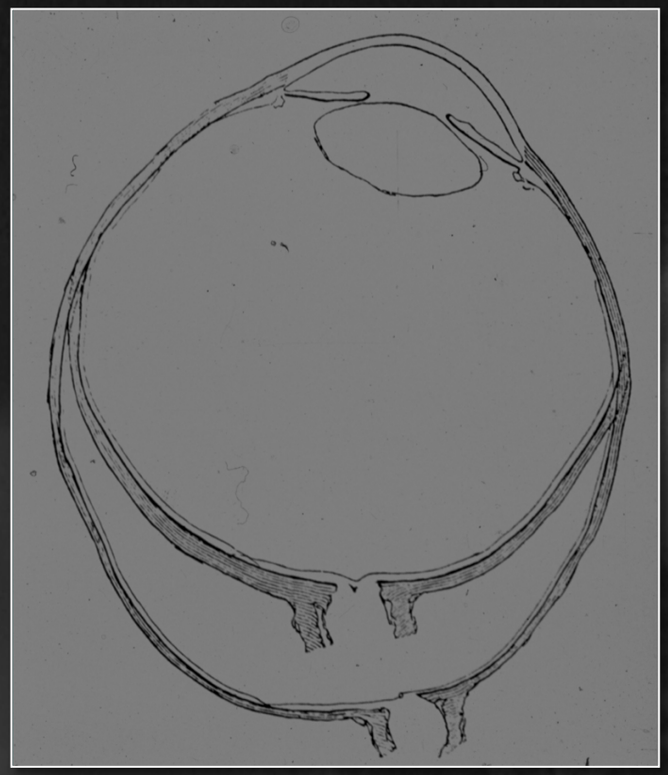
Symposium 32: Hot Topics 2015, AAO 2015, Las Vegas

5 year Clinical Trial on Atropine for the treatment of Myopia (ATOM2)



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(This presentation describes an off-label use of Atropine eyedrops as a form of myopia control)

ATOM1

Ophthalmology 2006;113:2285–2291

Atropine for the Treatment of Childhood Myopia

Wei-Han Chua, FRCSEd(Ophth), FAMS,[1,2] Vivian Balakrishnan, FRCS(Ed), FRCOphth,[1] Yiong-Huak Chan, PhD,[3] Louis Tong, FRCS(Ed),[1] Yvonne Ling, FRCS(Ed), FRCOphth,[1] Boon-Long Quah, FRCS(Ed), MMed(Ophth),[1] Donald Tan, FRCS(Ed), FRCOphth[1,2,3]

1% Atropine eyedrops have been around for many years, and are approved for use in babies and young children for the treatment of amblyopia (lazy eye), but previous studies have suggested that it may also slow down the progression of myopia in older children

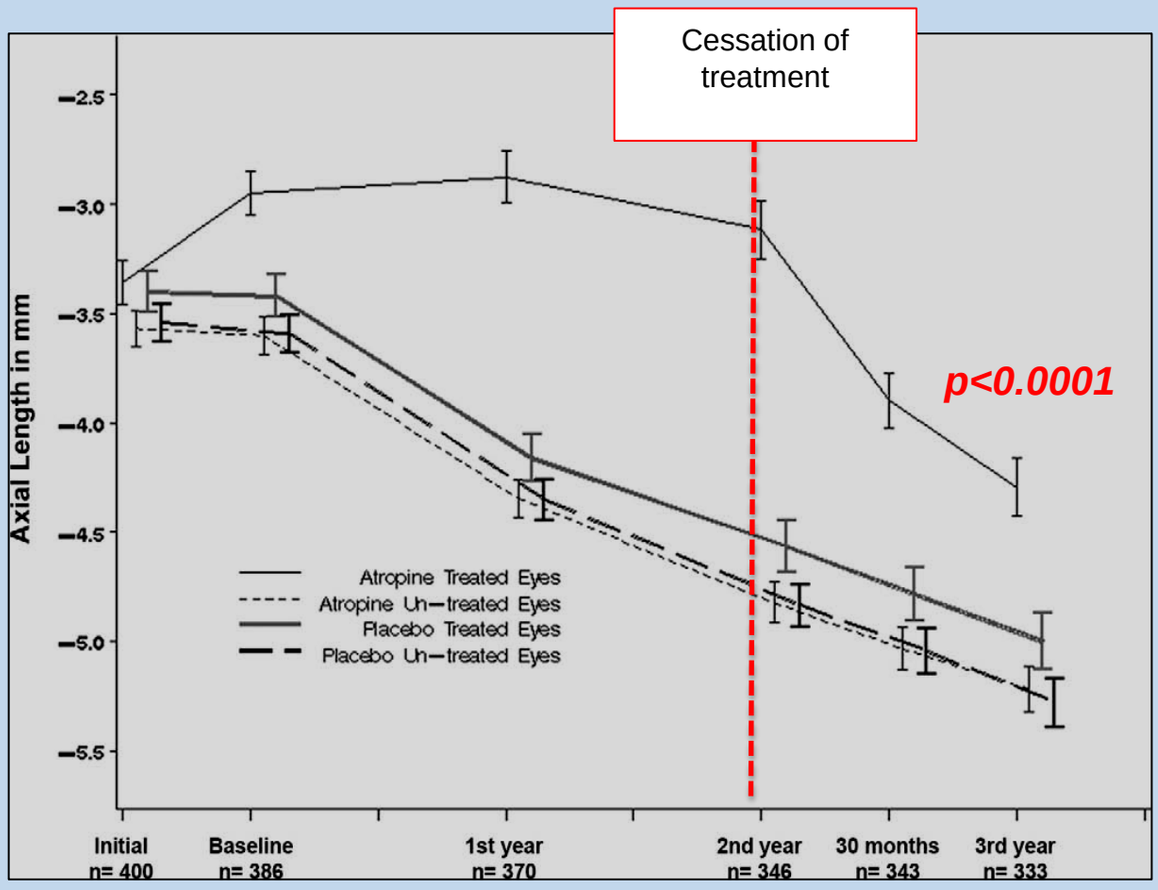
- *ATOM1: placebo-controlled double-masked RCT, 1999 to 2004*
- *400 children, 6-12 years, -1 to -6D, (mean: -3.5D)*
- *Treatment group: 1% atropine o.n. in one eye, other eye untreated*
- *Control group: Vehicle eyedrops in one eye, and other eye untreated*
- *3 year study: 2 years of treatment, 1 observational wash-out year*

Ophthalmology 2009;116:572–579

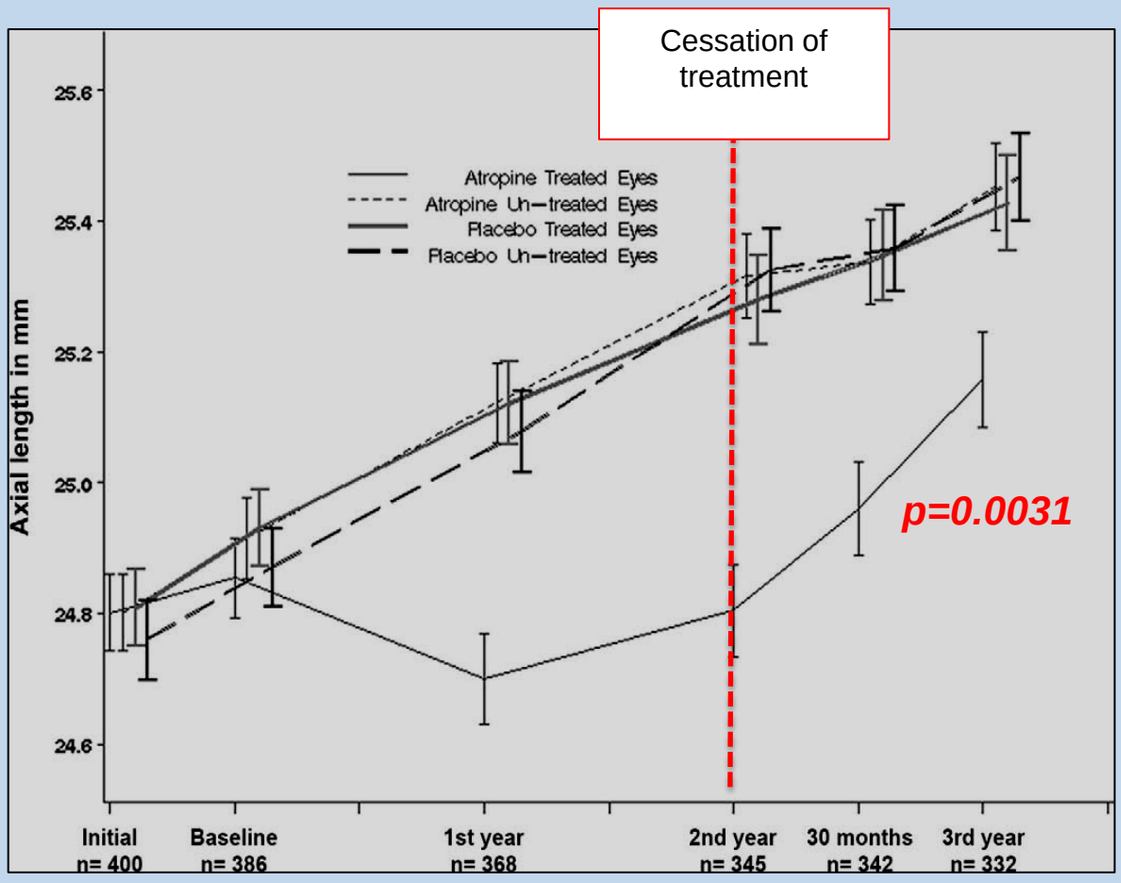
Atropine for the Treatment of Childhood Myopia: Effect on Myopia Progression after Cessation of Atropine

Louis Tong, FRCS, DM,[1] Xiao Ling Huang, BSc (Hons),[2] Angeline L. T. Koh, BHSc,[2] Xiaoe Zhang, MSc,[2] Donald T. H. Tan, FRCS, FRCOphth,[1,3,4] Wei-Han Chua, FRCSEd (Ophth), FAMS[1]

ATOM 1



Change in Refractive Error (D)



Axial length change (mm)

- *First 2 years: 77% **reduction** in mean progression of myopia, strong correlation with axial length*
- *Usual side-effects: **pupil dilation, glare, loss of accommodation***
- *Year 3: significant **rebound of myopia progression** upon cessation of atropine 1% eyedrops*

ATOM2

- *Study Aim: to compare safety and efficacy of 3 lower doses of atropine*
- *double-masked RCT, 2006 to 2012*
- *400 children, 6-12 years, ≥-2D,*
- *Randomized: 0.5% (n=161)*
  0.1% (n=155)
  0.01% (n=84)
- *Slightly older children (9.7 yrs vs 9.2 yrs), higher myopia (-4.7D vs -3.5D) vs ATOM1*
- *Bilateral eye treatment*
- *5 year study:*
  Treatment phase 1: 2 years of treatment

  Treatment phase 2: Year 3: wash-out year

  Treatment phase 3: Year 4,5: continuing progressors restarted on treatment with one dosage

Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1%, and 0.01% Doses (Atropine for the Treatment of Myopia 2)

Audrey Chia, FRANZCO,[1,2] Wei-Han Chua, FRCSEd(Ophth), FAMS,[1,2] Yin-Bun Cheung, PhD,[3,4] Wan-Ling Wong, Mbiostat,[2] Anushia Lingham, SRN,[4] Allan Fong, FRCSEd(Ophth),[1,2] Donald Tan, FRCS, FRCOphth[1,2,5]

Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A, Tan D. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology 2012;119(2):347-54.

Atropine for the Treatment of Childhood Myopia: Changes after Stopping Atropine 0.01%, 0.1% and 0.5%

AUDREY CHIA, WEI-HAN CHUA, LI WEN, ALLAN FONG, YAR YEN GOON, AND DONALD TAN

Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: Changes after stopping Atropine 0.01%, 0.1% and 0.5%. Am J Ophthalmol 2014;157:451-457

AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2

Myopia Control with Atropine 0.01% Eyedrops

Audrey Chia, FRANZCO, PhD,[1,2] Qing-Shu Lu, PhD,[3,4] Donald Tan, FRCS, FRCOphth[1,2,4,5]

E-pub (accepted July 2015), Ophthalmology

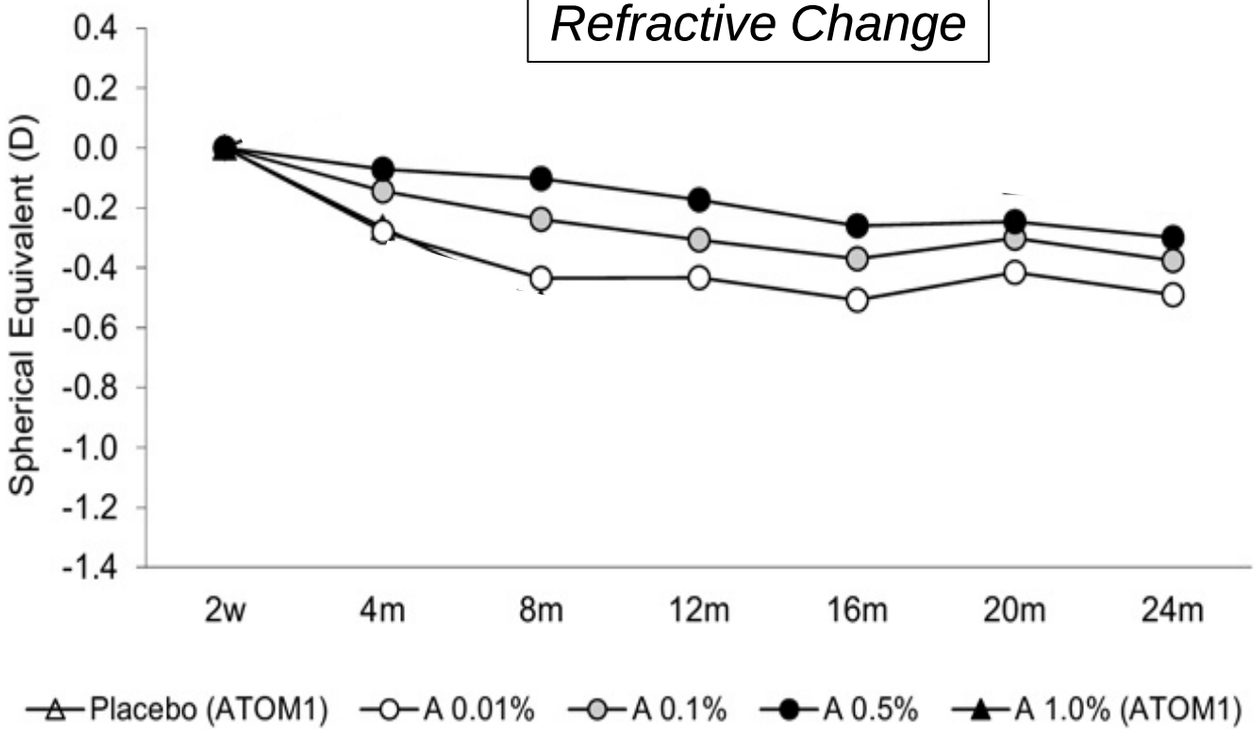
ATOM2

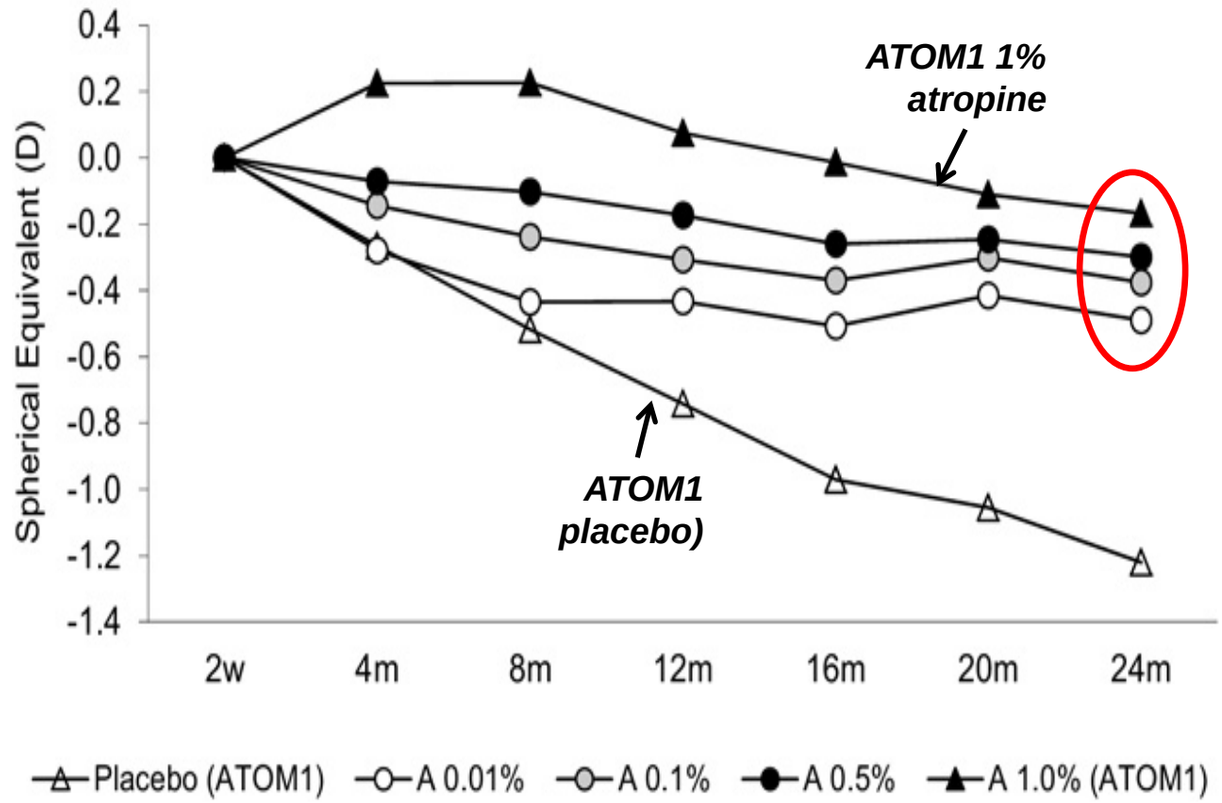
Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1%, and 0.01% Doses (Atropine for the Treatment of Myopia 2)

Audrey Chia, FRANZCO,[1,2] Wei-Han Chua, FRCSEd(Ophth), FAMS,[1,2] Yin-Bun Cheung, PhD,[3,4] Wan-Ling Wong, Mbiostat,[2] Anushia Lingham, SRN,[4] Allan Fong, FRCSEd(Ophth),[1,2] Donald Tan, FRCS, FRCOphth[1,2,5]

Ophthalmology 2012;119:347–354

Refractive Change





Dose-related response, but clinically small differences

Mean Spherical Equivalent:

Before study started: -4.7D

0.5% atropine: -4.6D (1.9)

0.1% atropine: -4.8D (1.4)

0.01% atropine: -4.9D (1.5) (p=0.20)

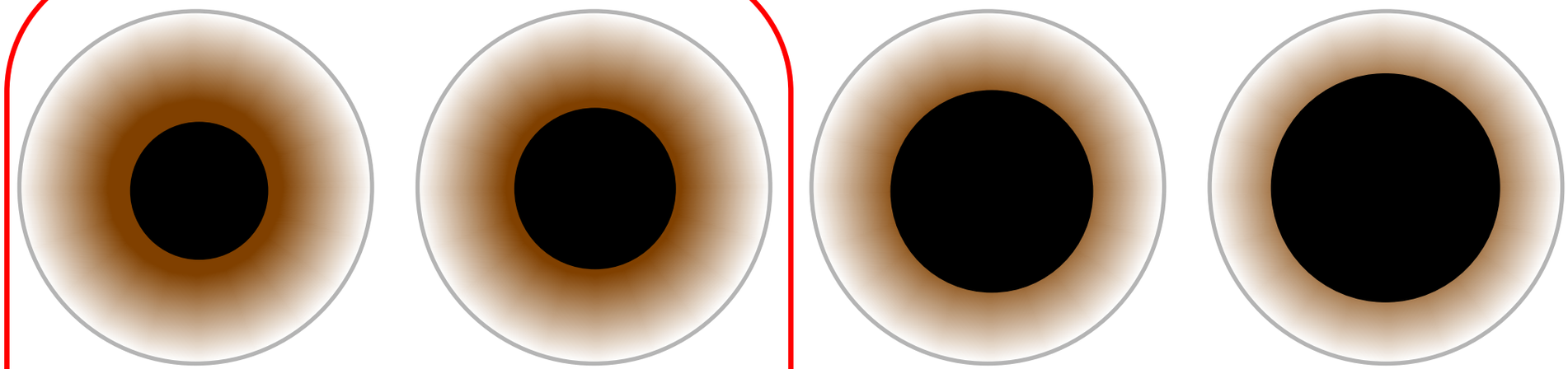
Consolidating ATOM 1 and 2, it appears that 0.01% atropine is clinically similar to 0.1%, 0.5% and 1.0% in efficacy, as compared to placebo

ATOM2

Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1%, and 0.01% Doses (Atropine for the Treatment of Myopia 2)

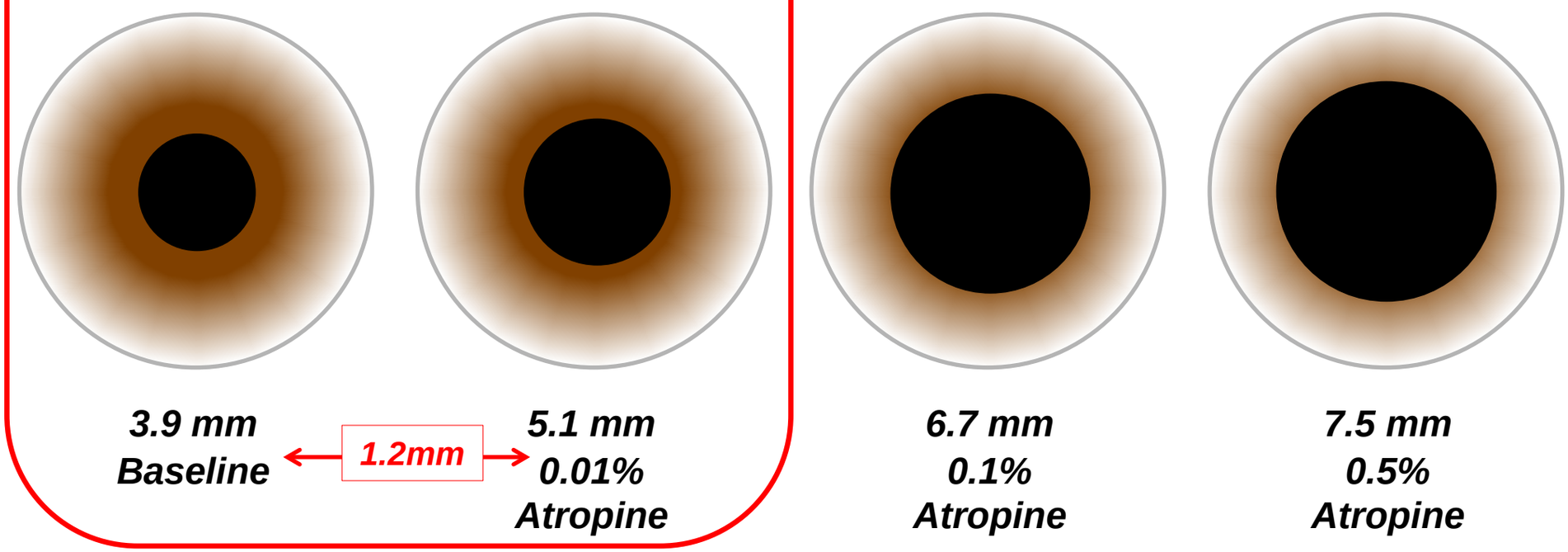
Audrey Chia, FRANZCO,[1,2] Wei-Han Chua, FRCSEd(Ophth), FAMS,[1,2] Yin-Bun Cheung, PhD,[3,4] Wan-Ling Wong, Mbiostat,[2] Anushia Lingham, SRN,[4] Allan Fong, FRCSEd(Ophth),[1,2] Donald Tan, FRCS, FRCOphth[1,2,5]

Mean Mesopic Pupil Size:



(P<0.001)

Mean Photopic Pupil Size:



(P<0.001)

ATOM1+2 Safety Data

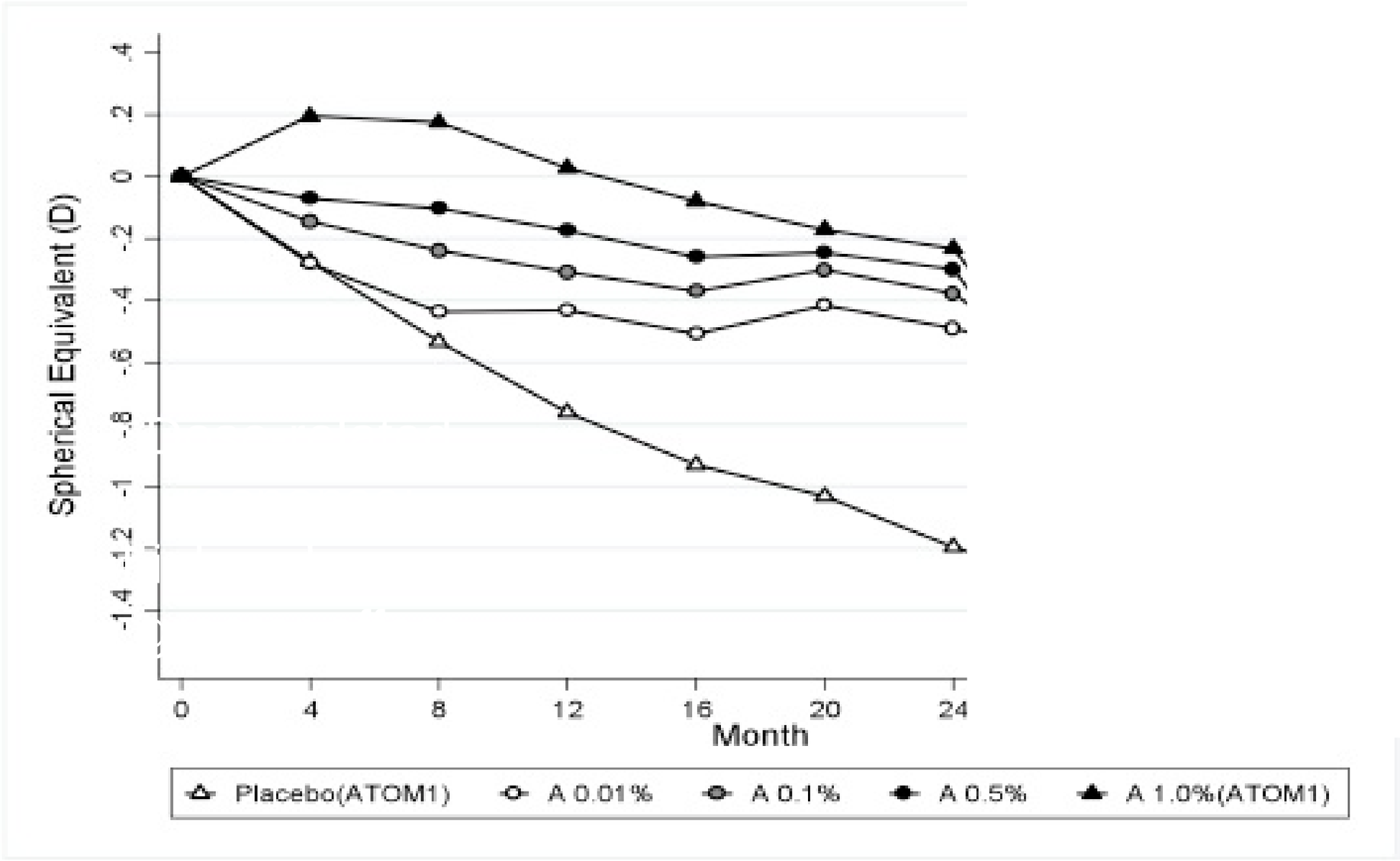
- *No serious adverse events during entire study – no cataract, glaucoma, retinal disease, no systemic side-effects*

- *Very minor side-effects : glare – 1%, no loss of near vision*

Luu CD, Lau AM, Koh AH, Tan D. Multifocal electroretinogram in children (ATOM1). BJO 2005;89:151-3

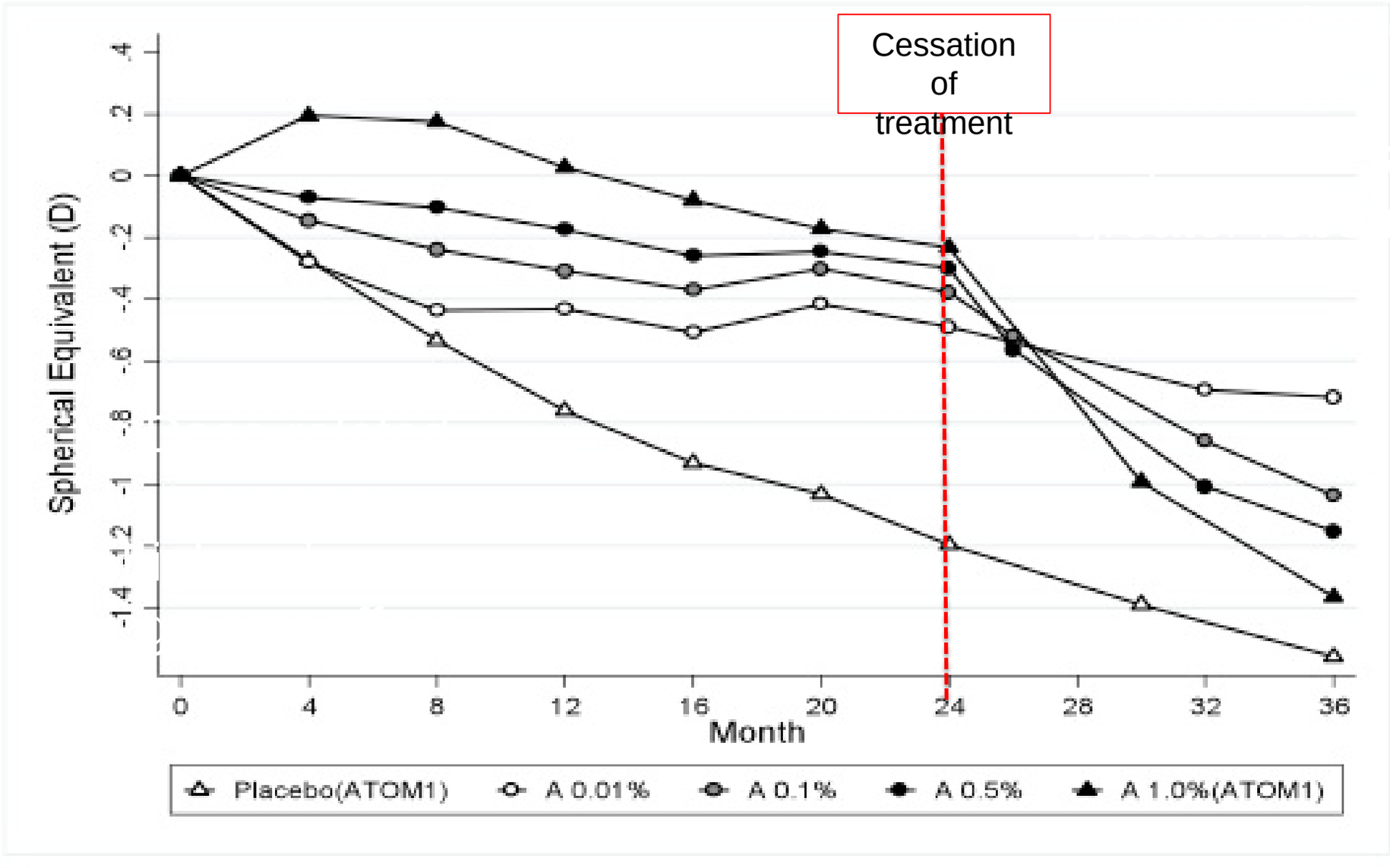
Chia A, Li W, Tan D, Luu CD. Full-field electroretinogram findings in children (ATOM2). Doc Ophthal. 2013;126:177-86

ATOM2 : Phase 2: washout stage (year 3)



- *Atropine treatment stopped at 24 months*
- *One year washout period: 365 children (89%)*
- *Pupil size, accommodation all returned to normal*

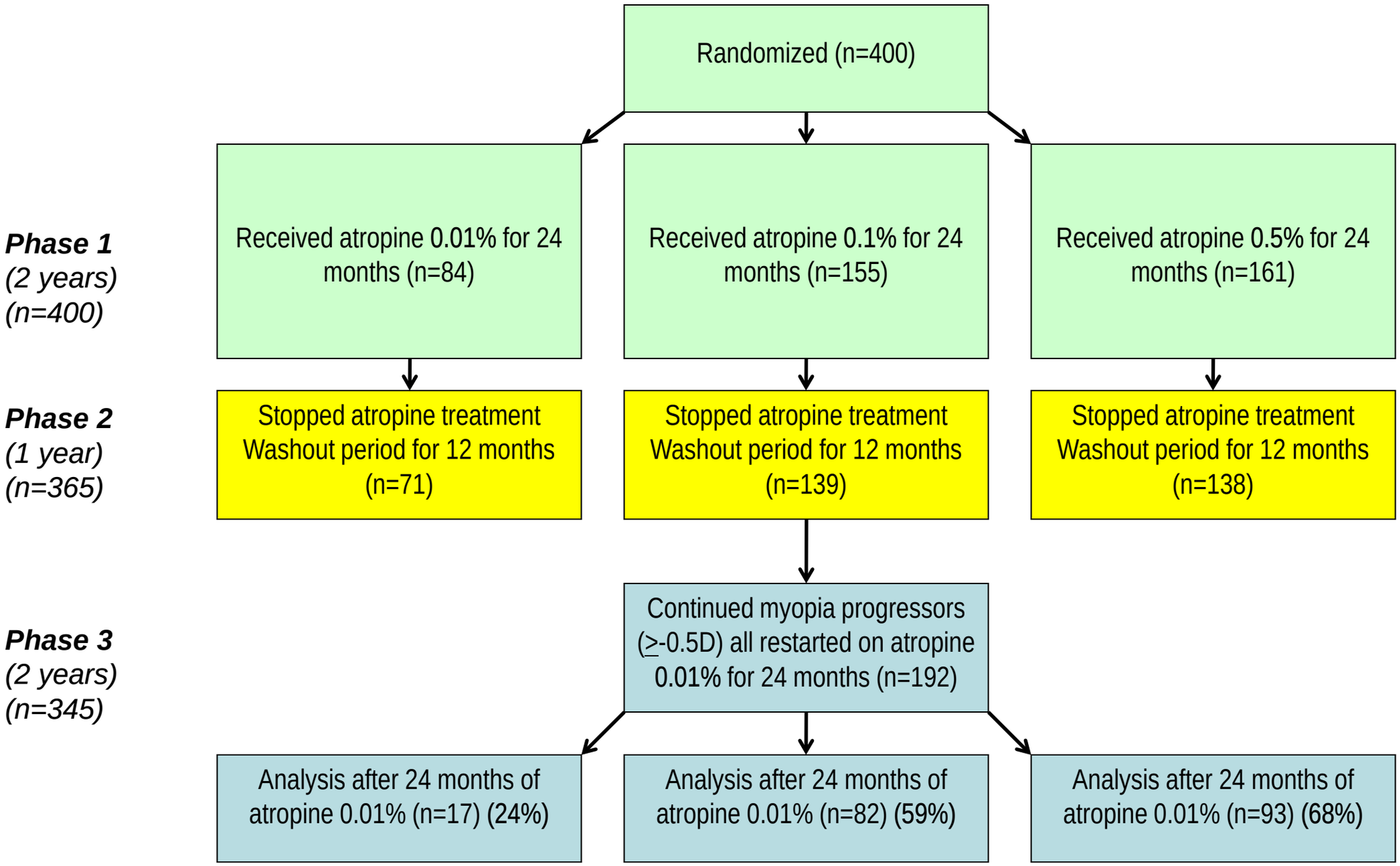
ATOM1+2 : Phase 2: washout stage (year 3)



- *Atropine treatment stopped at 24 months*
- *One year washout period: 365 children (89%)*
- *Pupil size, accommodation all returned to normal*

- *Clear rebound phenomenon, but dose-related*
- *0.01% atropine had minimal rebound*

ATOM2 : Phase 3: all those still progressing (5 years) restarted on Atropine 0.01% after Washout

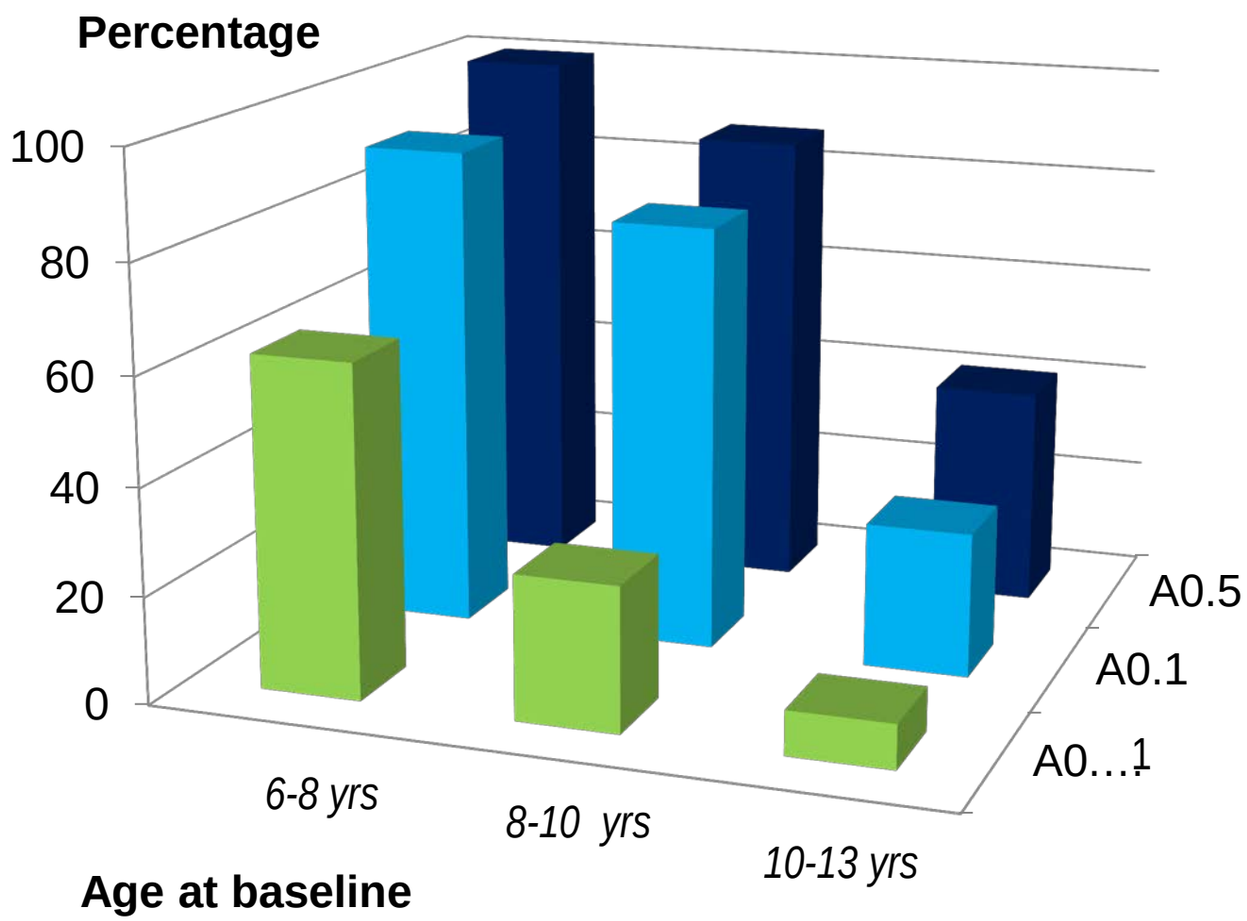


ATOM2 : Proportion that progressed >0.5D at (5 years) washout (between 24-36 months

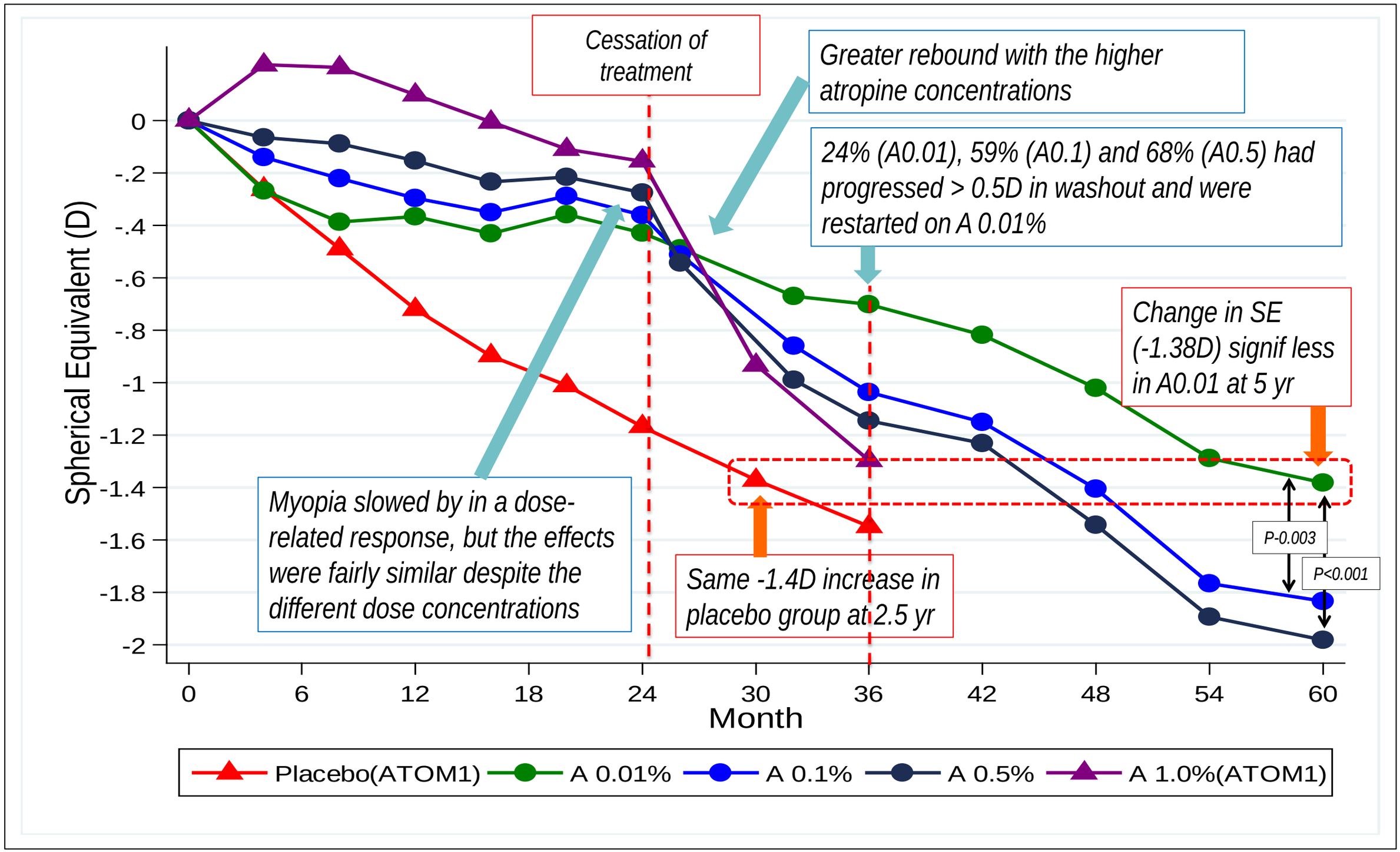
- *The percentage of children who continued to have progressive myopia after the washout period related to the original concentration of atropine used in Phase 1:*
  - *0.5% atropine group: 68% progressed*
  - *0.1% atropine group: 59% progressed*
  - *0.01% atropine group: 24% progressed*

- *Children requiring retreatment were:*
  - *younger*
  - *had less myopia at baseline*
  - *greater increase in myopia at Phase 1*

Percentage of children in each atropine group who required retreatment at 3 years because they had progressed by >0.5D



ATOM1 (3 year) and ATOM2 (5 year) data



So what have we learnt from the ATOM trials?
(in the last 14 years!)

- *Atropine eyedrops **reduces myopia progression and axial elongation** in children in a **dose-related** manner, but a **rebound phenomenon** occurs with the higher doses of atropine*

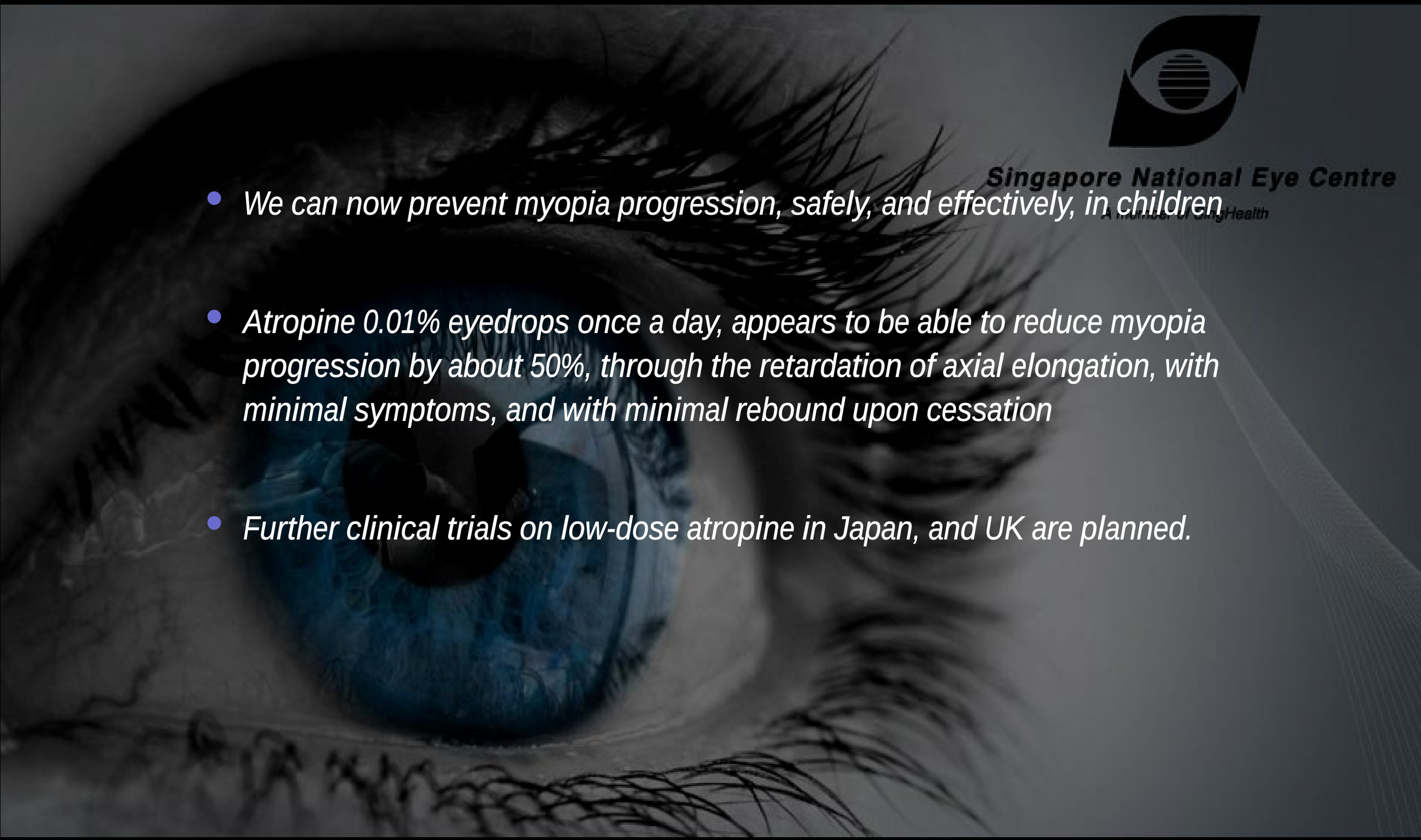
- *Atropine eyedrops are safe, with no serious adverse events, but in the higher doses, the side-effects of pupil dilatation, loss of accommodation and near vision limits practical use*

- *Atropine 0.01% has the best therapeutic index, with clinically insignificant amounts of pupil dilatation, near vision and accommodation loss, and yet is as effective as the higher doses*

- *Atropine 0.01% appears to retard myopia progression by 50%, and **retreatment** after a period of treatment cessation **still appears to be equally effective***

1. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the treatment of childhood myopia. Ophthalmology 2006;113:2285-91.
2. Tong L, Huang XL, Koh AL, et al. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. Ophthalmology 2009;116:572-9.
3. Chia A, Chua WH, Tan D. Effect of topical atropine on astigmatism. Br J Ophthalmol. 2009 Jun;93(6):799-802.
4. Luu CD, Lau AM, Koh AH, Tan D. Multifocal electroretinogram in children on atropine treatment for myopia. Br J Ophthalmol. 2005 Feb;89(2):151-3.
5. Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A, Tan D. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology 2012;119(2):347-54.
6. Chia A, Li W, Tan D, Luu CD. Full-field electroretinogram findings in children in the atropine treatment for myopia (ATOM2) study. Doc Ophthalmol. 2013 Jan 5.
7. Chia A, Chua WH, Li W, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping Atropine 0.01%, 0.1% and 0.5% (ATOM2). Submitted AJO 2013.
8. Chia A, Lu QS, Tan D. Myopic control in children re-started on Atropine 0.01% after a 12 month washout period (ATOM2). Being prepared for submission.

What is the Impact?



- *We can now prevent myopia progression, safely, and effectively, in children*
- *Atropine 0.01% eyedrops once a day, appears to be able to reduce myopia progression by about 50%, through the retardation of axial elongation, with minimal symptoms, and with minimal rebound upon cessation*
- *Further clinical trials on low-dose atropine in Japan, and UK are planned.*

Acknowledgements

SERI Leaders in Myopia Research

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Wallace Foulds

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Singapore National Eye Centre
A member of SingHealth

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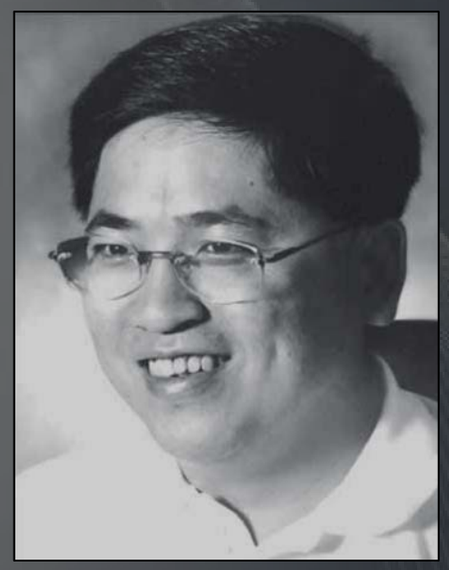

Dedicated to the memory of
Chew Sek-Jin
1959-1999