



RESEARCH UPDATES IN LOW-DOSE ATROPINE

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DISCLAIMERS

- Low dose Atropine is currently not approved by any regulatory body for myopia control
- Its use is considered off-label and is subject to local regulatory, legal and professional requirements that the ECP must understand and comply with to cover all aspects of off-label prescribing in their country
- Practitioners should obtain their own independent legal and professional advice before they prescribe off-label
- The intent of this presentation is to review published peer reviewed literature of low dose atropine when used in controlled investigational studies
- There is no intention for J&J to promote any off-label use and/or treatment

MYOPIA MANAGEMENT THERAPIES

Delay myopia onset



Lifestyle guidance
(outdoor, breaks from near work)

Slow myopia progression



Myopia control
spectacles



Orthokeratology



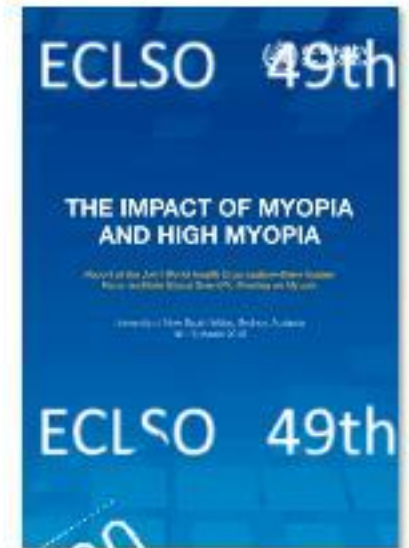
Myopia control soft
contact lenses



Low dose atropine



Combination therapy



WHAT IS ATROPINE?

- An anticholinergic drug derived from the *Atropa Belladonna* plant, commonly known as deadly nightshade¹
- Used systemically as a cardiovascular drug for bradycardia¹
- Used topically in eye care for mydriasis & cycloplegia in uveitis,² pediatric refraction³ & amblyopia treatment⁴



Image from [Woodland Trust UK](#)

1. McLendon K, Preuss CV. Atropine. [Updated 2021 Sep 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/3470551/>

2. Babu K, Manendradas P. Medical management of uveitis - current trends. Indian J Ophthalmol. 2013 Jun;61(6):277-83.

3. Sani RY, Hassan S, Habib SG, Ifeanyiichukwu EP. Cycloplegic effect of atropine compared with cyclopentolate-tropicamide combination in children with hypermetropia. Niger Med J. 2016 May-Jun;57(3):173-7.

4. Scheiman MM, Hertle RW, Kraker RT, Beck RW, Birch EE, Felius J, Holmes JM, Kundart J, Morrison DG, Repka MX, Tamkins SM; Pediatric Eye Disease Investigator Group. Patching vs atropine to treat amblyopia in children aged 7 to 12 years: a randomized trial. Arch Ophthalmol. 2008

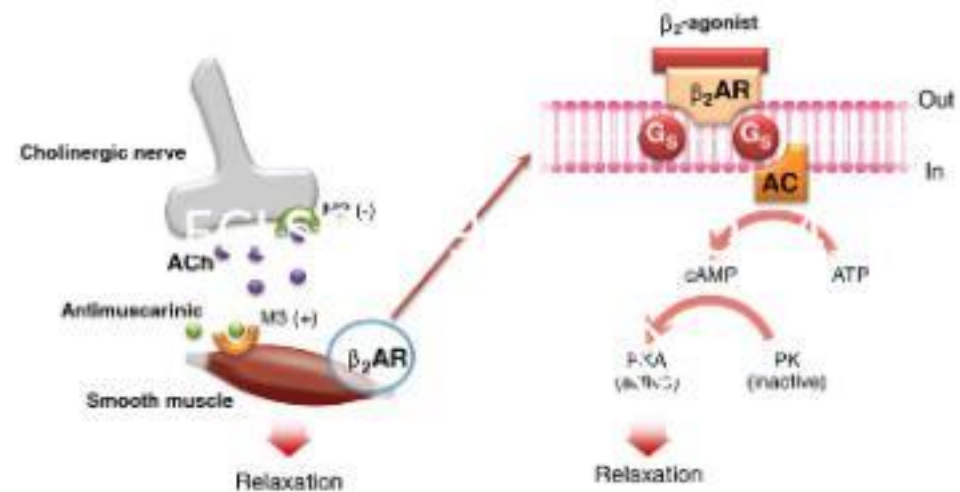
PHARMACOLOGIC ACTION OF ATROPINE

Muscarinic receptors found throughout the eye

- Iris sphincter, iris dilator, ciliary muscle, trabecular meshwork, conjunctival goblet cells.

Mechanism of action in myopia control unknown:


- Thought to act directly or indirectly on sclera via the choroid.
- Unlikely via accommodative pathway



TEN RANDOMISED CONTROL TRIALS (RCT)

Study	Location	Follow-up	Atropine dose %	Age (y)
Yen et al. 1989	Taiwan	12	1	6-14
Shih et al. 1999	Taiwan	24	0.5, 0.25, 0.1	6-13
Shih et al. 2001	Taiwan	18	0.5	6-13
Hsiao et al. 2005	Taiwan	18	0.5	6-13
Chua et al. 2006	Singapore	24	1	6-12
Liang et al. 2008	Taiwan	6	0.25, 0.5	6-15
Chia et al 2012	Singapore	24	0.5, 0.1, 0.01	6-12
Kumaran et al. 2015	Singapore	36	1	6-12
Yi et al. 2015	China	12	1	7-12
Yam et al. 2019, 2020	HK SAR	24	0.01, 0.025, 0.05	4-12

DOSE-RELATED OCULAR ADVERSE EFFECTS



Ocular adverse effect	Low dose atropine 0.01%	Moderate dose atropine > 0.01% to < 0.05%	High dose atropine 0.5% to 1.0%
Photophobia	0%	17.8%	43.1%
Poor near VA	2.3%	11.9%	11.9%
Allergic conjunctivitis	0%	2.9%	3.9%
Other (chalazion & systemic effect)	4.8%	11.0%	11.2%

1. Liang Q, Janiszewski J, Liu M, et al. Efficacy and Adverse Effects of Atropine in Childhood Myopia: A Meta-analysis. JAMA Ophthalmol. 2017;135(5):624-630. doi:10.1001/jamaophth.2017.1051

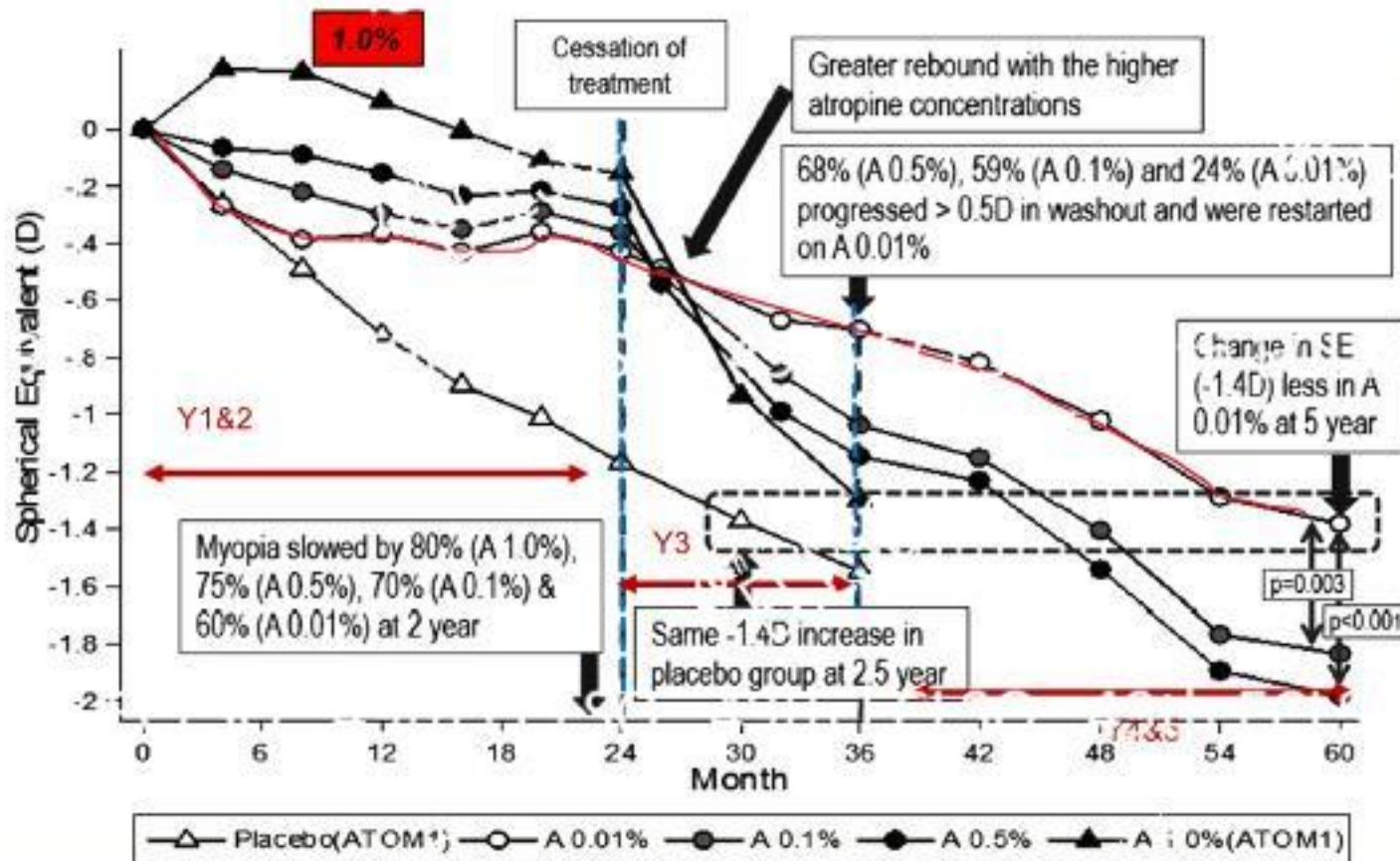
2. Shih KC, Chan TC, Ng AL, et al. Use of Atropine for Prevention of Childhood Myopia Progression in Clinical Practice. Eye Contact Lens. 2016;42(1):16-23. doi:10.1097/ICL.0000000000000189

THE ATOM2 FIVE-YEAR STUDY



Original Article
Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.1%, 0.01%, and 0.001% Doses (Atropine for the Treatment of Myopia 2)

Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2: Myopia Control with Atropine 0.01% Eye Drops. Ophthalmology. 2016 Feb;125(2):391-399.



0.01%

0.1%

0.5%

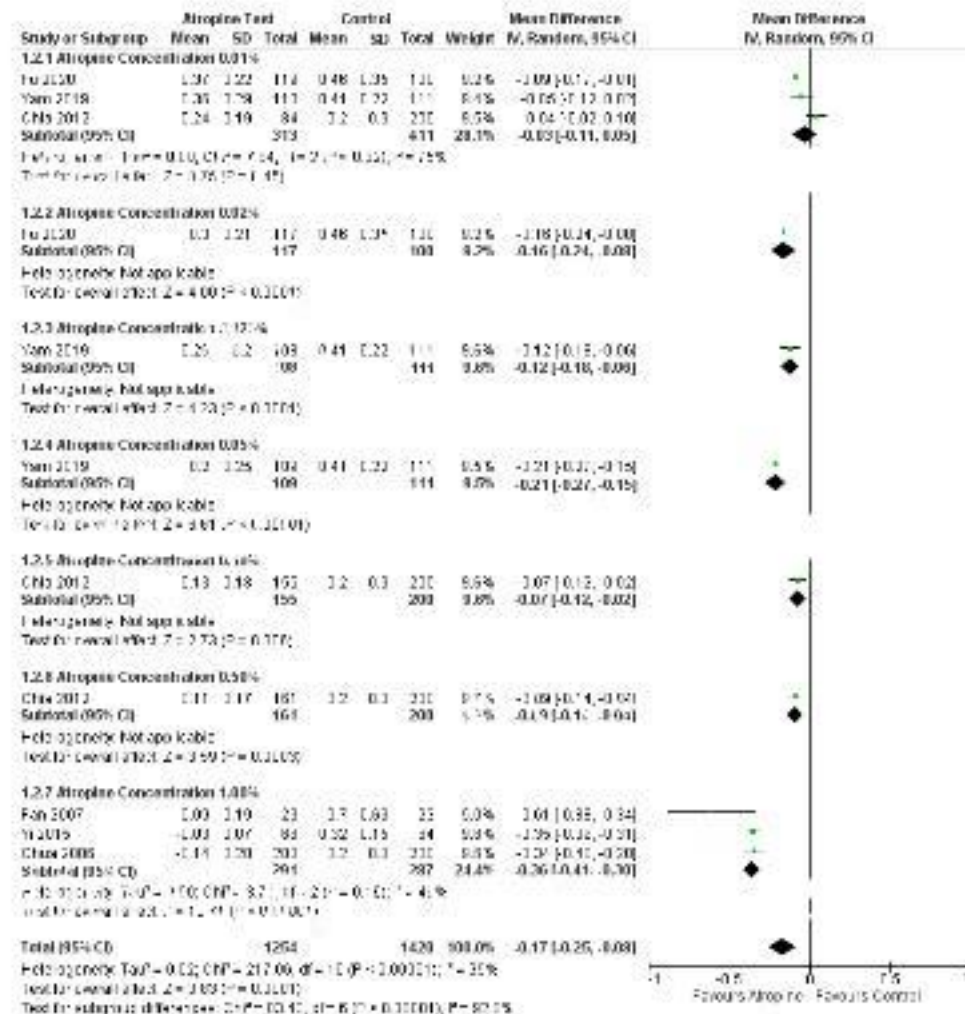
AXIAL ELONGATION

Peer Review Article

A Meta-Analysis Assessing Change in Pupillary Diameter, Accommodative Amplitude, and Efficacy of Atropine for Myopia Control

Hoang D.M. Tran, MD, PhD^{1,2*}, Thinhua S. Le^{1,2,3,4}, Doan B. Nguyen, PhD⁵,
Thuanh Nhatvuthi, PhD⁶, Phuc T.T. Luu, MD⁷, Tuan D. Tran, MD, PhD⁸,
Minh Anh, MD, PhD⁹, Minh C. Luu, MD, PhD, and Van H. Tran, MD, PhD¹⁰

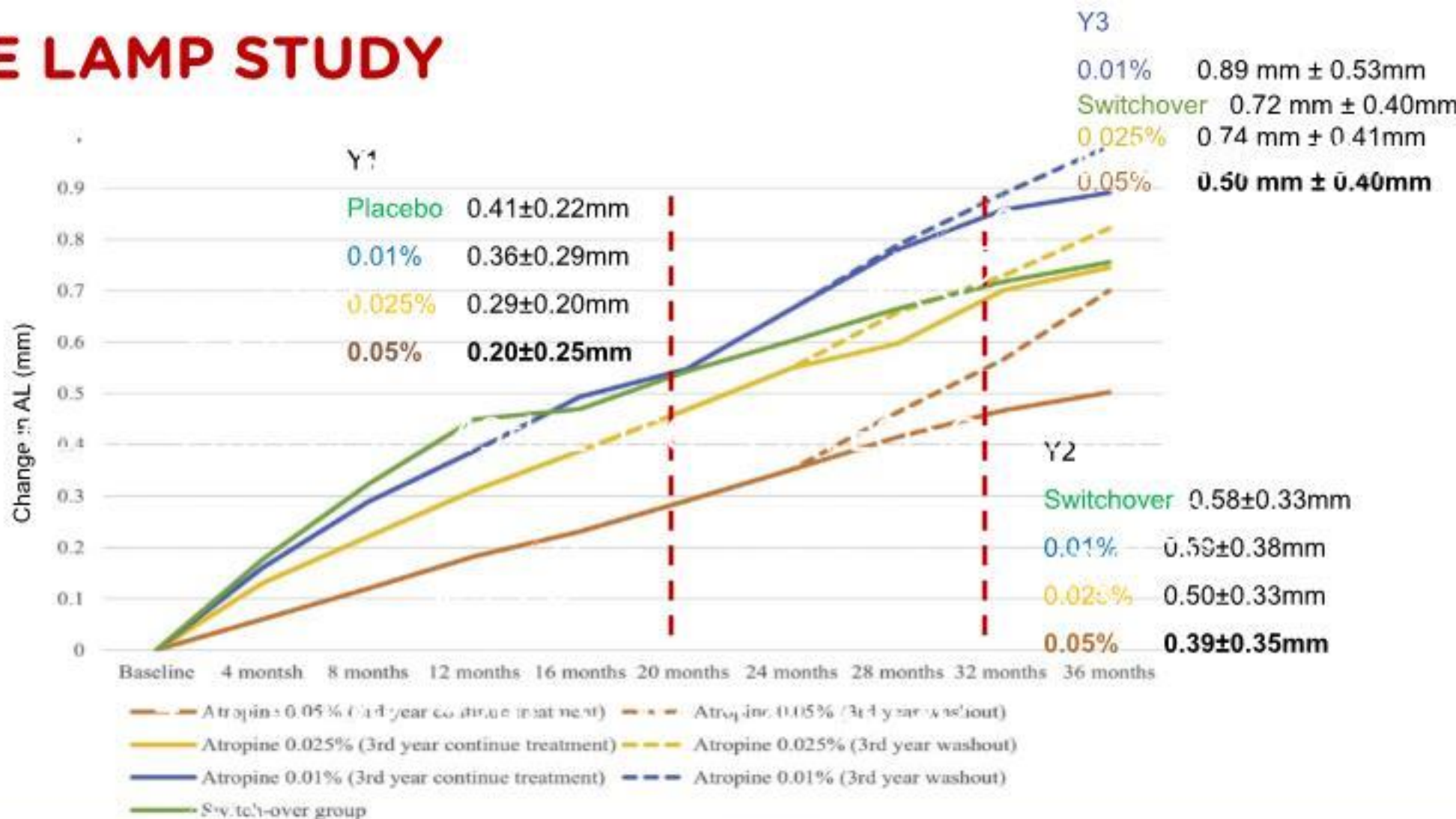
CLSO 49th ECLSO 4
Three well-conducted studies reported minor to insignificant effect of 0.01% atropine on axial elongation



UNSW SYDNEY



THE LAMP STUDY



FREQUENCY OF SIDE EFFECTS: LAMP STUDY



Very few required
a near add < 2%



Photophobia

At 2 weeks :

- 0.05% LDA = 31%
- 0.025% LDA = 19%
- 0.01% LDA = 6%
- Placebo = 13%

At one year:

- 2-7% across the groups
- not concentration dependent

HOW EFFECTIVE IS LOW DOSE ATROPINE?



Efficacy Comparison of 16 Interventions for Myopia Control in Children

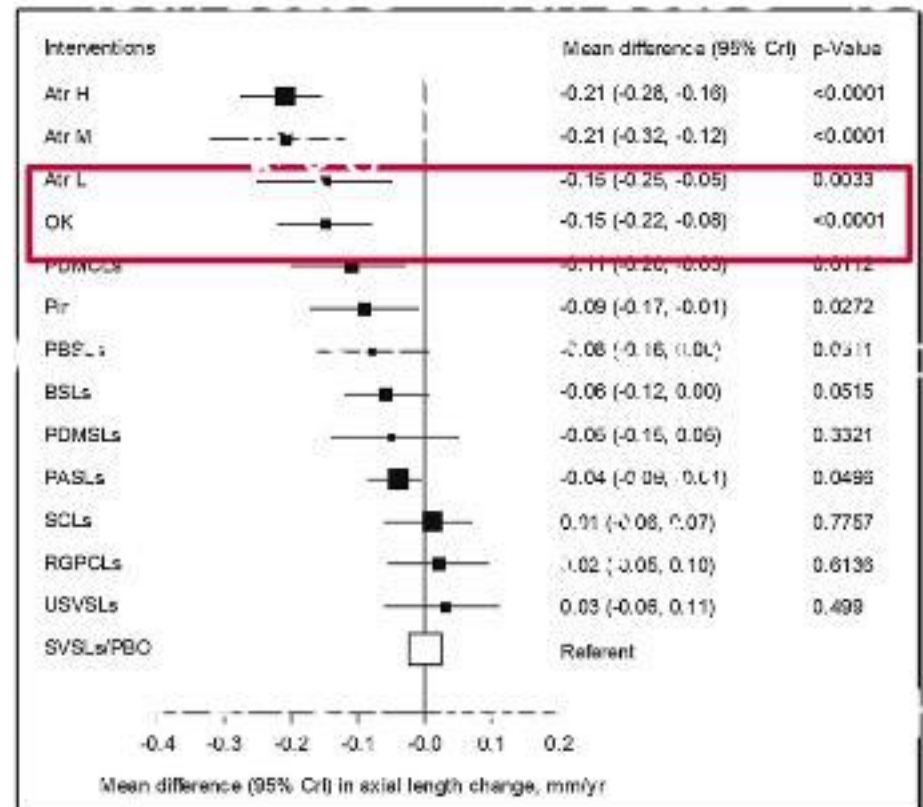
A Network Meta-analysis

Yin H, Huang J, Wang Q, Wang W, Chen H, Saw SM, Chen H, Bao F, Zhao Y, Hu L, Li X, Gao R, Lu W, Zhang Z, Jiang Q, Yu Y, Gu J. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. *Ophthalmology*. 2016 Apr;123(4):697-706. doi: 10.1016/j.ophtha.2015.11.010. Epub 2016 Jun 23. PMID: 26826749

Purpose: To determine the effectiveness of different interventions to slow down the progression of myopia in children.

- AL -0.15 mm / year
- - 0.40D

Both low-dose atropine and OK are similar in effectiveness



EARLY EVIDENCE: ATROPINE 0.01% IN COMBINATION TREATMENTS

Interval (months)	Axial elongation Mean \pm SD (mm)		p-value
	AOK n=34	OK n=35	
6	-0.02 \pm 0.10	0.07 \pm 0.08	< 0.001
12	0.08 \pm 0.08	0.11 \pm 0.09	0.309
18	0.04 \pm 0.07	0.08 \pm 0.07	0.044
24	0.06 \pm 0.07	0.08 \pm 0.07	0.090
FINAL	0.17 \pm 0.19	0.35 \pm 0.20	< 0.001



Ortho-k: significant additive effect¹⁻³



Centre distance MF +2.50 Add: no additive effect⁴

Pupil size larger in AOK group

- Δ 0.39mm (mesopic)
- Δ 0.55mm (photopic)

contactlens & ANTERIOR EYE BCLA

FULL LENGTH ARTICLE | ARTICLES IN PRESS, 101723

Combined 0.01% atropine with orthokeratology in childhood myopia control (AOK) study: A 2-year randomized clinical trial

Qi Tan, Alex LK Ng, George PM Cheng, Victor CP Woo, Pauline Cho

Published: May 31, 2022 • DOI: <https://doi.org/10.1016/j.clae.2022.101723>

1. Tan Q, Ng AL, Cheng GP, Woo VC, Cho P, Cheng PM, et al. Efficacy of combined orthokeratology and 0.01% atropine in childhood myopia control (AOK) study: A 2-year randomized clinical trial. *Cont Lens Contact*. 2022 May;50(10):25.
 2. Khoshdeli R, Kozani Y, Hamedani N, Karimi Y, Karimi M, Karimi T, Kabayashi A. Efficacy of combined orthokeratology and 0.01% atropine in childhood myopia control: a 2-year randomized trial. *Sci Rep*. 2020 Jul 29;10(1):12790.
 3. Wan L, Wei C-G, Chen C, Zhang C-Y, Liu C. The synergistic effects of Ortho-Keratology and Atropine in Slowing the Progression of Myopia in Children: A 2-Year Randomized Clinical Trial. *Optom*. 2019;90(11):28-33.
 4. Jang JH, Muo DQ, Jones-Jonker LA, Walker J. The Effect of Adding 0.01% Atropine with Soft PMMA Contact Lenses on Myopia Progression in Children. *Optom*. 2022 May;93(5):424-442.

CONCLUSION

The recent LAMP¹ study suggests that:

- monotherapy 0.05% atropine may be more clinically effective in slowing axial elongation in myopia with minimal adverse effects¹
- monotherapy 0.01% is not clinically effective in slowing axial elongation¹

Early studies suggest combination therapy enhances myopia control²

- 0.01% combined with ortho-k

Further work is needed to understand the mechanism by which atropine slows eye growth, & optimum dose



1. Yam JC, Zhang XJ, Zhang Y, Wang YM, Tang SM, Li FF, Kam KW, Ko ST, Yip BHK, Young AL, Tham CC, Chen LJ, Pang CP. Three-Year Clinical Trial of Low-Concentration Atropine for Myopia Progression (LAMP) Study: Continued Versus Washout: Phase 3 Report.

2. Tan Q, Ng AL, Cheng GP, Woo VC, Cho P. Combined 0.01% atropine with orthokeratology in childhood myopia control (AOK) study: A 2-year randomized clinical trial. Cont Lens Anterior Eye. 2022 May 30:101723.