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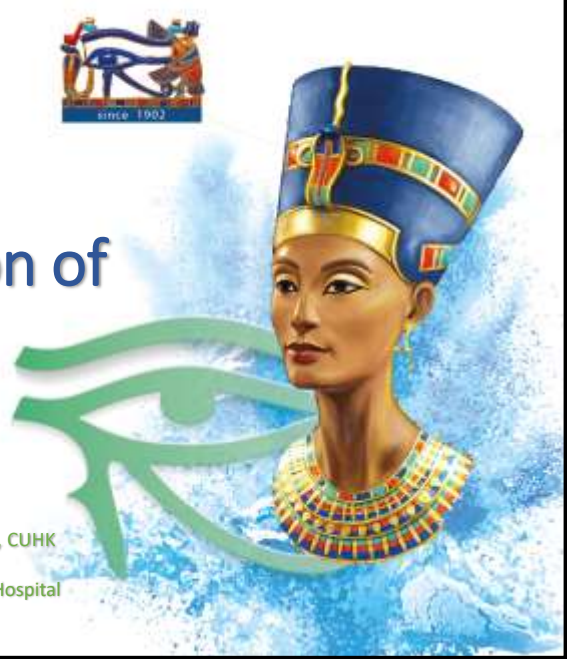

# Atropine for Prevention of Myopia Progression

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Chair of Education Committee & Myopia Committee, IPOSC

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## Disclosure

I have no financial interest to disclose



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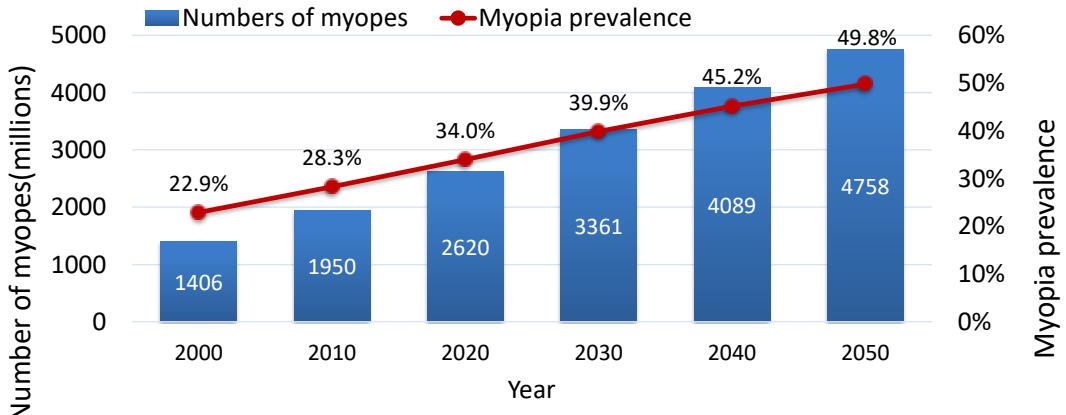
# Global Prevalence of Myopia




1. Nearly 50% of world's population myopic by 2050 [1]
2. Major public health concern, heavy health and economic burden [2]

[1] Holden, BA. et al. ***Ophthalmology.*** **2016**
[2] Holden, B. et al. ***Eye(Lond).*** **2014**

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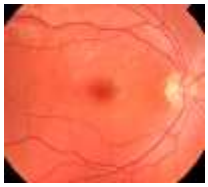
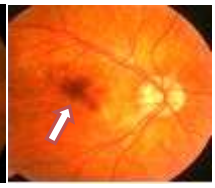
# Complications of Myopia

**Elongation of eyeball → Complications → Visual impairment (even blindness)**

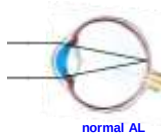
| Complications | High myopia (≤ -6.0D) OR | Moderate myopia (-6.0 to -3.0D) OR | Low myopia (-3.0 to -0.5D) OR |
|---|---|---|---|
| Myopic Macular degeneration | **850** | 73 | 14 |
| Retinal detachment | **13** | 9 | 3 |
| Cataracts | 5 | 3 | 1.5 |
| Glaucoma | 3 | 3 | 1.5 |

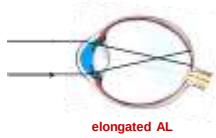

normal retina


retinal detachment


macular hemorrhage

| Axial length (AL) | Visual impairment by 60 years old |
|---|---|
| <24 mm (normal) | 1 (reference) |
| 24 – 26 mm (below -6D) | OR 0.7 (0.3 to 1.5) |
| 26 – 28 mm (-6D to -12D) | OR 3 (1.3 to 7.5) |
| 28 – 30 mm (-12D to -18D) | OR 10 (3.0 to 31) |
| >30 mm (over -18D) | **OR 100** (38 to 228) |


normal AL


elongated AL

Haarman et al. ***Invest Ophthalmol Vis Sci.*** **2020**
Wu et al, ***Asia-Pacific Journal of Ophthalmology***. **2016**

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## Our work on Myopia Prevention starts at childhood

**1. Hong Kong Children Eye Study**
Territory-wide, risk factors, lifestyle, parenting style, public education, community service

**2. Hong Kong Children Eye Genetics Study**
Biobanks, GWAS, WGS / WES for myopia genes for precision medicine

**3. Low-concentration Atropine for Myopia Progression (LAMP) Study**
Randomized controlled trial to establish the efficacy and safety of low concentration atropine to prevent myopia

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## Hong Kong Children Eye Study
## Hong Kong Children Eye Genetics Study

1. **Hong Kong Children Eye Study 香港兒童眼科計劃** (5000 children, 2015-2018)
2. **CUHK Jockey Club Children Eye Care Programme香港中文大學賽馬會瞳心護眼計劃** (30,000 children, 2018-2021)
3. **CUHK Jockey Club Myopia Prevention Programme 香港中文大學賽馬會瞳心童行計劃** (20,000 children, 2021- now)

**Community Impact:**
(a) Children health care through eye care
(b) Family eye care and health care

**Society Impact:**
(a) Proposal on school curriculum to Government Education Bureau
(b) Proposal on children eye screening to Government Health Bureau

**Medical Impact:**
(a) Territory-wide epidemiological data on school children + parents
(b) Biobank of school children + parents
(c) Myopia genetics: one single ethnic group/living environment

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## Hong Kong Children Eye Study

**CUHK Eye Centre 2015-2022 (09:00-18:00 every Saturday/Sunday 100 children 6-8 years + parents)**
**40,000 children + 80,000 parents**

### Comprehensive Ocular Examination by Ophthalmologists and Complete Ophthalmic Investigations

1. LogMAR BCVA
2. Cycloplegic refraction
3. Corneal biomechanics
4. Ocular biometrics (IOL Master)
5. Anterior segment OCT
6. OCT for posterior imaging (SD & SS OCT)
7. Fundus photos and wide field imaging
8. Visual field

### Bio Samples

1. Blood
2. Buccal swab

### Detailed Questionnaires by Nurses

**45 mins face-to-face interview on 7 questionnaires, 350 questions**




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## Hong Kong Children Eye Biobank

1. Hong Kong Children Eye Study (Phase II) (n=40000 (children); n=80000(adult))
2. Hong Kong Children Eye Study : Three-year follow up cohorts (n=3000)
3. Hong Kong High Myopia Cohort (n=1500)
4. Low-concentration Atropine for Myopia Progression (LAMP-1) (n=438)
5. Low-concentration Atropine for Myopia Prevention (LAMP-2) (n=480)

| Cohort Type | Age | Target number |
|---|---|---|
| Kindergarten Cohort | 3 – 5 | 5000 |
| Primary School Cohort | 6 – 8 | 35,000 |
| Parental Cohort | 25 – 50 | 80,000 |
| High Myopia Cohort | 6 – 70 | 1500 |
| Interventional Atropine Cohort | 4 – 12 | 1000 |

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6. **HK Research Grants Council GRF** *14105916, 14100917, 14103221* (CP Pang)
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10. **HK Food and Health Bureau HMRF** *7180256, 5160836* (LJ Chen)
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# Myopia pattern in Hong Kong children

Pre-COVID-19 era | During COVID-19 | Post-COVID-19 era

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# Prevalence of Myopia in Hong Kong

## pre-COVID era

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# High Prevalence of Myopia in Hong Kong (pre-COVID era)

## High Prevalence of Myopia in Children

- Hong Kong has high prevalence of myopia
- Mean age: 7.61 ± 0.97

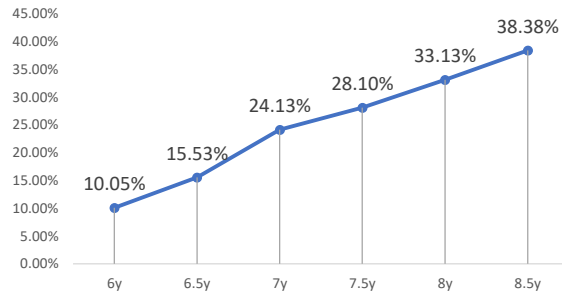
**➢6 years old: 12.7%**
**➢7 years old: 24.4%**
**➢8 years old: 36.1%**


Acta Ophthalmologica

High prevalence of myopia in children and their parents in Hong Kong Chinese Population: the Hong Kong Children Eye Study

**Hong Kong Children Eye Study (n=4257)**

Prevalence of Myopia in Children




Yam JC.. Pang CP. Acta Ophthalmol 2020

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**Lifestyle** is changed by Covid-19 outbreak.

**Myopia** progression increased during this period?

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## Myopia Prevalence and Progression During the COVID-19 Pandemic

JAMA Ophthalmology | Original Investigation

Progression of Myopia in School-Aged Children After COVID-19 Home Confinement

[1]

Jiaxing Wang, MD, PhD; Ying Li, MD, PhD; David C. Musch, PhD, MPH; Nan Wei, MD; Xiaoli Qi, MD; Gang Ding, MD; Xue Li, MD; Jing Li, MD; Linlin Song, [illegible]; Shuo Li, MD, PhD; Xuehan Qian, MD, [illegible]

Reports

COVID-19 Quarantine Reveals That Behavioral Changes Have an Effect on Myopia Progression

Research

JAMA Ophthalmology | Original Investigation

Rates of Myopia Development in Young Chinese Schoolchildren During the Outbreak of COVID-19

Yin Hu, MD; Feng Zhao, MD, PhD; Xiaohu Ding, MD, PhD; Sheng Zhang, MD; Zhouyue Li, MD, PhD; Yangfeng Guo, MD; Zhibin Feng, MD; Xianghua Tang, MD; Qian Li, MD; Lan Guo, MD, PhD; Ciyong Lu, MD, PhD; Xiao Yang, MD, PhD; Mingguang He, MD, PhD

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# Myopia Incidence in Hong Kong Children During Covid-19

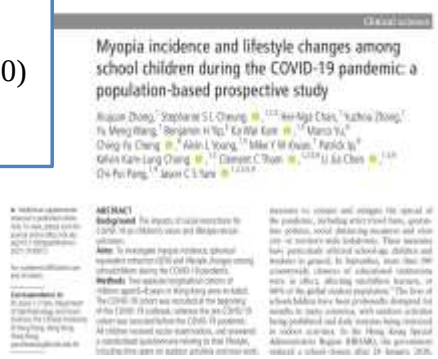




## Myopia Incidence and Progression During the COVID-19 Pandemic

**At the early stage of COVID-19 Pandemic:**
Pandemic control measures in Hong Kong

- School closures (January 25, 2020, to September 22, 2020)
- Flexible work arrangements for employees


Myopia incidence and lifestyle changes among school children during the COVID-19 pandemic: a population-based prospective study

**Research questions:**

Do myopia progression and associated lifestyle changes among schoolchildren during the COVID-19 pandemic?

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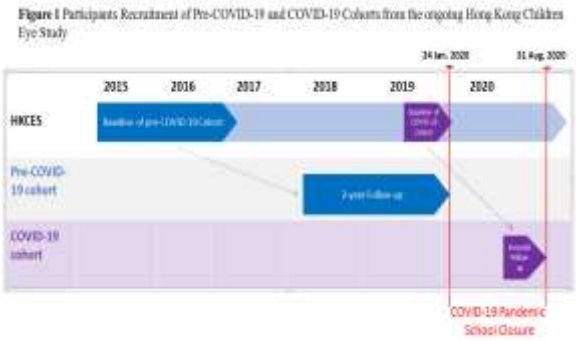
# Myopia Incidence and Progression During the COVID-19 Pandemic

- Study Design: A prospective population-based study
- Two longitudinal cohorts with 1,793 children aged 6 to 8 years old
  a) the COVID-19 cohort: 709 children, 8-m follow-up
  b) the pre-COVID-19 cohort: 1,084 children, 3-year follow-up

- Outcomes:
  1) **Myopia incidence** (new myopia cases during a specified period)
  2) **SE** (spherical equivalent) change
  3) **AL** (axial length) changes
  4) **Lifestyle changes**: time spent outdoors, screen time, and near work time

- **Participants recruited from Hong Kong Children Eye Study**

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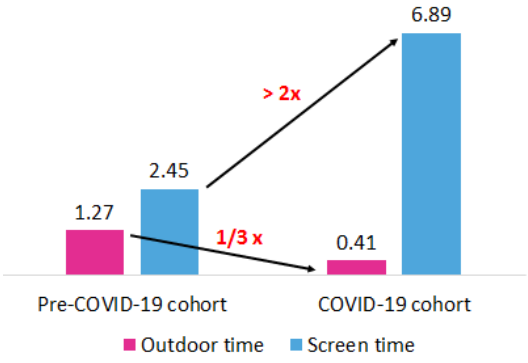
# Myopia Incidence and Progression During the COVID-19 Pandemic

## Lifestyle Change

**Change in outdoor time and screen time during the COVID-19 pandemic (hours/day)**




XJ Zhang,…Pang CP, Yam JC. BJO. 2021

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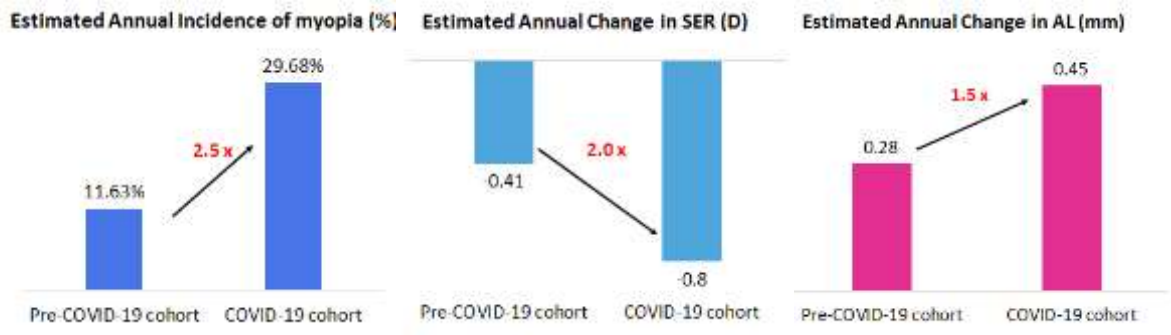
# Myopia Incidence and Progression During the COVID-19 Pandemic

## Increase in Myopia Incidence and Progression




***Lifestyles changed during the COVID-19 pandemic, aggravating myopia and its progression***

XJ Zhang,.... Pang CP, Yam JC. BJO. 2021

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- Burgeoning vaccination and the epidemic under control
- Lockdown measures were withdrawn

## Research Questions:

1. What is the myopia prevalence after relaxing restriction measures?
2. Did lifestyle such as time spent outdoors and screen time, change after restrictions were lifted?
3. Were there any risk factors influencing myopia during this period?


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# Myopia Pattern in Hong Kong Children From 2015 to 2021 (over 7 years)

**Before, During and After COVID-19 Restriction**

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## Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

### Purpose

1. To investigate myopia prevalence in school children during the consecutive 7 years across before, during and after COVID-19 restrictions (2005-2021)
2. To explore the lifestyle changes and the risk factors for myopia prevalence during this period

### Study Design

A repeated cross-sectional study


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# Myopia prevalence and associated factors before, during and after COVID-19 restrictions (from 2015 to 2021)

**Subjects:** **20,527** **children aged 6 to 8 years old in Hong Kong Children Eye Study from 2015 to 2021**

**Examinations:** **Cycloplegic refraction, Axial length (IOL master), and lifestyle questionnaires**

The quarantine policy of the Hong Kong Government

School closure

Half-day face-to-face class

Restriction eased

| Year of Examination | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | Total |
|---|---|---|---|---|---|---|---|---|
| Number of Participants | 1037 | 1536 | 1370 | 5516 | 7127 | 1211 | 2730 | 20527 |
| Age (yrs) Mean (SD) | 7.47 (0.77) | 7.37 (0.85) | 7.50 (0.83) | 7.19 (0.96) | 7.25 (0.89) | 7.34 (0.78) | 7.60 (0.84) | 7.33 (0.89) |
| Male-Female Ratio | 0.98 | 1.05 | 1.20 | 1.16 | 1.11 | 1.04 | 1.13 | 1.12 |

Before COVID-19

During

Outbreak of COVID-19

After COVID-19 restrictions

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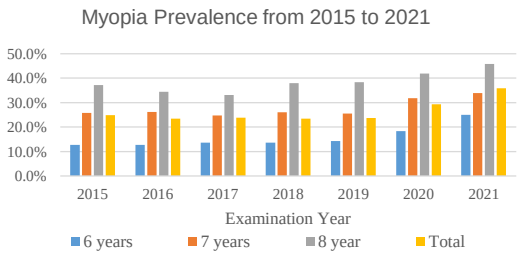
# Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

**Results:** **Prevalence of Myopia by Age in Each Year from 2015 to 2021**




| Age (yrs) | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
|---|---|---|---|---|---|---|---|
| 6 (n=7993) | 12.7% | 12.7% | 13.7% | 13.6% | 14.3% | 18.3% | 25.0% |
| 7 (n=7090) | 25.8% | 26.2% | 24.7% | 26.1% | 25.5% | 31.8% | 33.9% |
| 8 (n=5444) | 37.2% | 34.4% | 33.1% | 37.9% | 38.3% | 41.9% | 45.8% |
| Total (n=20527) | 24.9% | 23.5% | 23.8% | 23.4% | 23.7% | 29.4% | 35.9% |

***Prevalence of myopia:*** ***stable*** ***from*** ***2015 to 2019,*** ***increased*** ***in*** ***2020*** ***and*** ***2021***

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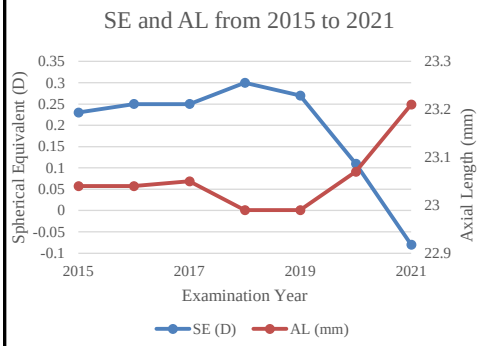
# Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

## Results: Spherical Equivalent and Axial Length by Age from 2015 to 2021




| Spherical Equivalent (D), Mean (SD) | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Age (years)** | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
| **6 (n=7993)** | 0.62 (0.96) | 0.65 (1.24) | 0.67 (1.12) | 0.65 (1.20) | 0.61 (1.20) | 0.43 (1.11) | 0.30 (1.48) |
| **7 (n=7090)** | 0.24 (1.23) | 0.20 (1.40) | 0.25 (1.31) | 0.23 (1.46) | 0.19 (1.58) | 0.08 (1.30) | -0.03 (1.47) |
| **8 (n=5444)** | -0.22 (1.54) | -0.19 (1.54) | -0.21 (1.58) | -0.24 (1.72) | -0.23 (1.68) | -0.34 (1.59) | -0.39 (1.65) |
| **Total (n=20527)** | 0.23 (1.29) | 0.25 (1.42) | 0.25 (1.38) | 0.30 (1.47) | 0.27 (1.51) | 0.11 (1.34) | -0.08 (1.56) |
| Axial Length (AL, mm), Mean (SD) | | | | | | | |
| **Age (years)** | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
| **6 (n=7993)** | 22.73 (0.68) | 22.74 (0.74) | 22.73 (0.72) | 22.69 (0.77) | 22.71 (0.81) | 22.78 (0.80) | 22.85 (0.94) |
| **7 (n=7090)** | 23.05 (0.90) | 23.08 (0.92) | 23.06 (0.87) | 23.09 (0.89) | 23.08 (0.90) | 23.12 (0.82) | 23.20 (0.90) |
| **8 (n=5444)** | 23.37 (0.85) | 23.38 (0.89) | 23.37 (0.95) | 23.39 (0.91) | 23.37 (0.95) | 23.43 (0.85) | 23.47 (0.96) |
| **Total (n=20527)** | 23.04 (0.86) | 23.04 (0.89) | 23.05 (0.89) | 22.99 (0.89) | 22.99 (0.92) | 23.07 (0.85) | 23.21 (0.96) |

***Similar* trends in *SE* and *AL***

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# Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

## Results: Outdoor Time, Near Work Time and Screen Time in Each Year from 2015 to 2021

| Outdoor time (hours per day), Mean (SD) | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Age (years)** | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
| **6 (n=7993)** | 1.40 (0.46) | 1.43 (0.65) | 1.45 (0.58) | 1.43 (0.60) | 1.50 (0.67) | 0.83 (0.56) | 1.26 (0.49) |
| **7 (n=7090)** | 1.40 (0.49) | 1.44 (0.71) | 1.48 (0.60) | 1.41 (0.58) | 1.44 (0.61) | 0.89 (0.53) | 1.25 (0.45) |
| **8 (n=5444)** | 1.40 (0.45) | 1.39 (0.66) | 1.41 (0.57) | 1.40 (0.58) | 1.43 (0.64) | 0.79 (0.52) | 1.29 (0.51) |
| **Total (n=20527)** | 1.40 (0.47) | 1.42 (0.68) | 1.45 (0.59) | 1.41 (0.59) | 1.46 (0.65) | 0.85 (0.53) | 1.26 (0.48) |
| Near work time (hours per day), Mean (SD) | | | | | | | |
| **Age (years)** | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
| **6 (n=7993)** | 3.34 (1.38) | 3.20 (1.32) | 3.27 (1.27) | 3.01 (1.21) | 3.11 (1.30) | 5.40 (1.33) | 4.53 (1.99) |
| **7 (n=7090)** | 3.53 (1.65) | 3.56 (1.24) | 3.56 (1.28) | 3.33 (1.35) | 3.37 (1.39) | 5.67 (1.51) | 4.59 (1.80) |
| **8 (n=5444)** | 3.62 (1.33) | 3.71 (1.59) | 3.55 (1.24) | 3.54 (1.36) | 3.57 (1.46) | 6.40 (2.10) | 4.75 (1.94) |
| **Total (n=20527)** | 3.49 (1.50) | 3.47 (1.39) | 3.47 (1.27) | 3.23 (1.31) | 3.30 (1.38) | 5.72 (1.61) | 4.64 (1.90) |
| Screen time (hours per day), Mean (SD) | | | | | | | |
| **Age (years)** | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
| **6 (n=7993)** | 1.89 (1.21) | 1.81 (1.07) | 1.91 (1.08) | 1.90 (1.19) | 2.01 (1.23) | 3.28 (1.15) | 2.95 (1.90) |
| **7 (n=7090)** | 1.94 (1.36) | 2.05 (1.15) | 2.12 (1.06) | 1.99 (1.14) | 2.06 (1.21) | 3.45 (1.36) | 2.90 (1.67) |
| **8 (n=5444)** | 1.95 (1.01) | 2.10 (1.25) | 2.20 (1.13) | 2.27 (1.29) | 2.27 (1.44) | 4.42 (2.03) | 3.02 (1.81) |
| **Total (n=20527)** | 1.93 (1.24) | 1.98 (1.16) | 2.08 (1.09) | 2.02 (1.21) | 2.09 (1.28) | 3.56 (1.50) | 2.96 (1.78) |

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# Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

**Results:** Association between COVID-19 Pandemic and Myopia Prevalence

| Dependent variable: Myopia (no as ref.) | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| | Exp (β) (95%CI) | P value | Exp (β) (95%CI) | P value | Exp (β) (95%CI) | P value | Exp (β) (95%CI) | P value |
| **COVID-19 pandemic (no as ref.)** | 1.58 (1.44, 1.73) | <0.001* | 1.38 (1.25, 1.51) | <0.001* | 1.39 (1.26, 1.54) | <0.001* | 1.86 (1.57, 2.20) | <0.001* |
| **Age (yrs)** | | | 1.84 (1.75, 1.92) | <0.001* | 1.88 (1.79, 1.97) | <0.001* | 1.88 (1.79, 1.98) | <0.001* |
| **Sex (female as ref.)** | | | 1.12 (1.03, 1.20) | 0.005* | 1.11 (1.03, 1.21) | 0.007* | 1.12 (1.03, 1.21) | 0.006* |
| **Low family income** | | | | | 1.05 (1.00, 1.09) | 0.04* | 1.05 (1.00, 1.09) | 0.03* |
| **No. of Parental Myopia** | | | | | 1.60 (1.51, 1.69) | <0.001* | 1.71 (1.60, 1.82) | <0.001* |

P value was generated by logistic regression; *Statistical significance was set at 0.05.
D = diopter, Exp (β) = odds ratio, SE = standard error.

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# Myopia prevalence and associated factors before, during and after COVID-19 restriction (from 2015 to 2021)

## Summary

1. Lifestyle changes, including increased digital learning, may persist beyond the period of the COVID-19 school closure
2. Myopia increased in children during the pandemic and will be sustainable even after restrictions were lifted in Hong Kong
3. The situation may be worsened in children of younger age or from the low-income family in the COVID era

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# Prevention and control of Myopia

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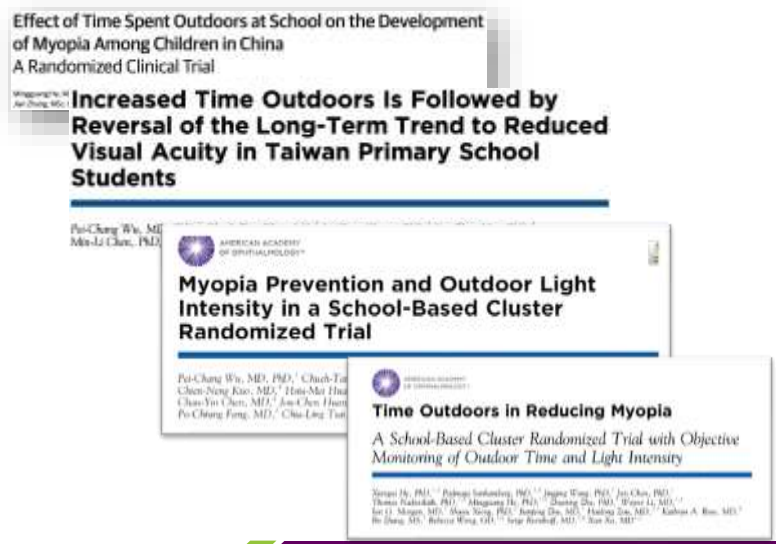
## Methods of Myopia Control

1. Increase outdoor time

2. Optical methods
   - Defocus spectacles
   - Contact lens
   - Orthokeratology

3. Pharmacological methods
   - Atropine eye drops

4. Red Light

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# Methods of Myopia Control

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# Methods of Myopia Control

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# Methods of Myopia Control

1. Increase outdoor time

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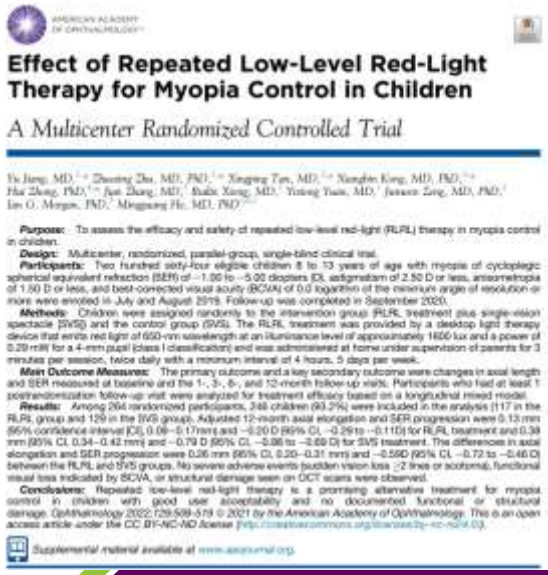

Effect of Repeated Low-Level Red-Light Therapy for Myopia Control in Children

A Multicenter Randomized Controlled Trial

Yu Jiang, MD,[1,2] Zhuoting Zhu, MD, PhD,[1,2] Xingyang Tan, MD,[1,2] Xianghui Kong, MD, PhD,[1,2] Hui Zhong, PhD,[1,2] Jian Zhang, MD,[1] Baifa Xiang, MD,[1] Yuting Yuan, MD,[1] Jiawen Zeng, MD, PhD,[1] Ian G. Morgan, PhD,[3] Mingguang He, MD, PhD[1,2,4]

**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], 0.09–0.17 mm) and −0.20 D (95% CI, −0.29 to −0.11 D) for RLRL treatment and 0.38 mm (95% CI, 0.34–0.42 mm) and −0.79 D (95% CI, −0.86 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 −0.58D (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 

Supplemental material available at www.aaojournal.org

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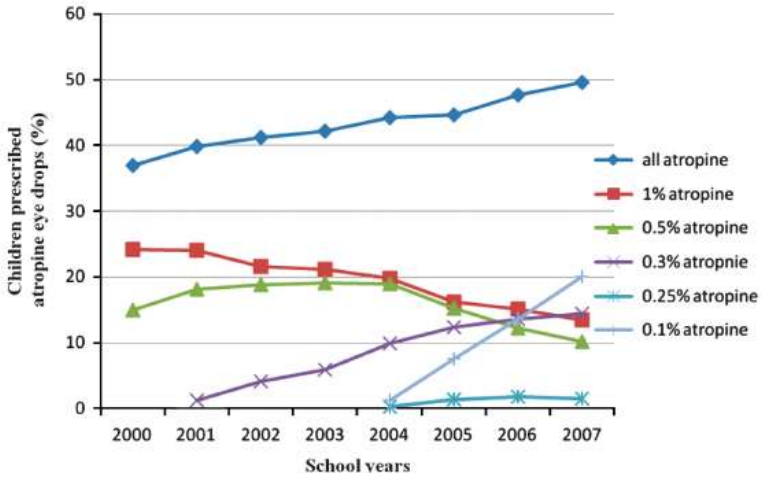
# Prevalent use of atropine in Taiwan




Fang YT, Chou YJ, Pu C et al. Prescription of atropine eye drops among children diagnosed with myopia in Taiwan from 2000 to 2007: a nationwide study. Eye 2013: 418-424

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## Singapore ATOM Studies

**1. Atropine for the Treatment of Childhood Myopia( ATOM1)**

- Intervention:
  - one eye no treatment
  - one eye received treatment once nightly x 2 year
    - 1% atropine eye drop
    - Placebo eye drop

**2. Atropine for the Treatment of Myopia 2 (ATOM2)**

- Intervention:
  - 0.5%, 0.1%, and 0.01% (2:2:1 ratio)
  - Once nightly, BE x 2 year
- Outcome measures:
  - Change in SE refraction (cycloplegic refraction)
  - Change in AL

1. Chia A. et al. ***Ophthalmology***. 2012
2. Chua, WH. et al. ***Ophthalmology***. 2006



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## Remaining questions

1. Efficacy compared with placebo ?
2. Concentration-dependent response?
3. Optimal Concentration?
4. Any effect on corneal and lens power ?
5. Factors associated with treatment response?
6. Any biomarker for treatment efficacy?
7. Continue treatment or stop treatment after 2 years?
8. Rebound effect?
9. Long-term efficacy of different low concentration atropine?
10. Can atropine delay myopia onset ?



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# Low-concentration Atropine for Myopia Progression (LAMP-1) Study

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## LAMP-1 Study

- First randomized placebo-controlled trial on low-concentration atropine
- 438 children included (4-12 years)
- <-1.0D in both eyes, and ≥0.5 D increase in the previous year
- Receive 0.05%, 0.025%, 0.01% atropine or placebo eye drops randomly
- Once a night, one drop for each eye

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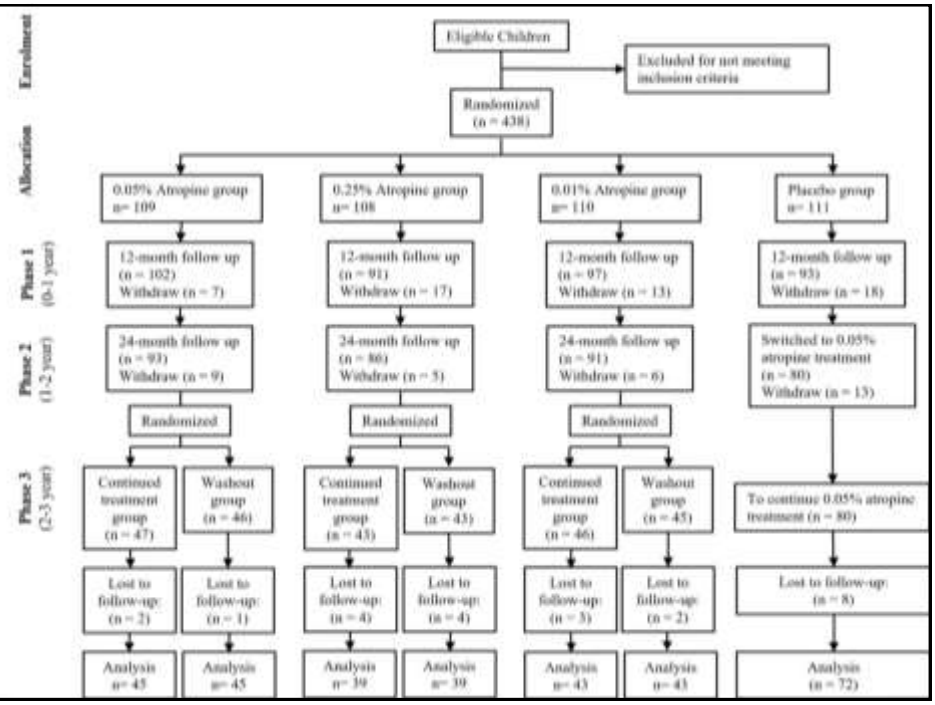
# LAMP-1 Study

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# LAMP Study Series


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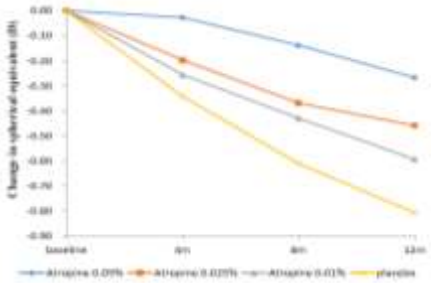
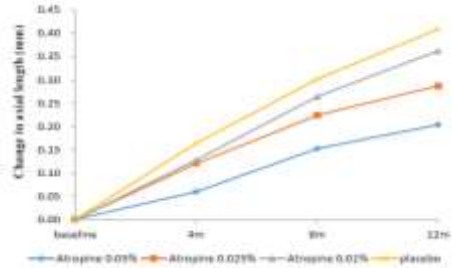
# LAMP: First year report

## Results Myopic progression & AL elongation over 1 year

| | 0.05% | 0.025% | 0.01% | Placebo |
|---|---|---|---|---|
| Change_SE Mean (SD) | -0.27 (0.61)* | -0.46 (0.45)* | -0.59 (0.61)** | -0.81 (0.53) |
| Change_AL Mean (SD) | 0.20 (0.25)* | 0.29 (0.20)* | 0.36 (0.29)# | 0.41 (0.22) |

No significant difference in AL elongation between 0.01% and placebo group





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# LAMP: First year report

## Results Efficacy compared with placebo group

| | Mean change in SE | % reduction in myopia progression | Axial length change | % reduction in AL elongation |
|---|---|---|---|---|
| Atropine 0.05% | -0.27 (0.61) | 67% | -0.20 (0.25) | 51% |
| Atropine 0.025% | -0.46 (0.45) | 43% | 0.29 (0.20 ) | 29% |
| Atropine 0.01% | -0.59 (0.61) | 27% | 0.36 (0.29) | 12% |
| Placebo | -0.81 (0.53) | | 0.41 (0.22) | |

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CUHK Ophthalmology and Visual Sciences

# LAMP: First year report

## Results Changes in accommodation, pupil diameter and visual acuity

VA = visual acuity; logMAR = logarithm of the minimum angle of resolution; D = diopter
Repeated measure analysis was performed for the ophthalmic parameters with treatment group, time and interaction of time and group included in the model setup, followed by testing the treatment group effects at each time point. Multiple comparisons were performed after the overall treatment group effect.
*significant at 0.05





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# LAMP: First year report

## Results Side effects and adverse events

| | 0.05% (n=109) | | 0.025% (n=108) | | 0.01% (n=110) | | placebo (n=111) | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | p-value |
| Photochromatic glasses needed | 33 | 30.3% | 37 | 34.3% | 33 | 30.0% | 44 | 39.6% | 0.39 |
| Progressive glasses needed | 1 | 0.9% | 0 | 0.0% | 2 | 1.8% | 1 | 0.9% | 0.86 |
| Photophobia at 2 week | 34 | 31.2% | 20 | 18.5% | 6 | 5.5% | 14 | 12.6% | <.001*[a] |
| Photophobia at 1 year[b] | 8 | 7.8% | 6 | 6.6% | 2 | 2.1% | 4 | 4.3% | 0.27 |
| Allergic conjunctivitis | 3 | 2.8% | 7 | 6.5% | 7 | 6.4% | 7 | 6.3% | 0.57 |
| Hospitalization | 3 | 2.8% | 5 | 4.6% | 3 | 2.7% | 2 | 1.8% | 0.66 |

a, 0.05% differed from placebo, 0.01% and 0.025% significantly; 0.025% differed from 0.01% significantly

b, only subjects at one year follow up were included

*significant at 0.05

No significant difference in clinical side effect at 1 year.

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# LAMP: First year report

**Results** Values of VFQ domains at 1 year [a]

| | 0.05% (n=102) | | 0.025% (n=91) | | 0.01% (n=97) | | placebo (n=93) | | |
|---|---|---|---|---|---|---|---|---|---|
| | mean | sd | mean | sd | mean | sd | mean | sd | p-value |
| General Health | 70.34 | 22.45 | 73.39 | 20.79 | 75.00 | 22.47 | 73.35 | 23.21 | 0.51 |
| General Vision | 83.92 | 15.93 | 79.57 | 18.88 | 83.00 | 14.32 | 81.98 | 14.92 | 0.27 |
| Ocular Pain | 92.89 | 10.48 | 91.26 | 14.60 | 93.00 | 10.56 | 92.45 | 11.91 | 0.74 |
| Near Activities | 96.81 | 7.23 | 94.35 | 10.07 | 95.67 | 7.15 | 94.23 | 9.10 | 0.11 |
| Distance Activities | 95.34 | 9.62 | 93.82 | 12.31 | 95.38 | 8.64 | 94.09 | 11.08 | 0.62 |
| Social Functioning | 98.86 | 5.67 | 97.92 | 5.70 | 99.36 | 2.78 | 99.16 | 3.67 | 0.16 |
| Mental Health | 93.14 | 7.69 | 90.39 | 9.06 | 92.31 | 8.13 | 90.68 | 9.86 | 0.11 |
| Role Difficulties | 95.59 | 9.90 | 93.55 | 14.81 | 95.13 | 9.55 | 94.09 | 13.48 | 0.63 |
| Dependency | 97.63 | 7.07 | 97.04 | 8.48 | 97.92 | 6.42 | 96.23 | 9.64 | 0.48 |
| Color Vision | 99.49 | 3.54 | 96.94 | 13.42 | 98.71 | 8.36 | 96.63 | 13.69 | 0.18 |
| Peripheral Vision | 98.28 | 7.26 | 95.11 | 12.43 | 98.25 | 6.41 | 97.25 | 10.83 | 0.07 |
| VFQ-25 Composite | 92.91 | 4.89 | 91.13 | 8.33 | 93.01 | 4.80 | 91.79 | 6.79 | 0.12 |

VFQ = visual function questionnaires
a. only subjects at one year follow up were included

No significant difference in the vision-related quality of life among all groups.

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# LAMP: First year report

## Summary

1. Low-concentration atropine (0.05%, 0.025%, 0.01%) is effective compared to placebo.
2. The difference in axial elongation between 0.01% atropine and placebo groups was not significant.
3. Concentration-related response among low-concentration atropine
4. All low concentration groups are well tolerated
5. 0.05% atropine is an optimal concentration among other low concentration groups at one year FU

Yam JC, Jiang Y, Tang SM, Law AKP, Chan JJ, Wong E, Ko ST, Young AL, Tham CC, Chen LJ, Pang CP. 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* 6 July 2018.

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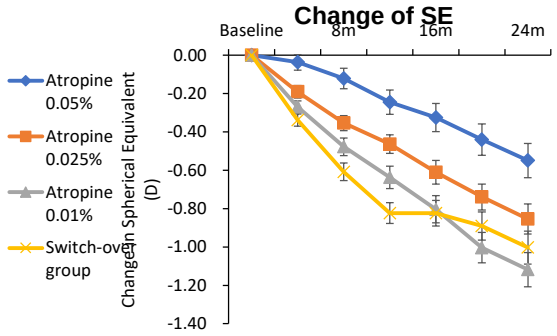
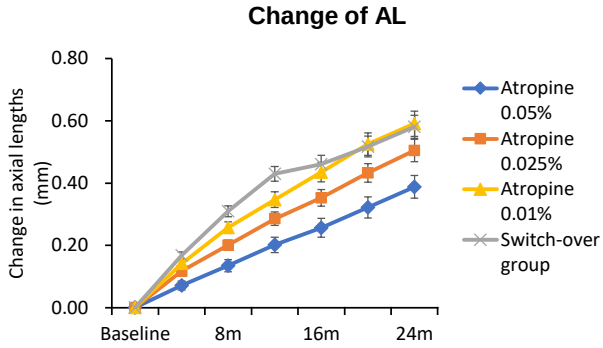
# LAMP: Second year report

## Results: 0.05% remained the most efficacious concentration over 2 years

| | 0.05% | 0.025% | 0.01% | Switch-over group |
|---|---|---|---|---|
| SE Change over 2 years (D) | -0.55 | -0.85 | -1.12 | -1.00 |
| AL Change over 2 years (mm) | 0.39 | 0.50 | 0.59 | 0.58 |

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Yam JC. Ophthalmology 2020 47

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# LAMP: Second year report

## Summary

1. 0.05% atropine is the optimal concentration amongst the concentrations studied for myopia control over a two-year period
2. 0.01% atropine was mildly more effective in the second year than the first year, but not in 0.05% and 0.025% atropine.
3. All concentrations of atropine were well-tolerated without apparent adverse effects on the quality of life.
4. The efficacy of 0.05% atropine observed was double that observed with 0.01% atropine in SE progression over two years.

Yam JC, Li FF, Zhang XJ, Tang SM, Yip BH, Kam KW, Ko ST, Young AL, Tham CC, Chen LJ, Pang CP. Two-Year Clinical Trial of the Low-concentration Atropine for Myopia Progression (LAMP) Study: Phase 2 Report. Ophthalmology. 2020

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## Observed Discrepancy on the Effect for SE progression and AL elongation ?

| | LAMP 0.01% | LAMP 0.025% | LAMP 0.05% |
|---|---|---|---|
| | Compared with placebo group | | |
| Slowing SE progression | 27% | 43% | 67% |
| Slowing AL elongation | 12% | 29% | 51% |

A better antimyopic effect in terms of SE progression than AL elongation.

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## Observed Discrepancy on the Effect for SE progression and AL elongation ?

Gong et al. speculate that "the unexpected **distinction** between the refractive error and axial length data may have resulted from interactions between atropine effects in the eye and the development of the cornea with some **change of corneal curvature or corneal power**"

Gong Q. et al. *JAMA Ophthalmol*. (2018)

**Clinical question:**

Whether the anti-myopic effect of low concentration atropine is mediated via **retarding axial elongation** or **other associated biometric changes?**

*Myopic complications are mainly caused by excessive axial length elongation*

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# LAMP: Ocular biometrics study

## Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study

### Purpose:

To evaluate changes in ocular biometrics in groups receiving 0.05%, 0.025%, and 0.01% atropine compared with placebo over 1 year based on the Low-Concentration Atropine for Myopia Progression (LAMP) study.

Li FF,...Pang CP, Yam JC. Ophthalmology 2020

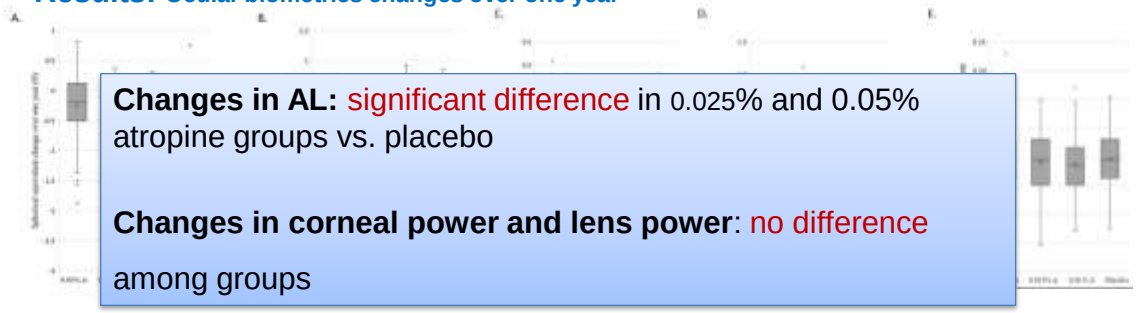






# LAMP: Ocular biometrics study

### Results: Ocular biometrics changes over one year



**Changes in AL:** significant difference in 0.025% and 0.05% atropine groups vs. placebo

**Changes in corneal power and lens power**: no difference among groups

Change in SE | Change in AL | Change in corneal power | Change in lens power | Change in ACD

**Box plots of changes in refractive error and ocular biometrics in treatment groups over one year.**

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# LAMP: Ocular biometrics study

## Results: Contribution of ocular biometrics changes to myopia progression

| | 0.05% atropine | | | 0.025% atropine | | | 0.01% atropine | | | Placebo | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | β | SE | P value | β | SE | P value | β | SE | P value | β | SE | P value |
| Model 1£ | | | | | | | | | | | | |
| Δ Axial length (mm) | -2.21 | 0.11 | <.001* | -1.77 | 0.11 | <.001* | -2.07 | 0.10 | <.001* | -2.11 | 0.13 | <.001* |
| Adjusted R-squared | | 80.4% | | | 72.6% | | | 81.2% | | | 75.3% | |
| Model 2£ | | | | | | | | | | | | |
| Δ Axial length (mm) | -2.67 | 0.09 | <.001* | -2.28 | 0.09 | <.001* | -2.64 | 0.07 | <.001* | -2.74 | 0.10 | <.001* |
| Δ Lens power (D) | -0.54 | 0.06 | <.001* | -0.47 | 0.04 | <.001* | -0.57 | 0.04 | <.001* | -0.61 | 0.05 | <.001* |
| Adjusted R-squared | | 89.3% | | | 87.9% | | | 93.7% | | | 90.2% | |
| Model 3£ | | | | | | | | | | | | |
| Δ Axial length (mm) | -2.77 | 0.05 | <.001* | -2.46 | 0.07 | <.001* | -2.73 | 0.06 | <.001* | -2.77 | 0.06 | <.001* |
| Δ Lens power (D) | -0.71 | 0.03 | <.001* | -0.56 | 0.04 | <.001* | -0.65 | 0.04 | <.001* | -0.64 | 0.03 | <.001* |
| Δ Corneal power (D) | -1.21 | 0.08 | <.001* | -1.04 | 0.13 | <.001* | -0.85 | 0.14 | <.001* | -1.03 | 0.09 | <.001* |
| Adjusted R-squared | | 97.0% | | | 93.0% | | | 95.6% | | | 96.1% | |
| Model 4¶ | | | | | | | | | | | | |
| Δ Axial length (mm) | -2.79 | 0.05 | <.001* | -2.43 | 0.08 | <.001* | -2.74 | 0.07 | <.001* | -2.73 | 0.07 | <.001* |
| Δ Lens power (D) | -0.71 | 0.03 | <.001* | -0.58 | 0.04 | <.001* | -0.66 | 0.04 | <.001* | -0.65 | 0.03 | <.001* |
| Δ Corneal power (D) | -1.21 | 0.08 | <.001* | -1.07 | 0.13 | <.001* | -0.90 | 0.14 | <.001* | -1.05 | 0.09 | <.001* |
| Gender (M1,F2) | -0.01 | 0.02 | 0.50 | -0.04 | 0.02 | 0.07 | -0.05 | 0.02 | 0.02 | -0.07 | 0.02 | 0.003* |
| Age | -0.01 | 0.01 | 0.23 | 0.01 | 0.01 | 0.14 | 0.002 | 0.01 | 0.86 | 0.011 | 0.01 | 0.14 |
| Adjusted R-squared | | 97.0% | | | 93.2% | | | 95.7% | | | 96.4% | |

Δ =change over one yea
£Model 1, 2, 3 are the ec
¶Model 4 is the equation
*Significant level set at p

1. Axial elongation alone contributed to the SE change variance ranging from 75% to 81%.
2. Remaining variance was accounted for by lens and corneal factors.
3. Contributions were similar among groups.

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# LAMP: Ocular biometrics study

## Discussion

1. AL alone, SE variance 72% to 81%
2. Children's AL elongation includes normal age-related growth

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# LAMP: Ocular biometrics study

## Summary

1. Low-concentration atropine has no effect on corneal power and lens power.
2. Contributions to SE progression from axial length, corneal and lens power in each atropine concentration and placebo were similar.
3. Its antimyopic effect acts via retarding axial elongation, and thus can reduce risk of myopia complications

Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study. Li FF, Kam KW, Zhang Y, Tang SM, Young AL, Chen LJ, Tham CC, **Pang CP, Yam JC**. ***Ophthalmology***. 2020 Jun 7:S0161-6420(20)30520.

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# What is the associated factors for treatment responses to low concentration atropine ?

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# LAMP: Risk factors study

**Purpose**: To investigate the effect of age at treatment and other factors on the treatment response to atropine in the Low-concentration Atropine for Myopia Progression (LAMP) study

**Design:** Secondary analysis from a randomized trial.


Ophthalmology

FULL LENGTH ARTICLE | ARTICLES IN PRESS

Age effect on treatment responses to 0.05%, 0.025%, and 0.01% atropine: Low-concentration Atropine for Myopia Progression (LAMP) Study

Fan Fan Li • Yuzhou Zhang • Xiujuan Zhang • Benjamin Hon Kei Yip • Shu Min Tang • Ka Wai Kam • Alvin L. Young • Li Jia Chen • Clement C. Tham • Chi Pui Pang • Jason C. Yam Jr. +Show less

Published: January 07, 2021 • DOI: https://doi.org/10.1016/j.ophtha.2020.12.036

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# LAMP: Risk factors study

## Result

Table 1. Factors on change in spherical equivalent over two years in each treatment group

| | 0.05% Atropine | | | 0.025% Atropine | | | 0.01% Atropine | | |
|---|---|---|---|---|---|---|---|---|---|
| | N=81 | | Adjusted | N=88 | | Adjusted | N=91 | | Adjusted |
| | (Unadjusted) | Standard error | p-value | (Unadjusted) | Standard error | p-value | (Unadjusted) | Standard error | p-value |
| Age (years) | 0.14 | 0.03 | 0.01* | 0.13 | 0.04 | <0.001* | 0.30 | 0.03 | <0.001* |
| Gender (n, %) | | | | | | | | | |
| Female | 0 | | | 0 | | | 0 | | |
| Male | -0.01 | 0.16 | 0.97 | -0.03 | 0.14 | 0.81 | 0.15 | 0.13 | 0.24 |
| Baseline SE (D) | 0.01 | 0.05 | 0.32 | 0.07 | 0.04 | 0.07 | 0.01 | 0.04 | 0.83 |
| Outdoor activity (hours per day) | 0.02 | 0.08 | 0.78 | -0.03 | 0.07 | 0.63 | -0.01 | 0.06 | 0.91 |
| Near work (diopter hours per day) | 0.01 | 0.02 | 0.60 | 0.03 | 0.02 | 0.06 | 0.03 | 0.02 | 0.10 |
| Parental myopia status (n, %) | -0.24 | 0.16 | 0.13 | -0.10 | 0.14 | 0.47 | -0.10 | 0.16 | 0.52 |
| one parent or less with moderate myopia | | | | | | | | | |
| both parents with moderate or high myopia | 0 | | | 0 | | | 0 | | |
| Treatment compliance (days per week) | 0.09 | 0.12 | 0.45 | 0.16 | 0.08 | 0.20 | -0.03 | 0.08 | 0.72 |

SE=Spherical equivalent.

Generalized estimating equations were used to adjust the correlation between eyes.

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# LAMP: Risk factors study

## Result

Table 2. Factors on axial length elongation over two years in each treatment group

| | 0.05% Atropine | | | 0.025% Atropine | | | 0.01% Atropine | | |
|---|---|---|---|---|---|---|---|---|---|
| | N=93 | | Adjusted | N=84 | | Adjusted | N=93 | | Adjusted |
| | β(adjusted) | Standard error | p-value | β(adjusted) | Standard error | p-value | β(adjusted) | Standard error | p-value |
| Age (years) | -0.10 | 0.02 | <0.001* | -0.11 | 0.02 | <0.001* | -0.12 | 0.02 | <0.001* |
| Gender (n,%) | | | | | | | | | |
| Female | 0 | | | 0 | | | 0 | | |
| Male | -0.01 | 0.08 | 0.93 | 0.00 | 0.08 | 0.99 | -0.01 | 0.07 | 0.72 |
| Baseline SE (D) | -0.02 | 0.02 | 0.38 | -0.03 | 0.02 | 0.05 | -0.01 | 0.02 | 0.31 |
| Outdoor activity (hours per day) | -0.01 | 0.03 | 0.72 | 0.02 | 0.03 | 0.51 | 0.01 | 0.04 | 0.79 |
| Near work (dioptic hours per day) | -0.004 | 0.01 | 0.61 | -0.008 | 0.01 | 0.28 | -0.009 | 0.01 | 0.31 |
| Parental myopia status (n,%) | | | | | | | | | |
| one parent or less with moderate myopia | 0 | | | 0 | | | 0 | | |
| both parents with moderate or high myopia | 0.07 | 0.08 | 0.24 | 0.04 | 0.08 | 0.44 | 0.03 | 0.07 | 0.43 |
| Treatment compliance (days per week) | -0.04 | 0.05 | 0.43 | -0.04 | 0.05 | 0.23 | 0.00 | 0.04 | 0.99 |

SE=Spherical equivalent.
Generalized estimating equations were used to adjust the correlation between eyes.

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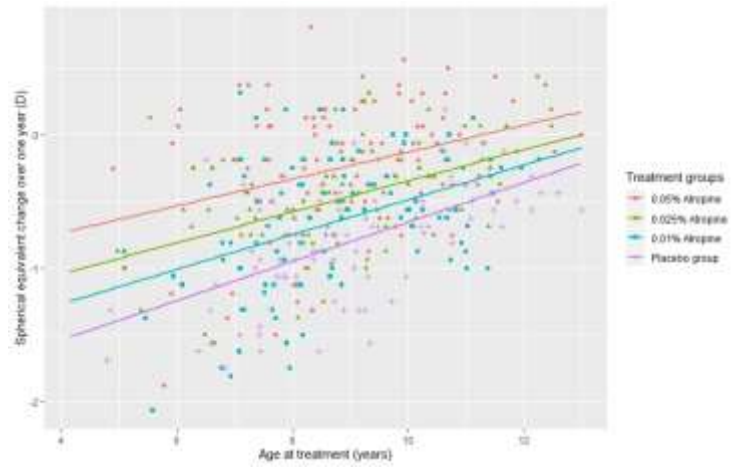
# LAMP: Risk factors study

## Result

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# LAMP: Risk factors study

## Result

Table 3. Estimated mean of myopia progression over two years in different ages of active treatment groups.

| | 0.05% Atropine | | 0.025% Atropine | | 0.01% Atropine | | P-trend |
|---|---|---|---|---|---|---|---|
| Age (Years) | N | Estimated mean (95%CI) | N | Estimated mean (95%CI) | N | Estimated mean (95%CI) | |
| 4 | 1 | -1.20 (NA) | 1 | -1.60 (NA) | NA | NA | 0.03*# |
| 5 | 4 | -1.12 (-1.19, -1.04) | 2 | -1.44 (-1.53, -1.36) | 4 | -1.75 (-1.98, -1.52) | |
| 6 | 6 | -0.90 (-0.99, -0.82) | 7 | -1.23 (-1.34, -1.12) | 7 | -1.54 (-1.72, -1.36) | <0.001* |
| 7 | 17 | -0.79 (-0.87, -0.71) | 17 | -1.04 (-1.15, -0.94) | 20 | -1.40 (-1.46, -1.34) | <0.001* |
| 8 | 24 | -0.57 (-0.63, -0.51) | 21 | -0.89 (-0.94, -0.83) | 22 | -1.24 (-1.31, -1.18) | <0.001* |
| 9 | 18 | -0.45 (-0.52, -0.39) | 15 | -0.81 (-0.87, -0.75) | 12 | -1.05 (-1.17, -0.93) | <0.001* |
| 10 | 16 | -0.27 (-0.35, -0.21) | 12 | -0.61 (-0.68, -0.54) | 13 | -0.92 (-0.99, -0.85) | <0.001* |
| 11 | 5 | -0.07 (-0.17, 0.02) | 8 | -0.40 (-0.49, -0.32) | 12 | -0.80 (-0.91, -0.69) | 0.01* |
| 12 | 2 | 0.07 (-0.24, 0.39) | 3 | -0.24 (-0.38, -0.10) | 1 | -0.55 (NA) | |

Estimated mean was generated in generalized estimating equations by adjusted age, gender, baseline refraction, outdoor time, near work activities, parental myopia, treatment compliance, and treatment groups.
N=number of subjects; 95% CI=95% confidence interval; NA=not available, mean or SD is not available due to the insufficient sample sizes.
P-trend of each age group were generated by using treatment groups as ordinal data (3, 0.05% atropine; 2, 0.025% atropine; 1, 0.01% atropine).
#age 4 and 5 were combined to generate the P-trend because of insufficient sample sizes
##age 11 and 12 were combined to generate the P-trend because of insufficient sample sizes
*Significant level set at p <0.05.

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# LAMP Risk factors study

## Summary

1. Age-dependent effect in each treatment group 0.05%, 0.025% and 0.01% atropine
2. Younger children required the higher concentration to achieve similar efficacy as older children on lower concentrations.
3. A higher concentration should be administered as a starting dosage for younger children

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# Any biomarkers for treatment responses to low concentration atropine ?



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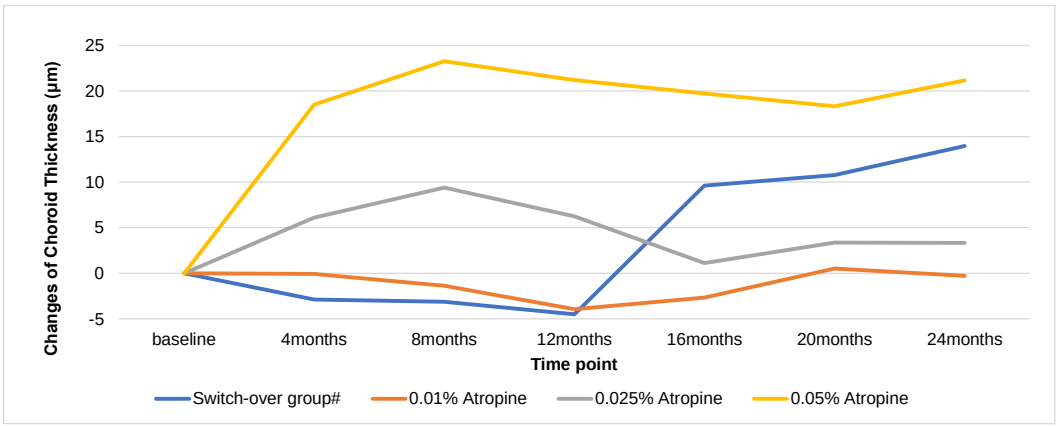
## LAMP: Choroidal thickness study

**Result** Changes of Subfoveal Choroidal Thickness Against Different Time Points among Different Groups




#Switch-over group: placebo in the first year and switchover to 0.05% atropine group in the second year

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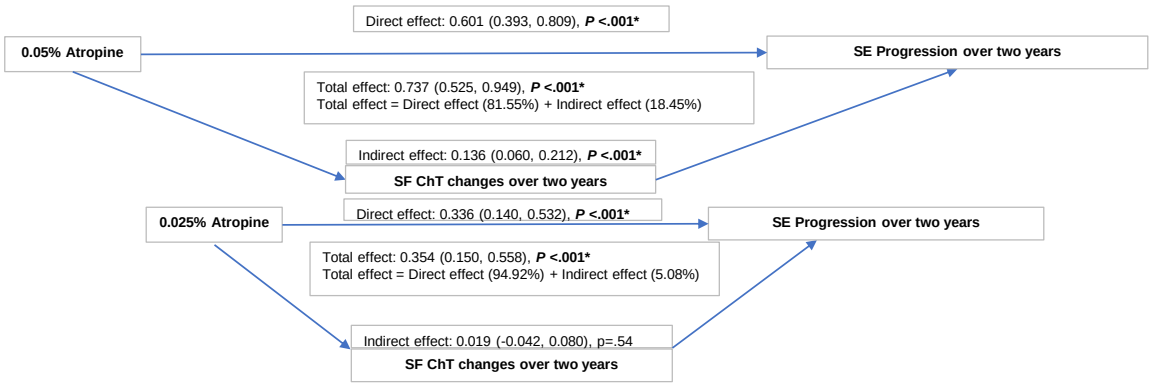
# LAMP: Choroidal thickness study

## Result Mediation Analysis




SE = spherical equivalent; SFChT = subfoveal choroidal thickness * Significant level set at P<.05.

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# LAMP: Choroidal thickness study

## Summary

1. Low concentration atropine induced a choroidal thickening effect along a concentration-dependent response throughout the treatment period.

2. The choroidal thickening was associated with a slower SE progression and AL elongation among all the treatment groups.

3. Choroidal response can be used for assessment of long-term treatment outcomes and as a guide for concentration titrations of atropine

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# LAMP: Third year report

## Purpose:

1. To compare the efficacy of continued and stopping treatment for 0.05%, 0.025% and 0.01% atropine during the third year.
2. To evaluate the efficacy of continued treatment over 3 years.
3. To investigate the rebound phenomenon and its determinants after cessation of treatment.



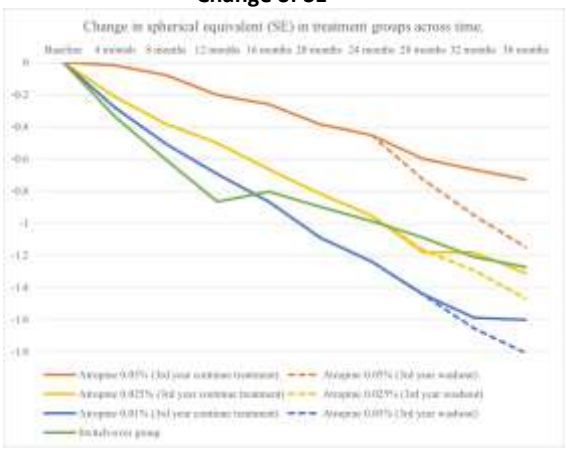




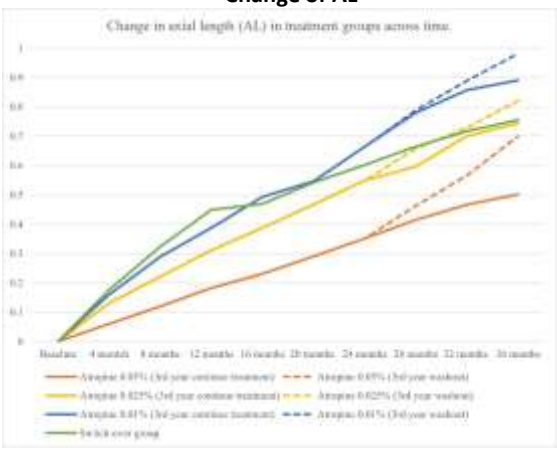

# LAMP: Third year report

## Result

**Change of SE**




**Change of AL**



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# LAMP: Third year report

## Result Change in Ophthalmic Parameters over Three Years in the 0.05% Atropine, 0.025% Atropine, and 0.01% Atropine groups

| | 3) 0.05% Atropine (n=90) | | 2) 0.025% Atropine (n=78) | | 1) 0.01% Atropine (n=86) | | Overall P values | Pairwise comparisons P values† (3 vs. 2; 3 vs. 1; 2 vs. 1) |
|---|---|---|---|---|---|---|---|---|
| **Change** | Mean | SD | Mean | SD | Mean | SD | | |
| **Spherical Equivalent (D)** | | | | | | | | |
| **Baseline to 36 Months** | | | | | | | | |
| **Continue** | -0.73 | 1.04 | -1.31 | 0.92 | -1.60 | 1.32 | 0.001* | 0.01*, 0.002*, 0.38 |
| **Washout** | -1.15 | 1.13 | -1.47 | 0.77 | -1.81 | 1.10 | 0.03* | 0.09, 0.03*, 0.34 |
| **P values** | 0.04* | | 0.34 | | 0.45 | | | |
| **24 to 36 Months‡** | | | | | | | | |
| **Continue** | -0.28 | 0.42 | -0.35 | 0.37 | -0.38 | 0.49 | 0.65 | 0.99, 0.99, 0.99 |
| **Washout** | -0.68 | 0.49 | -0.57 | 0.38 | -0.56 | 0.40 | 0.15 | 0.39, 0.16, 0.48 |
| **P values** | <0.001* | | 0.004* | | 0.04* | | | |
| **Axial Length (mm)** | | | | | | | | |
| **Baseline to 36 Months** | | | | | | | | |
| **Continue** | 0.50 | 0.40 | 0.74 | 0.41 | 0.89 | 0.53 | <0.001* | 0.002*, 0.001*, 0.42 |
| **Washout** | 0.70 | 0.47 | 0.82 | 0.37 | 0.98 | 0.48 | 0.04* | 0.10, 0.05*,0.51 |
| **P values** | 0.04* | | 0.28 | | 0.54 | | | |
| **24 to 36 Months‡** | | | | | | | | |
| **Continue** | 0.17 | 0.14 | 0.20 | 0.15 | 0.24 | 0.18 | 0.19 | 0.36, 0.24, 0.52 |
| **Washout** | 0.33 | 0.17 | 0.29 | 0.14 | 0.29 | 0.15 | 0.003* | 0.22, 0.002*, 0.22 |
| **P values** | <0.001* | | 0.001* | | 0.13 | | | |

Mean and SD was calculated with both eye data. SD = Standard Deviation; *Significant was set at 0.05.

P values were generated by generalized estimating equation models with age, sex and baseline SE/AL adjustment for comparisons among groups and comparisons within different treatment groups; †Sequential Bonferonni correction was applied for the pairwise comparisons; ‡ SE/AL in 24 months was used to adjust for the comparisons of SE/AL changes.

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# LAMP: Third year report

## Result Multiple Regression Models of SE/AL Changes during Third Year in Washout Group

| Spherical Equivalent (D) Change at Third year | | | | Axial Length (mm) Change at Third year | | | |
|---|---|---|---|---|---|---|---|
| | Beta (β) | Standard Error | P values | | Beta (β) | Standard Error | P values |
| **Age at Treatment Cessation (years)** | 0.08 | 0.02 | <0.001* | Age at Treatment Cessation (years) | -0.05 | 0.01 | <0.001* |
| **Sex (Male as Reference)** | -0.10 | 0.07 | 0.14 | Sex (Male as Reference) | -0.01 | 0.03 | 0.61 |
| **SE at Treatment Cessation (D)** | 0.01 | 0.02 | 0.46 | SE at Treatment Cessation (D) | -0.01 | 0.01 | 0.39 |
| **Parental Myopia Status** | | | | Parental Myopia Status | | | |
| **One or less moderate or high myopia** | 0 | | | One or less moderate or high myopia | 0 | | |
| **Both moderate or high myopia** | 0.03 | 0.07 | 0.64 | Both moderate or high myopia | 0.01 | 0.02 | 0.55 |
| **Outdoor Activity (hours per day)[a]** | 0.03 | 0.04 | 0.41 | Outdoor Activity (hours per day)[a] | -0.03 | 0.01 | 0.09 |
| **Nearwork (dioptic hours per day)[b]** | -0.01 | 0.01 | 0.33 | Nearwork (dioptic hours per day)[b] | 0.00 | 0.00 | 0.11 |
| **Treatment Groups** | | | | Treatment Groups | | | |
| **0.05% Atropine** | -0.20 | 0.08 | 0.02* | 0.05% Atropine | 0.08 | 0.03 | 0.01* |
| **0.025% Atropine** | -0.03 | 0.08 | 0.74 | 0.025% Atropine | 0.03 | 0.03 | 0.29 |
| **0.01% Atropine** | 0 | | | 0.01% Atropine | 0 | | |

Generalized estimating equations (GEEs) were used to adjust the correlation between eyes; D = diopter; *Significant was set at 0.05.

a, outdoor activity = outdoor exercise + outdoor leisure activity; b, nearwork = 3*(homework + reading + playing cell phone) + 2*(using computer + playing video game) + 1*(watching TV).

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# LAMP: Third year report

## Result Change in Ophthalmic Parameters over Three Years in the 0.05% Atropine, 0.025% Atropine, and 0.01% Atropine groups

| | 3) 0.05% Atropine (n=90) | | 2) 0.025% Atropine (n=78) | | 1) 0.01% Atropine (n=86) | | Overall P values | Pairwise comparisons P values† (3 vs. 2; 3 vs. 1; 2 vs. 1) |
|---|---|---|---|---|---|---|---|---|
| Change | Mean | SD | Mean | SD | Mean | SD | | |
| Spherical Equivalent (D) | | | | | | | | |
| Baseline to 36 Months | | | | | | | | |
| Continue | -0.73 | 1.04 | -1.31 | 0.92 | -1.60 | 1.32 | 0.001* | 0.01*, 0.002*, 0.38 |
| Washout | -1.15 | 1.13 | -1.47 | 0.77 | -1.81 | 1.10 | 0.03* | 0.09, 0.03*, 0.34 |
| P values | 0.04* | | 0.34 | | 0.45 | | | |
| 24 to 36 Months‡ | | | | | | | | |
| Continue | -0.28 | 0.42 | -0.35 | 0.37 | -0.38 | 0.49 | 0.65 | 0.99, 0.99, 0.99 |
| Washout | -0.68 | 0.49 | -0.57 | 0.38 | -0.56 | 0.40 | 0.15 | 0.39, 0.16, 0.48 |
| P values | <0.001* | | 0.004* | | 0.04* | | | |
| Axial Length (mm) | | | | | | | | |
| Baseline to 36 Months | | | | | | | | |
| Continue | 0.50 | 0.40 | 0.74 | 0.41 | 0.89 | 0.53 | <0.001* | 0.002*, 0.001*, 0.42 |
| Washout | 0.70 | 0.47 | 0.82 | 0.37 | 0.98 | 0.48 | 0.04* | 0.10, 0.05*,0.51 |
| P values | 0.04* | | 0.28 | | 0.54 | | | |
| 24 to 36 Months‡ | | | | | | | | |
| Continue | 0.17 | 0.14 | 0.20 | 0.15 | 0.24 | 0.18 | 0.19 | 0.36, 0.24, 0.52 |
| Washout | 0.33 | 0.17 | 0.29 | 0.14 | 0.29 | 0.15 | 0.003* | 0.22, 0.002*, 0.22 |
| P values | <0.001* | | 0.001* | | 0.13 | | | |

Mean and SD was calculated with both eye data. SD = Standard Deviation; *Significant was set at 0.05.

P values were generated by generalized estimating equation models with age, sex and baseline SE/AL adjustment for comparisons among groups and comparisons within different treatment groups; †Sequential Bonferonni correction was applied for the pairwise comparisons; ‡ SE/AL in 24 months was used to adjust for the comparisons of SE/AL changes.

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# LAMP: Third year report

## Summary

1. During the third year, continued atropine treatment achieved a better effect
2. 0.05% atropine remained the optimal concentration over 3 years in Chinese children.
3. Stopping treatment at an older age and lower concentration is associated with a smaller rebound.
4. The difference in rebound effects were clinically small across all three studied atropine concentrations.
5. All atropine concentrations were well-tolerated without apparent adverse effects on vision-related quality of life.
6. We suggest that treatment using 0.05% atropine should be continued into the third year in Asian children.

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# Low-concentration Atropine for Myopia Prevention (LAMP-2) Study

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## LAMP2 Research Question

Can low concentration atropine drops (0.05%, 0.01%) prevent myopia onset in children ?

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JAMA | Original Investigation

## Effect of Low-Concentration Atropine Eyedrops vs Placebo on Myopia Incidence in Children
### The LAMP2 Randomized Clinical Trial

Jason C. Yam, MPH; Xiu Juan Zhang, PhD; Yuzhou Zhang, PhD; Benjamin H. K. Yip, PhD; Fangyao Tang, PhD; Emily S. Wong, MBChB; Christine H. T. Bui, PhD; Ka Wai Kam, MSc; Mandy P. H. Ng, MHM; Simon T. Ko, MBBS; Wilson W.K. Yip, MBChB; Alvin L. Young, MMedSc; Clement C. Tham, BM, BCh; Li Jia Chen, PhD; Chi Pui Pang, DPhil

- First randomized placebo-controlled trial on delaying myopia onset with atropine
- 474 children included (4-9 years) without myopia
- Receive 0.05%, 0.01% atropine or placebo eye drops randomly
- Once a night, one drop for each eye
- Every 4 months follow up, over two years

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# Primary Outcomes

**1. Cumulative incidence of myopia**

- cycloplegic spherical equivalent of at least −0.50D in either eye over 2 years

2. **Percentage of participants with fast myopic shift**

- cycloplegic spherical equivalent myopic shift of at least 1.00 D in either eye over 2 years

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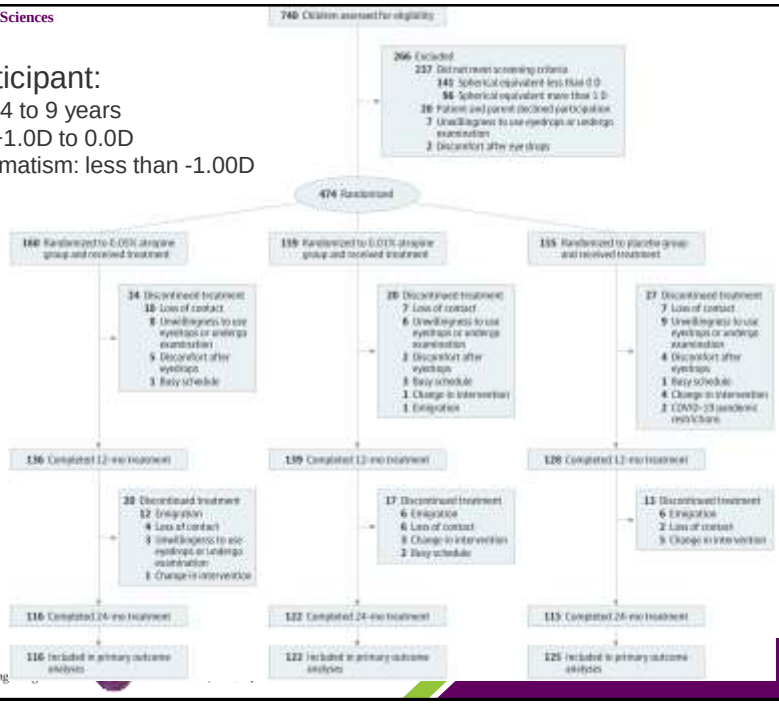
## Participant:

Age: 4 to 9 years
SE: +1.0D to 0.0D
Astigmatism: less than -1.00D

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## Baseline Demographic and Clinical Characteristics in Children

| | 0.05% atropine (n=160) | 0.01% atropine (n=159) | Placebo (n=155) |
|---|---|---|---|
| | Mean (SD) | Mean (SD) | Mean (SD) |
| Age, years | 6.86 (1.42) | 6.88 (1.35) | 6.75 (1.27) |
| Sex, No. (%) | | | |
| Male | 81 (50.6%) | 78 (49.1%) | 78 (50.3%) |
| Female | 79 (49.4%) | 81 (50.9%) | 77 (49.7%) |
| BMI, kg/m$^2$ | 15.66 (2.60) | 15.58 (2.10) | 15.47 (2.00) |
| Spherical equivalent, D [a] | 0.50 (0.33) | 0.51 (0.33) | 0.53 (0.31) |
| Axial length, mm [b] | 22.82 (0.72) | 22.89 (0.70) | 22.80 (0.64) |
| Central corneal thickness, um [c] | 556.07 (32.13) | 555.78 (31.58) | 553.14 (31.71) |
| IOP, mmHg [d] | | | 15.97 (1.91) |
| Photopic pupil size, mm [e] | | | 3.69 (0.72) |
| Mesopic pupil size, mm [e] | 6.36 (0.68) | 6.34 (0.74) | 6.53 (0.74) |
| Accommodation amplitude, D [f] | 13.34 (2.69) | 13.60 (2.67) | 13.33 (2.74) |
| Distance VA, logMAR [g] | 0.03 (0.09) | 0.02 (0.09) | 0.03 (0.07) |
| Near VA, logMAR [g] | 0.04 (0.10) | 0.03 (0.10) | 0.02 (0.09) |
| Outdoor activity, hours per day [h] | 1.48 (0.51) | 1.50 (0.48) | 1.46 (0.48) |
| Near work, diopter hours per day [i] | 10.55 (3.55) | 10.20 (3.64) | 10.54 (3.69) |
| No. of parental myopia | | | |
| 1 | 66 (37.4%) | 62 (39.0%) | 58 (41.2%) |
| 2 | 94 (62.6%) | 97 (61.0%) | 97 (58.8%) |
| Baseline visit before the COVID-19 pandemic (January 1, 2020) | 94 (58.8%) | 102 (64.2%) | 92 (59.4%) |

No significant differences between baseline parameters

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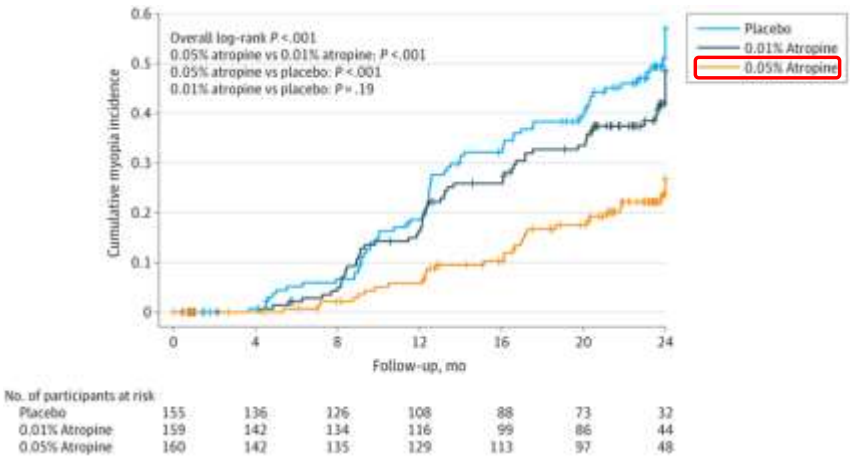
## Time to Myopia Onset by Treatment Group




**Significant lower 2-year cumulative myopia incidence in 0.05% atropine**





## Myopia incidence and Participants with Fast Myopic Shift Over 2 Years

Table 2. Primary Outcomes of Myopia Incidence and Participants With Fast Myopic Shift Over 2 Years

| Follow-up | No./total No. (%) | | | P value | | Difference (95% CI), % | | | P value[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0.05% Atropine | 0.01% Atropine | Placebo | For trend[a] | For trend (adjusted)[b] | 0.05% Atropine vs 0.01% atropine | 0.05% Atropine vs placebo | 0.01% Atropine vs placebo | 0.05% Atropine vs 0.01% atropine | 0.05% Atropine vs placebo | 0.01% Atropine vs placebo |
| Cumulative myopia incidence (defined as spherical equivalent ≤ −0.50 D) | | | | | | | | | | | |
| 4 mo | 1/138 (0.7) | 4/127 (3.1) | 8/130 (6.2) | .02 | .01 | 2.4 (−1.1 to 7.2) | 5.4 (1.4 to 11.0) | 3.0 (−2.5 to 8.9) | .15 | .01 | .25 |
| 8 mo | 8/133 (6.1) | 20/131 (15.3) | 21/120 (17.5) | .007 | .001 | 9.2 (1.8 to 17.1) | 11.4 (3.7 to 19.9) | 2.2 (−7.0 to 11.7) | .02 | .004 | .63 |
| 12 mo | 13/126 (9.6) | 33/109 (25.2) | 36/126 (30.5) | <.001 | <.001 | 15.6 (6.9 to 24.5) | 20.9 (11.8 to 30.4) | 5.3 (−5.4 to 16.0) | <.001 | <.001 | .33 |
| 16 mo | 23/124 (18.5) | 43/132 (32.6) | 44/124 (35.5) | .004 | .001 | 14.0 (3.4 to 24.4) | 16.9 (6.0 to 27.7) | 2.9 (−8.7 to 14.5) | .01 | .003 | .62 |
| 20 mo[c] | 26/95 (27.4) | 36/93 (39.1) | 38/88 (43.2) | .03 | .01 | 11.8 (−1.7 to 24.9) | 15.8 (2.0 to 29.2) | 4.1 (−10.3 to 18.2) | .08 | .03 | .58 |
| 24 mo | 33/116 (28.4) | 56/122 (45.9) | 61/115 (53.0) | <.001 | <.001 | 17.5 (5.2 to 29.2) | 24.6 (12.0 to 36.4) | 7.1 (−5.8 to 19.6) | .005 | <.001 | .27 |
| Participants with fast myopic shift (defined as spherical equivalent myopic shift ≥0.50 D over the first 12 mo and ≥1.00 D over 24 mo) | | | | | | | | | | | |
| 12 mo | 39/136 (28.7) | 68/139 (48.9) | 81/128 (63.3) | <.001 | <.001 | 20.2 (8.8 to 31.2) | 34.6 (22.5 to 45.2) | 14.4 (2.4 to 25.9) | <.001 | <.001 | .02 |
| 24 mo | 29/116 (25.0) | 55/122 (45.1) | 62/115 (53.9) | <.001 | <.001 | 20.1 (8.0 to 31.6) | 28.9 (16.5 to 40.5) | 8.8 (−3.9 to 21.3) | .001 | <.001 | .17 |

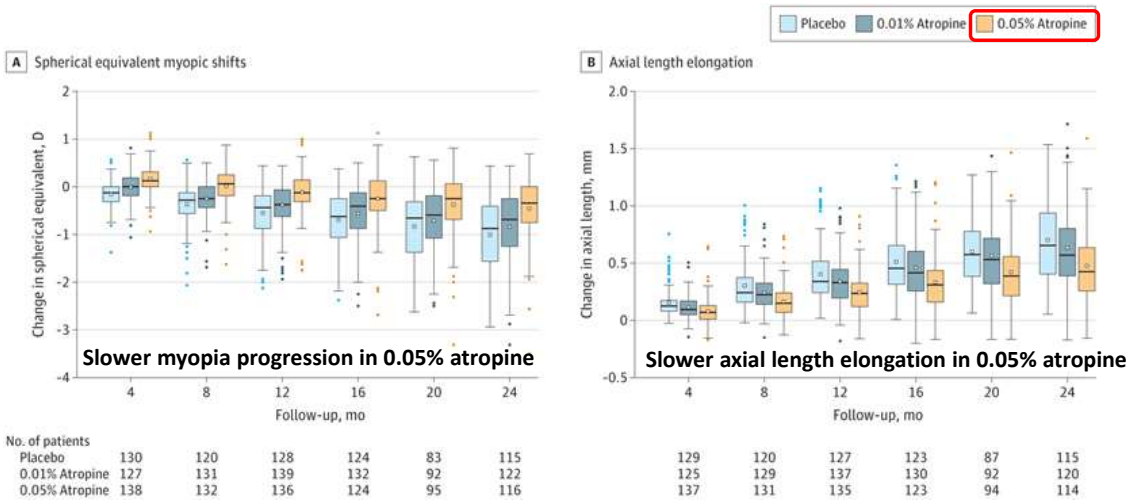
[a] P values for trend were calculated via logistic regression without adjustment.
[b] Adjusted P values for trend were calculated via logistic regression with adjustment of baseline age, sex, baseline spherical equivalent/axial length, outdoor time, near-work time, and parental myopia.
[c] P values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.
[d] A proportion of participants did not attend the 20-month visit because of infection control restrictions during the COVID-19 pandemic.

2-year Myopia Incidence:
- 0.05% Atropine: 28.4%
- 0.01% Atropine: 45.9%
- Placebo: 53.0%

2-year Fast Myopic Shift Rate:
- 0.05% Atropine: 25.0%
- 0.01% Atropine: 45.1%
- Placebo: 53.9%

**Significant lower myopia incidence and fast myopic shift rate over 2 years in 0.05% atropine**

## Spherical Equivalent Myopic Shifts and Axial Length Elongation Over 2 Years

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## Spherical Equivalent Myopic Shifts and Axial Length Elongation Over 2 Years

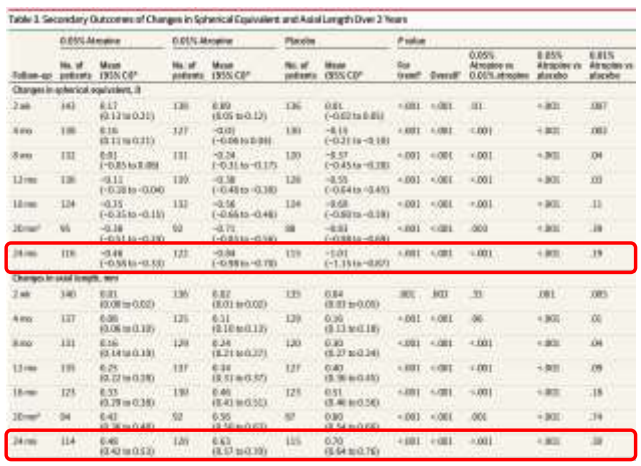

Table 3. Secondary Outcomes of Changes in Spherical Equivalent and Axial Length Over 2 Years

| Follow-up | 0.05% Atropine: No. of patients | 0.05% Atropine: Mean (95% CI)* | 0.01% Atropine: No. of patients | 0.01% Atropine: Mean (95% CI)* | Placebo: No. of patients | Placebo: Mean (95% CI)* | P value: For trend† | P value: Overall† | P value: 0.05% Atropine vs 0.01% Atropine | P value: 0.05% Atropine vs placebo | P value: 0.01% Atropine vs placebo |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Changes in spherical equivalent, D | | | | | | | | | | | |
| 2 wk | 143 | 0.17 (0.12 to 0.21) | 130 | 0.09 (0.05 to 0.12) | 136 | 0.01 (−0.02 to 0.05) | <.001 | <.001 | .01 | <.001 | .007 |
| 4 mo | 138 | 0.16 (0.11 to 0.21) | 127 | −0.01 (−0.06 to 0.04) | 130 | −0.13 (−0.21 to −0.18) | <.001 | <.001 | <.001 | <.001 | .002 |
| 8 mo | 132 | 0.01 (−0.05 to 0.05) | 131 | −0.24 (−0.31 to −0.17) | 120 | −0.57 (−0.65 to −0.50) | <.001 | <.001 | <.001 | <.001 | .04 |
| 12 mo | 136 | −0.11 (−0.16 to −0.06) | 139 | −0.38 (−0.46 to −0.30) | 128 | −0.93 (−0.04 to −0.85) | <.001 | <.001 | <.001 | <.001 | .03 |
| 18 mo | 124 | −0.35 (−0.35 to −0.15) | 132 | −0.56 (−0.66 to −0.46) | 124 | −0.68 (−0.80 to −0.58) | <.001 | <.001 | <.001 | <.001 | .11 |
| 26 mo† | 95 | −0.38 (−0.51 to −0.26) | 92 | −0.71 (−0.85 to −0.58) | 88 | −0.83 (−0.98 to −0.68) | <.001 | <.001 | .003 | <.001 | .18 |
| 24 mo | 116 | −0.46 (−0.56 to −0.36) | 122 | −0.84 (−0.98 to −0.70) | 119 | −1.01 (−1.15 to −0.87) | <.001 | <.001 | <.001 | <.001 | .19 |
| Changes in axial length, mm | | | | | | | | | | | |
| 2 wk | 140 | 0.01 (0.00 to 0.02) | 130 | 0.02 (0.01 to 0.02) | 135 | 0.04 (0.03 to 0.05) | .001 | .003 | .33 | .001 | .005 |
| 4 mo | 137 | 0.06 (0.06 to 0.10) | 125 | 0.11 (0.10 to 0.12) | 129 | 0.26 (0.13 to 0.18) | <.001 | <.001 | .06 | <.001 | .01 |
| 8 mo | 131 | 0.16 (0.14 to 0.18) | 129 | 0.24 (0.21 to 0.27) | 120 | 0.40 (0.37 to 0.44) | <.001 | <.001 | <.001 | <.001 | .04 |
| 12 mo | 135 | 0.25 (0.22 to 0.28) | 137 | 0.34 (0.31 to 0.37) | 127 | 0.49 (0.46 to 0.53) | <.001 | <.001 | <.001 | <.001 | .09 |
| 18 mo | 125 | 0.33 (0.29 to 0.38) | 130 | 0.46 (0.41 to 0.51) | 125 | 0.61 (0.46 to 0.56) | <.001 | <.001 | <.001 | <.001 | .15 |
| 26 mo† | 94 | 0.42 (0.36 to 0.48) | 92 | 0.56 (0.50 to 0.63) | 87 | 0.80 (0.74 to 0.86) | <.001 | <.001 | .001 | <.001 | .34 |
| 24 mo | 114 | 0.48 (0.42 to 0.53) | 120 | 0.63 (0.57 to 0.70) | 115 | 0.70 (0.64 to 0.76) | <.001 | <.001 | <.001 | <.001 | .38 |

2-year SE progression:

- 0.05% Atropine: -0.46 D
- 0.01% Atropine: -0.84 D
- Placebo: -1.01 D

2-year AL elongation:

- 0.05% Atropine: 0.48 mm
- 0.01% Atropine: 0.63 mm
- Placebo: 0.70 mm

**Significant lower SE progression and AL elongation over 2 years in 0.05% atropine**

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## Side Effects

| | First year | | | Second year | | |
|---|---|---|---|---|---|---|
| | 0.05% Atropine | 0.01% Atropine | Placebo | 0.05% Atropine | 0.01% Atropine | Placebo |
| Photochromic glasses needed | 0 (0.0%) | 1 (0.7%) | 0 (0.0%) | 0 (0.0%) | 2 (1.6%) | 2 (1.7%) |
| Progressive glasses needed | 0 (0.0%) | 0 (0.0%) | 1 (0.8%) | 0 (0.0%) | 1 (0.8%) | 0 (0.0%) |
| Photophobia | 28 (20.6%) | 29 (20.9%) | 13 (10.2%) | 15 (12.9%) | 23 (18.9%) | 14 (12.2%) |
| Allergic conjunctivitis | 5 (3.7%) | 7 (5.0%) | 8 (6.3%) | 5 (4.3%) | 3 (2.5%) | 2 (1.7%) |
| Hospitalization [a] | 1 (0.7%) | 5 (3.6%) | 2 (1.6%) | 5 (4.3%) | 2 (1.6%) | 1 (0.9%) |

a. Hospitalization was not related to the medication.

**0.05%, 0.01% Atropine group had no significant side effects**

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## Conclusions

1. First study, 2-year randomized clinical trial to evaluate the effect of low-concentration atropine on delaying the onset of myopia
2. 0.05% atropine, but not 0.01% atropine, reduced both the incidence of myopia and the percentage of children with fast myopic shift
3. 46.7% relative reduction in 2-year cumulative myopia incidence
4. Good tolerability for both 0.05% atropine and 0.01% atropine without severe adverse events

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# Take Home Messages

## LAMP Studies

1. Low-concentration atropine (0.05%, 0.025%, 0.01%) is effective to reduce myopia progression along concentration-related response
2. Concentration-dependent response was maintained throughout 3 year follow up
3. All low concentration groups are well tolerated through 3 years of follow-up
4. Low-concentration atropine has no effect on corneal power and lens power.
5. Age-dependent effect in each treatment group with 0.05%, 0.025%, and 0.01% atropine
6. Low concentration atropine induced a choroidal thickening effect along a concentration-dependent response throughout the treatment period
7. During the third year, continued atropine treatment achieved a better effect across all concentrations compared to the washout regimen
8. Stopping treatment at an older age and lower concentration is associated with a smaller rebound
9. The difference in rebound effect was clinically small across all three studied atropine concentrations.
10. 0.05% atropine is effective to delay the onset of myopia





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**Hong Kong Children Eye Study**
**Hong Kong Children Eye Genetics Study**
**Low-Concentration Atropine for Myopia Progression (LAMP) Study**

# Children Health Care Through Eye Care


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