myopia have a higher IQ. A similar relationship has been described by other researchers from the USA, the Czech Republic, Denmark, Israel, New Zealand, and Singapore. In other related studies, it was reported that myopic children regardless of their IQ gain better school achievements--table 1. It was also observed that schoolchildren with hyperopia have a lower IQ and gain worse school achievements--table 2. Several hypotheses explaining the relationship between refractive errors and intelligence have been published. Recently, Saw et al. concluded that higher IQ may be associated with myopia, independent of books read per week, in schoolchildren. According to them "the association between genetically driven IQ and myopia of hereditary predisposition could be forged because of a pleiotropic relationship between IQ and myopia in which the same causal factor is reflected in both genetic traits. There may be similar genes affecting eye size or growth (associated with myopia) and neocortical size (possibly associated with IQ)". **CONCLUSIONS:** The conducted clinical observations suggest that children with myopia may have a higher IQ. This relationship is most probably determined by genetic and environmental factors.

Does refractive surgery damage the IQ?

Types of myopia....

Alcohol myopia: Its prized and dangerous effects.

Steele, Claude M.; Josephs, Robert A.

[View Article](#)



American Psychologist. Vol 45(8), Aug 1990, 921-933.



[Current issue feed](#)

This article explains how alcohol makes social responses more extreme, enhances important self-evaluations, and relieves anxiety and depression, effects that underlie both the social destructiveness of alcohol and the reinforcing effects that make it an addictive substance. The theories are based on alcohol's impairment of perception and thought—the myopia it causes—rather than on the ability of alcohol's pharmacology to directly cause specific reactions or on expectations associated with alcohol's use. Three conclusions are offered: (a) Alcohol makes social behaviors more extreme by blocking a form of response conflict. (b) The same process can inflate self-evaluations. (c) Alcohol myopia, in combination with distracting activity, can reliably reduce anxiety and depression in all drinkers by making it difficult to allocate attention to the thoughts that provoke these states. These theories are discussed in terms of their significance for the prevention and treatment of alcohol abuse. (PsycINFO Database Record (c) 2009 APA, all rights reserved)

a lack of foresight or discernment : a narrow view of something

How much Nature, how much Nurture

- Accommodation and myopia

Uncertain relationship**

- 3 recent studies* show increased outdoor activity protective against myopia
- Night lights
- Maternal smoking protective!

**Rose & Morgan 2008 [X2], Dirani 2009*

*** McBrien NA, Adams DW. Invest Ophthalmol Vis Sci 1997;38:321–33*

Overview of stats

- <5% of infants born @ term, then declines
- Preschool: 2-3%
- 11-13yo: 5%
- **15% by age 15**
- US adults: 33%

F > M, younger > older , whites > African- or Mexican- Americans

- Prematurity: 25 - 50%

increased corneal curvature bigger factor than increased axial length

TERRY YOUNG
MYOPIA GENETICS

CURRENT OPINION OPHTHALMOLOGY 2009

- Jon Ruddle [Melbourne] :
gene on 5q for axial length
- Twin studies: increased concordance of refractive error & all of the refractive components in mono- c.f. di- zygotic twins

from TERRY YOUNG

Table 1 Identified myopia loci as approved by the Human Genome Organization Gene Nomenclature Committee

Locus	OMIM	Cytogenetic location	Reference study	Myopia severity: age of onset
MYP1	310460	Xq28	[14–16]	High: –6.75 to –11.25 D Early: 1.5–5 years
MYP2	160700	18p11.31	[17–19]	High: –6 to –21 D Early: 6.8 years (average)
MYP3	603221	12q21–q23	[20,21,22*,23]	High: –6.25 to –15 D Early: 5.9 years (average)
MYP4	608367	7q36	[24]	High: –13.05 D (average)
MYP5	608474	17q21–q22	[25]	High: –5.5 to –50 D Early: 8.9 years (average)
MYP6	608908	22q12	[26–28]	Mild-moderate: –1.00 D or lower
MYP7	609256	11p13	[29]	–12.12 to +7.25 D
MYP8	609257	3q26	[29]	–12.12 to +7.25 D
MYP9	609258	4q12	[29]	–12.12 to +7.25 D
MYP10	609259	8p23	[29,30]	–12.12 to +7.25 D
MYP11	609994	4q22–q27	[31]	High: –5 to –20 D Early: before school age
MYP12	609995	2q37.1	[32,33]	High: –7.25 to –27 D Early: before 12 years
MYP13	HGNC:32582	Xq23–q25	[34]	High: –6 to –20 D Early: before school age
MYP14	610320	1p36	[35]	
Miscellaneous Loci			[11,36**–38**,39*,40,41*,42,43,44*]	

D, diopters; HUGO, Human Genome Organization; MYP, myopia locus; p, short arm of a chromosome; q, long arm of a chromosome. OMIM, Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>). HGNC- HUGO Gene Nomenclature Committee (<http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/searchgenes>).

Waardenburg's textbook, Genetics and Ophthalmology of 1961-3 "axial myopia may be due to different genes, either by itself or as part of syndromes."

EYE SHAPE & PERIPHERAL RETINA

Does peripheral optical defocus cause myopia ?

- Most myopic eyes are prolate

Peripheral retina

~1DS less myopic.

Literature ++ for 50+ years.

- 'improved' by laser refractive surgery

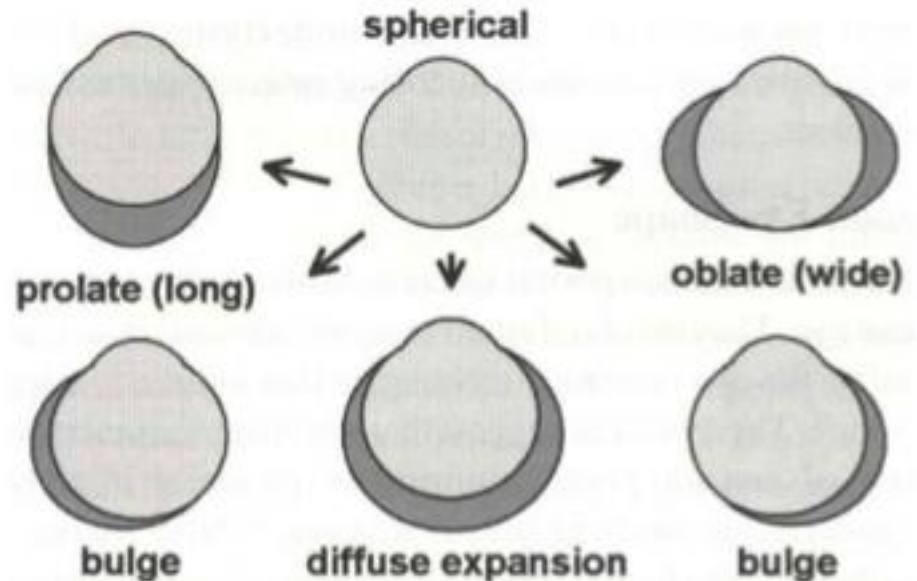


Fig. 1. Shapes of the vitreous chamber forms in chick. The vitreous chamber shape can be predictably modified in chick by altering visual input, changing photoperiod or administering pharmaceutical agents. The vitreous chamber can become diffusely enlarged, selectively elongated along the visual axis or selectively widened in the equatorial dimension. Asymmetries or local bulges can be induced in the posterior eye wall by altering the visual experience in part of the visual field. Each pattern is illustrated, superimposed on a spherical representation of the eye.

'CONGENITAL' MYOPIA

Hiatt, Costenbader, Albert 1965

- ..@ birth or by 6y
- N= 177; 120 studied. C's office 1936-64. M=F
- 1st exam 2m to 6y, av 3y4m. Myopia -0.4 to -17, av. -8
- Final exam 4-18y, av 10y7m.

Av -0.6 DS greater.

+ve FH: slightly greater increase -0.9 c.f. -0.2 [p=0.05]

43 showed decrease - range 0.25 to 4.5 DS.

- 46% FH of some type of myopia
- 13% prematurity \approx 'normals'
- 58%: typical fundus findings of myopia
- 50% strabismus. Most ET. Also XT, vertical, CN, SN

Selection bias: Costenbader was famous pediatric ophthalmologist and strabismus surgeon [First in USA] .

Myopic infants in Cambridge

Ehrlich, Atkinson, Braddick... Vis Res 1995

- Changes in Cyclo Refraction from 8m to 38m
- Myopes ≤ -3.5 DS : trend to low+
- Low+ controls: little/ no change

Selection bias: population study

Medium to **high** grade myopia in infancy and early childhood..

Lavrich, Nelson,... Wills, Albany, 1993

- Bilateral myopia ≥ -3 by age 4 R: -3 to -19.5
- N=45. M>F.
- 19/45: seen ≥ 2 y later:
- 12/38 eyes : progressed ≥ 1 DS [range -1 to -7, median -3]
- 7/38 : hyperopic shift ≥ 1 DS [1 to 6 DS, median 2.25]
- 40% strab, ET >> XT
- FH 51%

Selection bias: pediatric ophthalmology offices

Early / birth myopia

- Many change very little
- Many improve or get worse
- Some get better. Low myopes tend to emmetropise
- FH ~ 50%
- Strab ~50%

STABILITY OF REFRACTION IN CHILDHOOD ANISOMYOPIA

Caputo, Frosini,,, Strabismus 2001

- 46 anisomyopes age <10, followup $\geq 2y$
- 14 ET, 11 XT, 3 nystag, 2 IOOA
- W -4 to -18 [-8 \pm 3 DS] *Worse eye - More myopic W*
- B +4.5 to -6.5 [-1 \pm 2] *Better eye - Less Myopic B*
- W-B [aniso]: -7.5 \pm 3, end -6 \pm 4
- B: Myopic shift [p<0.001]74%, hyperopic shift 6%
- W: stable refraction [p=0.8]. Myopic shift 50%, hyperopic shift 40%

STABILITY OF REFRACTION IN ADULT MYOPIA

Nizam..Waring..PERK study group J Ref Corneal Surg 1992

- Manifest and cyclo refraction over 5y
- Unoperated eye [other had RK]
- Age 21 to 57y. 82 eyes

37 non- CL wearers:

- **13%** progressed ≥ 1 DS [max 2DS]
- 3% [n=1] less myopic by 1DS

45 CL users:

- **38%** progressed ≥ 1 DS
- MR > CR in 37% by 0.5 to 1.5 DS

STABILITY OF REFRACTION IN ADULT MYOPIA

Bullimore...OhioSU.. IOVS 2002

- Manifest refraction in 291 CL wearers age 20-40 over 5y
 - Baseline $-3.3 \text{ DS} \pm 2$, age $28 \pm 5\text{y}$
 - **21% progressed** by $\geq 1 \text{ DS}$ over 5y
 - ROMP decreased with increasing age $p=0.006$
 - Progressorscf non-progressors:
- independent of h/d of reading/ writing, computer use, education level, FH myopia, age onset myopia, age CL wear

Oculometry findings in high myopia at adult age: considerations based on oculometric follow-up data over **28 years** in a cohort-based Danish high-myopia series. [Fledelius HC](#), [Goldschmidt E](#). ActaOphthal 3/2009

...adults with high myopia followed between the ages of 26 and 54 years.

Myopia increased in **most** , average 1.0 D [\pm 1.84].

Ultrasound measurements over the 28 y:
correlation between axial eye elongation and myopia progression ($r = 0.65$).

Many eyes with high myopia had steeper corneas than expected

ADULT MYOPES

Some / many have modest
increases in their myopia

Rate Of Myopia Progression

- Number / complexity of proposed explanations of myopia progression proportional to the imagination and IQ of the investigators
- Number of trials to try and decrease the Rate Of Myopia Progression exceeded only by the persistence of the investigators

PREVENTING MYOPIA PROGRESSION: MECHANISM

*Many Interesting Innovative and Credible
Theories – no proof*

1. disruption of emmetropisation
2. form deprivation
3. optical defocus – central, peripheral
4. excessive accommodation
5. incremental retinal defocus theory
Hung & Ciuffreda ARVO 01
6. abnormal scleral collagen

MECHANISM

Genetic aspects

Many different genes

Will there be a phenotype / genotype correlation?

? Each genetic type of myopia has a **UNIQUE MECHANISM / ROMP / RESPONSE TO DIFFT TREATMENTS**

Hong Kong

? 90% incidence of myopia

Genetic influences less credible

MAINSTREAM TREATMENTS TO ARREST MYOPIA

OPTICAL

1. ↓ duration of spectacle wear
2. planned under correction
2. Bifocals / PALs
3. contact lenses / orthoK

PHARMACOLOGICAL

4. *atropine / pirenzepine*
5. ocular hypotensives
6. 7-methylxanthine

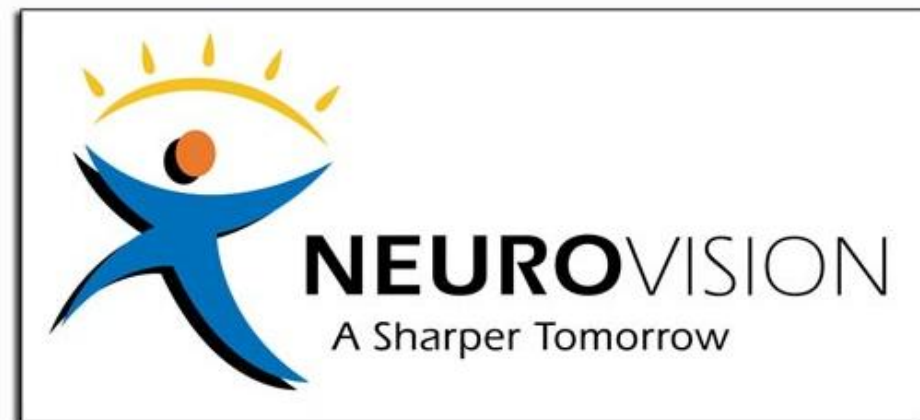
NON- MAINSTREAM TREATMENTS TO ARREST MYOPIA

OFFICE BASED

1. HELMHOLTZ – trans-scleral laser with infrasound pneumatic massage and 2,5% phenylephrine drops
2. EnergieEyrelax – franchises available
3. NeuroVision - franchises available

SURGERIES

1. Scleral reinforcement USSR, USA
2. Implantation of placenta & injections of extracts from whole eyes
(Vance et al, Bull, et mem. Soc. Franc.Opht., 82:507-24, 1970).



IDEAL STUDY FOR Rx TO REDUCE ROMP

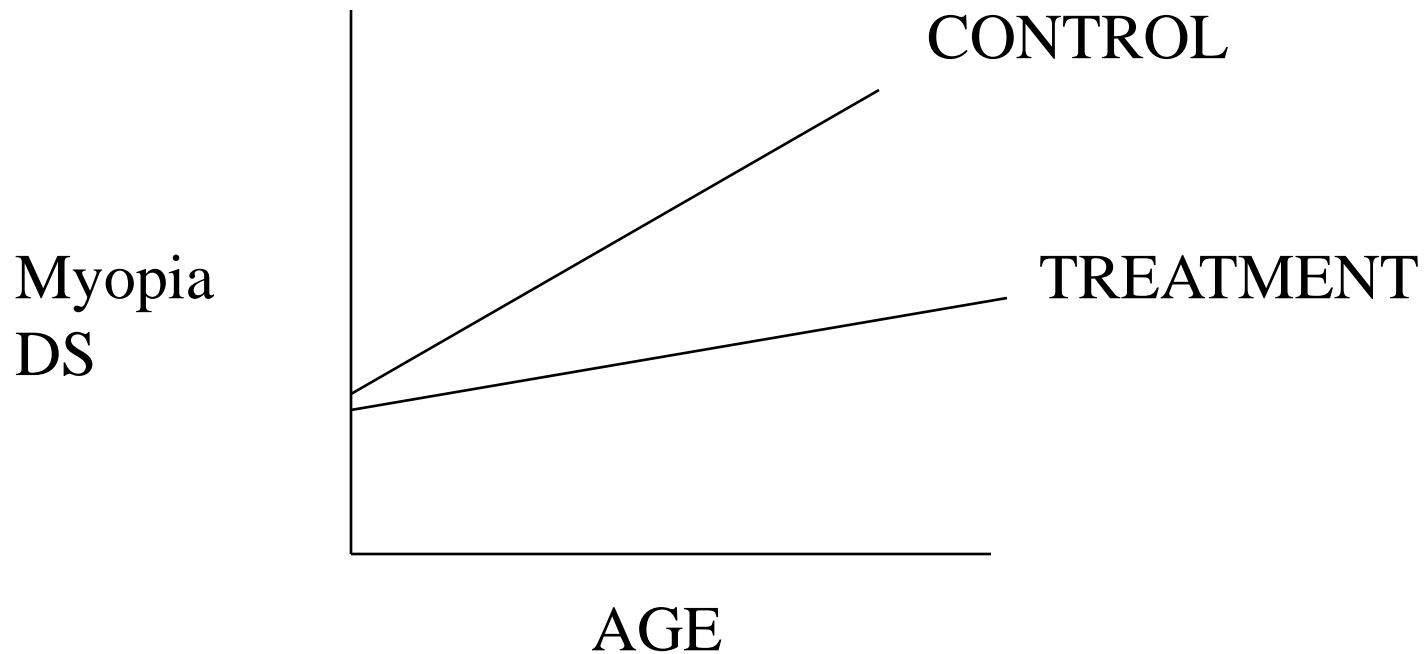
Prospective Randomised Double blind

? Monocular control [systemic absorption]

*Determine optimal timing & duration of Rx

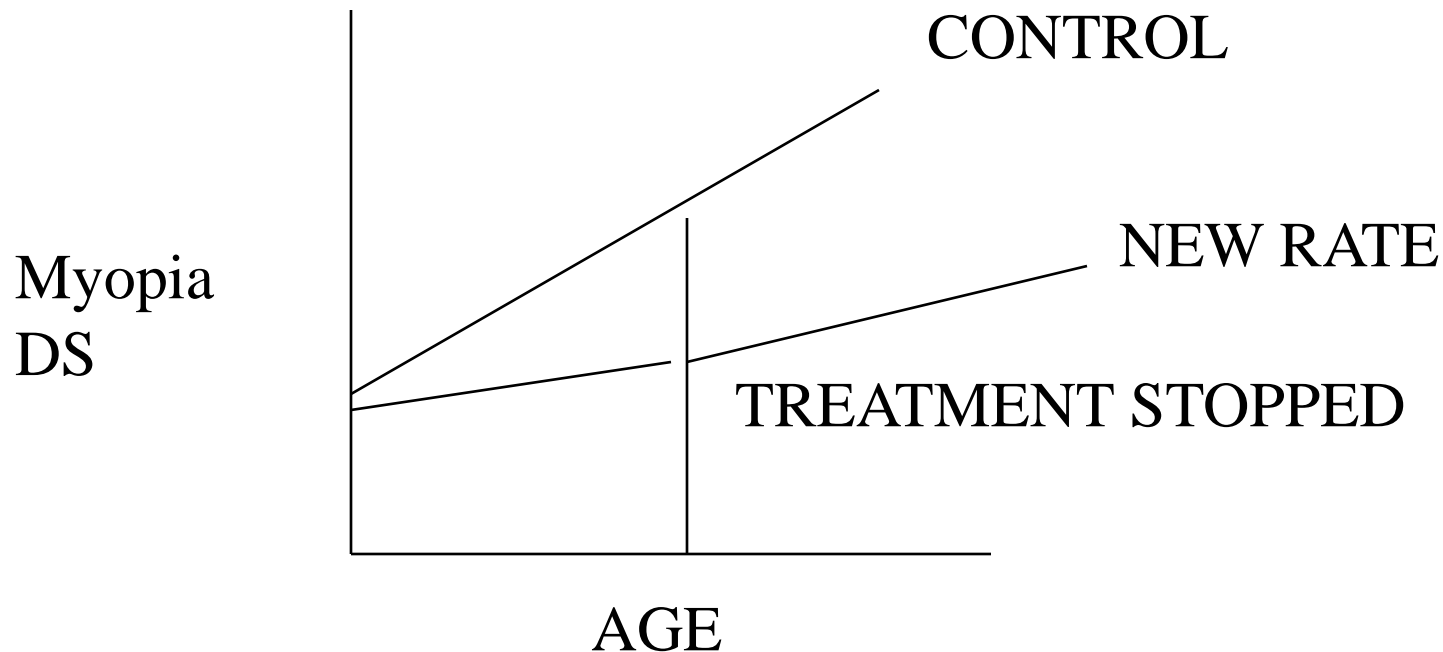
**Detect catch-up after stopping Rx

APPARENTLY EXCELLENT RESULT



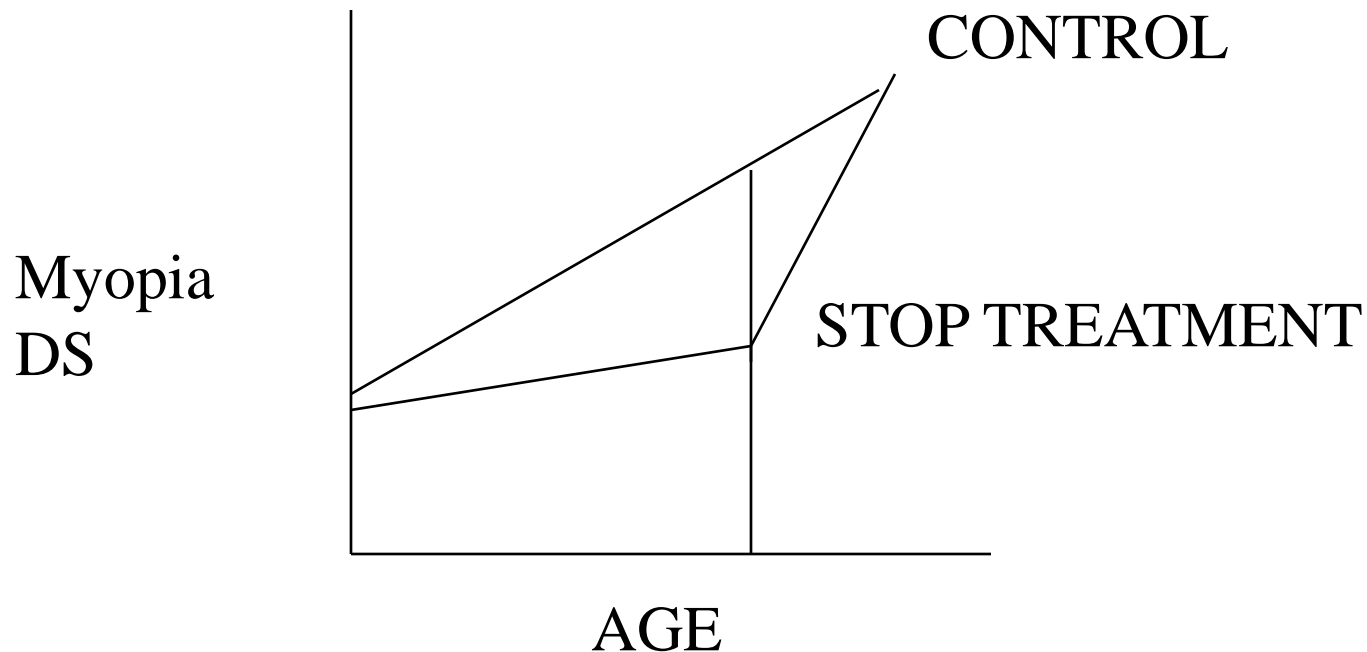
EXCELLENT RESULT

AFTER STOPPING Rx, ROMP @
'NEW' [LOWER] RATE



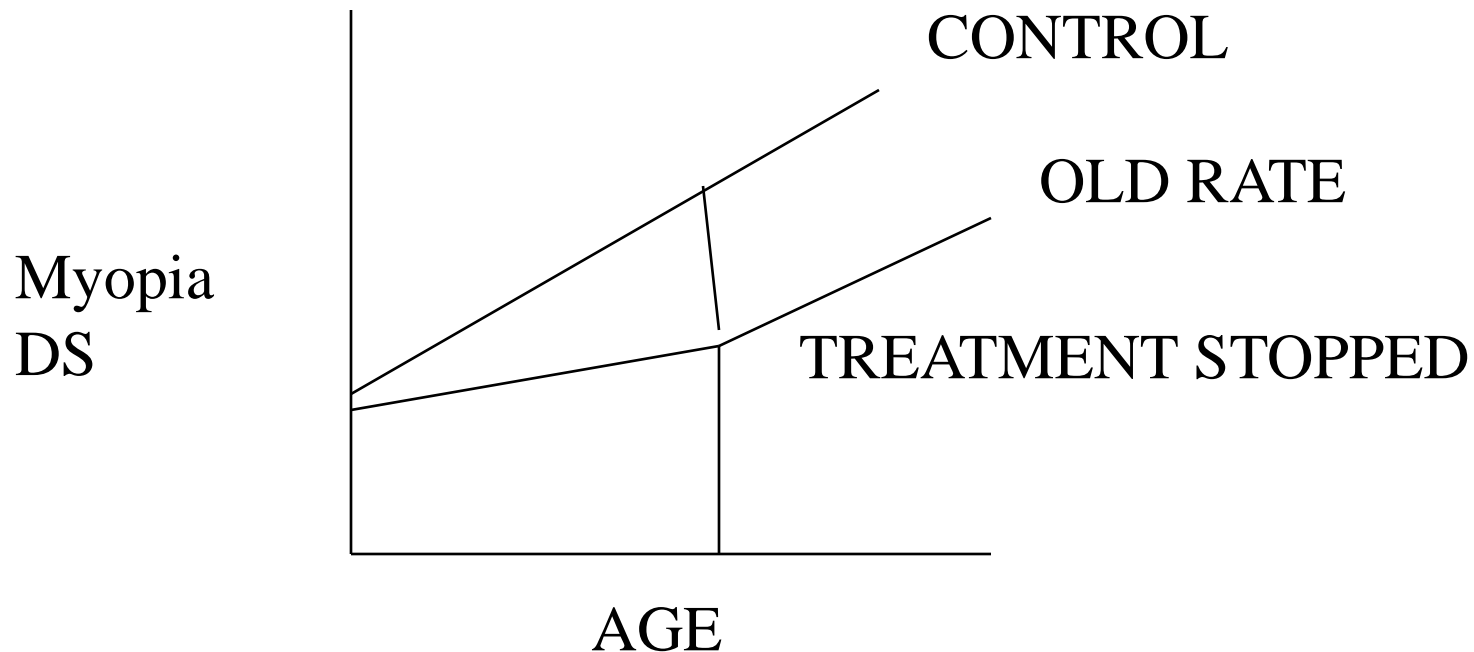
SIMULATED EXCELLENT RESULT-1

CATCH UP ON STOPPING Rx



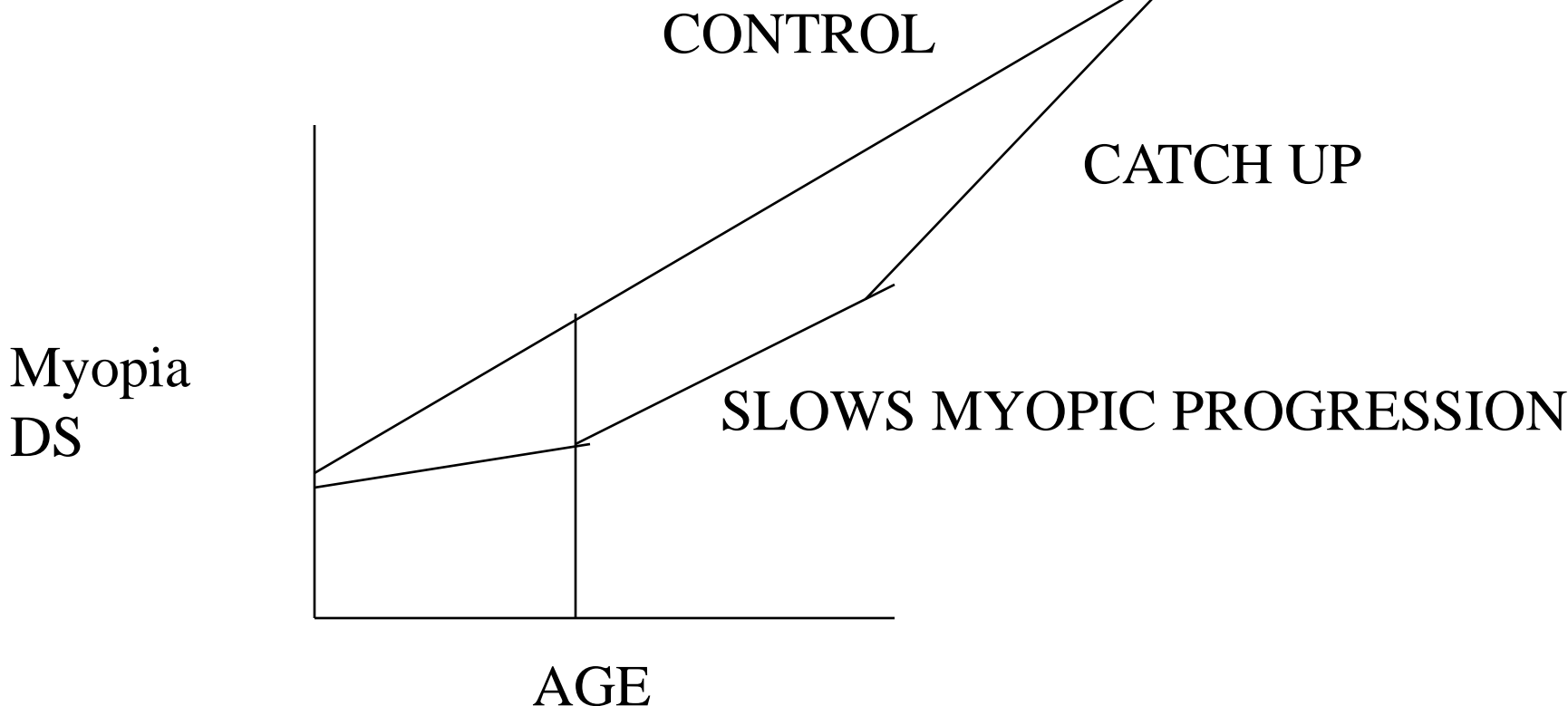
SIMULATED EXCELLENT RESULT- 2

AFTER STOPPING Rx,
ROMP @ 'OLD' [control] RATE

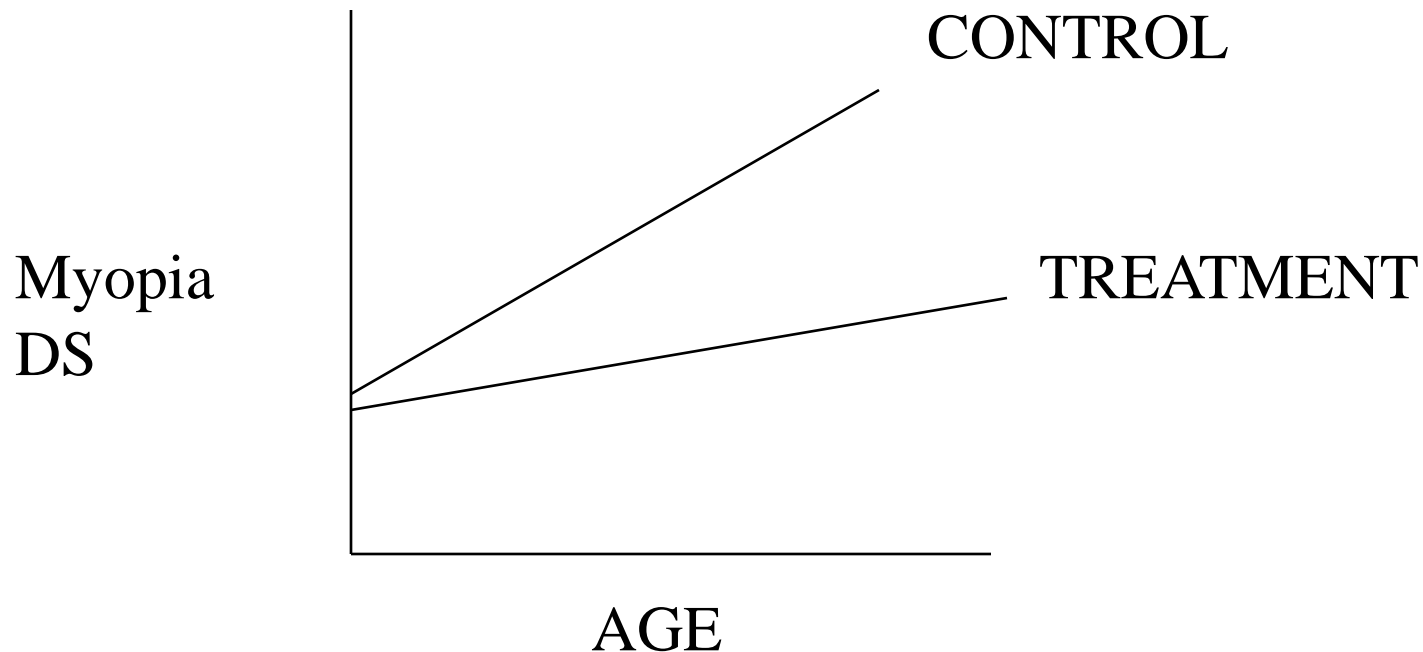


SIMULATED EXCELLENT RESULT-3

Rx SLOWS ROMP. MYOPIA CATCHES UP
DESPITE CONTINUING / AFTER STOPPING Rx



APPARENTLY EXCELLENT RESULT :
EASILY SIMULATED
**MUST HAVE GOOD & LONG
FOLLOWUP**



STUDY QUESTIONS

- 1. CONTROL GROUP
- 2. DURATION OF TREATMENT
- 3. DURATION OF FOLLOW UP

....ANY OTHER CRITERIA

- ***4. DATA AFTER TREATMENT STOPPED***

TREATMENTS TO ARREST MYOPIA

OPTICAL

1. ↓ duration of spectacle wear
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PHARMACOLOGICAL

4. *atropine / pirenzepine*
5. ocular hypotensives

OPTICAL Rxs

Saw : BJO, Ophthalmology 2002

1. < full time wear of full Rx
2. Under correction
3. B-F & PALs

< FULL TIME WEAR #1

Saw, BJO 2002

NRCT N= 43 3y

a. full time specs wear

b. wear for distance → full time

c. wear for distance

d. non wear

RESULT: Non Significant differences

< Full time wear #2

NMRCT Finland n= 240 9-11y f/u: 3y

a. SV, full correc, cont use

b. SV, full correc, distance only

c. Bifocals

RESULT: ROMP: Non Significant differences

Planned undercorrection / 1

Straub: Fully correc / Under correc

ROMP: NS

Tokoro and Kabe:

Fully corrected $-0.83\text{D}/\text{y}$

Under corrected $-0.47\text{D}/\text{y}$

$p < 0.01$

Planned undercorrection /2

CHUNG...O'LEARY VIS RES 2002

CHILDREN UNDERCORRECTED BY -0.75

SMALL [STATS SIGN] *INCREASE* ROMP OVER 2y

0.25D *GREATER* THAN FULLY CORRECTED

BIFOCALS / PALs

Saw BJO 2002

3 well designed RCT

USA, DENMARK, FINLAND

Bifocals +1 to +2 adds

Sample sizes 32-240

Result : Non Significant differences

PALS - Non Significant differences

Leung and Brown Hong Kong

36: +1.5 - +2 add. ROMP -3.67 to -3.73D.

32: SV. ROMP -3.67D.

Shih and colleagues Taiwan

227 6-12y

PALs -1.19D/y. SV -1.40D/y.

CORRECTION OF MYOPIA EVALUATION TRIAL (COMET) PALs vs. SV

IOVS 2003

3 y. N= 469. age 6-11y

MULTICENTRE USA RANDOMISED

DOUBLE MASKED. SE -1.25 to -4.50

PALs

Slight \downarrow ROMP, AL, # of Rx changes

RECOMMENDATIONS

Effects too small to change your current routine

CORRECTION OF MYOPIA

Multifocal CLs vs. glasses

Howell:

CLs retard ROMP more than glasses

The effectiveness of progressive addition lenses on the progression of myopia in Chinese children

Ophthalmic Physiol Opt. 2009 Jan;29(1):41-8.

[Yang Z](#), [Lan W](#), [Ge J](#), [Liu W](#), [Chen X](#), [Chen L](#), [Yu M](#). Guangzhou, China.

- 178 Chinese juvenile-onset acquired myopes (aged 7-13 years, -0.50 to -3.00 D spherical refractive error), who did not have moderately or highly myopic parents.
- 149 (75 in SV and 74 in PAL) completed the 2-year study.
- The myopia progression (mean +/- S.D.) in the SV and PAL groups was -1.50 +/- 0.67 and -1.24 +/- 0.56 D, respectively.
- This difference of 0.26 D over 2 years was statistically significant ($p = 0.01$).
- The lens type ($p = 0.02$) and baseline spherical equivalent refraction ($p = 0.05$) were significant contributing factors to myopia progression.
- Mean increase in the depth of vitreous chamber * was 0.70 +/- 0.40 and 0.59 +/- 0.24 mm, respectively. This difference of 0.11 mm was statistically significant ($p = 0.04$).
- Age ($p < 0.01$) was the only contributing factor to the elongation of vitreous chamber.
- Different near phoria ($p < 0.01$) and gender ($p = 0.02$) caused different treatment effects when wearing SV lenses. However, there were no factors found to influence the treatment effect of wearing PALs.
- CONCLUSIONS:
 - **ROMP was found to be retarded by PALs to some extent in Chinese children without moderately or highly myopic parents**, especially for subjects with near esophoria or females.
- * reported by Neville McBrien Acta Ophthalmologica 1987

Myopia Progression in Children Wearing Spectacles vs. Switching to Contact Lenses.

- Optom Vis Sci. 2009
- [Marsh-Tootle WL, ...Gwiazda J](#), [COMET]
- **No clinically significant difference in ROMP**

SUMMARY

< Full time wear / undercorrection

>5 STUDIES

MOST NOT SIGNIFICANT

2 SIGNIFICANT :

1 ROMP WORSE!

SUMMARY

BIFOCALS & PALs

>9 studies : NS

~2-3 PAL studies: Stats Significant

All clinically insignificant

ATROPINE

EASILY UNDERSTOOD EFFECT:

Muscarinic antagonist → blocks accommodation

If Xs accom → ↑ axial length, Atropine may block this

Non – Accom Effects [McBrien]:

* Affects dopamine release ?influence retinal signals ?control eye growth

* Suppresses GH

ATROPINE STUDIES

BEDROSSIAN

Ophthalmology 1979 n = 62

1% Atropine hs ONE eye for 12 mo.

Fellow eye treated in Y2 [previously
Rx'd eye now control].

Atropine: ↓ ROMP

**Post Atropine: ROMP @ 'new' [lesser]
rate**

ATROPINE STUDIES

KENNEDYMAYO

Transactions AOS 1995

Olmsted county study

Excellent review of older literature
on ROMP

Mayo Clinic study

KENNEDYMAYO

Transactions AOS 1995

Olmsted county study

N=214. Median age 11y, R6-15

Duration 3.5y [18w to 11.5y]

Follow up 11y

**ROMP Atropine: 0.05DS/Y,
Control 0.36 DS/Y [p<0.001]**

ATROPINE STUDIES

RCT X3 TAIWAN

At **0.1** to 1%

Result: ROMP significantly ↓

Lower % better tolerated

ATROPINE & B-F BRODSTEIN

OPHTHALMOLOGY 1984

n = 253. 1% Atropine od.

9y f/up.

↓ ROMP during Rx

ROMP after Rx = Control group

ROMP fastest age 8 -12

ATROPINE & B-F UCLA

BVQ 2002

15 Myopes / 15 control

Atropine 1% OU mean 29m [3-96]

ROMP:

Atropine : 0.05D Controls : 0.84D

p = 0.00021!!

Using same pair of glasses [months]:

Atropine : 25.1 (+/-19.3)

Control: 13.5 (+/-10.3) p = 0.049

ATROPINE & B-F WILMER

CASE SERIES RETRO / INTER / NON COM

n = 706 age 6-16 y

B-F : full cyclo / +2.25 add

Atropine 1% 1/w. 3w - 10 y

Result: 496 Fully Compliant. 210 Partly

ROMP:

F/ Compliant 0.08D / y. Partly 0.23D / y

p < 0.001 !!

ATOM STUDY

ARVO 2003 CHUA [SINGAPORE]

RANDOMIZED / DOUBLE MASKED / PLACEBO CONTROLLED

n=400 -1D to -6D 6-12 y

1% Atropine Control: Isoptotears 1/d

F/U: 4 monthly for 2 y. 90% @ 12mo, 80+% @ 2y

Cyclo ref / axial length CR / AL

ATOM STUDY #2: RESULTS

12 mo: CR C: $-0.76D$. Atropine : $+0.3D$!!

AL: C: $+0.2$ mm. Atropine reduction 0.14 mm

2yrs : CR / AL

C: $-1.20D$ / $+0.38$ mm

At $-0.25D$ / AL unchanged from baseline

$p < 0.0001$ @ 12 mo & 2 y

myopia progression after cessation of atropine.

Ophthalmology. 2009 Mar;116(3):572-9.

[Tong L](#), [Huang XL](#), [Koh AL](#), [Zhang X](#), [Tan DT](#), [Chua WH](#), SNEC

Subjects were followed up for 12 mo after stopping treatment [either 1% atropine or vehicle eyedrops once nightly for 2 y]. Only 1 eye of each subject was chosen through randomization for treatment.

RESULTS: **After cessation of atropine drops, the mean progression in the atropine-treated group was -1.14 ± 0.80 D over 1 year, whereas the progression in placebo-treated eyes was -0.38 ± 0.39 D ($P < 0.0001$).**

After 3 y of participation in the trial (with 2 years on atropine treatment), **eyes randomized to atropine have less severe myopia than other eyes.** Spherical equivalent was -4.29 ± 1.67 D in the atropine-treated eyes compared with -5.22 ± 1.38 D in the placebo-treated eyes ($P < 0.0001$).

Spherical equivalents in atropine-untreated and placebo-untreated eyes were -5.00 ± 1.62 D and -5.28 ± 1.43 D, respectively.

Over the 3 years, the increase in axial length of the atropine-treated eyes was 0.29 ± 0.37 mm compared with 0.52 ± 0.45 mm in the placebo-treated eyes ($P < 0.0001$)

PIRENZEPINE

Selective M1subtype muscarinic antagonist

Animal studies:

blocks \uparrow AL 2^o to form deprivation

PIRENZEPINE #1

ARVO 2003 SIATKOWASKI

MULTICENTRE RCT n=13 USA

N = 174 8-12 y Rx / C : 2:1

BD for 12 mo

ENTRY : BCVA 20/25 or better

REF ERROR -0.75 to -4.00 D SE

CYL ≤ 1 D

PIRENZEPINE #1 RESULTS

OUTCOME : CYCLO A/REF @ 12 mo

Entry Ref Error: PIR -2.10; C -1.93

ROMP: PIR -0.26D; C -0.53D $p < 0.001$

2% PIR >1D Myopic progression @ 12 mo

20% C > 1D Myopic Progression @ 12 mo

$p < 0.001$

PIR 11% withdrew; C: 0%.

PIRENZEPINE : STUDY #2

1yr Asian Trial

353 children 6-12 y

a. PIR bd

b. Placebo morning+ PIR Evening

c. Placebo bd

Ref error / AL

PIRENZEPINE – ASIA /2

ROMP @ 12 mo

- a. -0.40D (PIR bd)
- b. -0.70D (PIR 1/d)
- c. -0.80D (C)

a / b : $p < 0.001$

a / c : $p < 0.001$

b / c : NS

PIRENZEPINE – ASIA /3

AXIAL LENGTH

- a. +0.21mm (PIR bd)
- b. +0.30mm (PIR 1/d)
- c. +0.33mm (C)

All comparisons NS

OCULAR HYPOTENSIVES

↑ IOP → stretch sclera ↑ axial length ↑ myopia

Labetolol / Timolol

Several studies : no Controls, not randomised

Danish study 150 child. 0.25% timolol [2y]

ROMP: Timolol -0.59D/y

Single vision -0.57D/y

SUMMARY

PHARMACOLOGICAL STUDIES

1. ATROPINE many studies

Most : Stats significant

One study : post Rx ROMP @ reduced 'new' rate

2. PIRENZEPINE 2% GEL 2 studies Sig

3. OCULAR HYPOTENSIVES NS

MYOPIA

- 1. Major personal / societal problem
- 2. Convincing data on ↓ ROMP with At / Pir. Need longer f/up.
- 3. No convincing evidence on optical treatments
- 4. ? Genetic segregation first & repeat optical and drug studies

THANKS