Supplemental Online Content

Yam JC, Zhang XJ, Zhang Y, et al. Effect of Low-Concentration Atropine Eyedrops vs Placebo on Myopia Incidence in Children. *JAMA.* Published online February 14, 2023. doi:10.1001/jama.2022.24162

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix Table 1. Summary of Randomized Controlled Trials (RCTs) in Atropine for Myopia Control

Author (s), Year	Area	Follow-up, months	Sample Size	Age, years	Arms and Treatments	Baseline Spherical Equivalent, D	Baseline Axial Length, mm	Change in Spherical Equivalent, D	Change in Axial Length, mm
Yen, MY. et al, 1989[1]	Taiwan	12	96	6 to 14		-0.5 to -4.0 D			
			32	10.5	1 % Atropine	-1.52 (0.96)	NA	-0.22 (0.54) D/year	NA
			32	10.0	1% Cyclopentolate	-1.45 (0.85)	NA	-0.58 (0.49) D/year	NA
			32	10.4	Placebo	-1.59 (0.92)	NA	-0.91 (0.58) D/year	NA
Shih, YF. et al,1999[2]	Taiwan	24	200	6 to 13		-0.5 to -7.0 D			
			41	9.8	0.5 % Atropine	-4.89 (2.06)	NA	-0.04 (0.63) D/year	NA
			47	9.7	0.25 % Atropine	-4.24 (1.74)	NA	-0.45 (0.55) D/year	NA
			49	8.9	0.1 % Atropine	-4.41 (1.47)	NA	-0.47 (0.91) D/year	NA
			49	8.3	0.5% Tropicamide	-4.50 (1.86)	NA	-1.06 (0.61) D/year	NA
Shih, YF. et al, 2001[3]	Taiwan	18	227	6 to 13					
			76	N/A	0.5 % Atropine+multi-focal lenses	-3.20 (0.14)	24.75 (0.10)	-0.41 (0.07) D/year	0.22 (0.03) mm/year
			75	N/A	Multi-focal lenses	-3.34 (0.14)	24.80 (0.09)	-1.19 (0.07) D/year	0.49 (0.03) mm/year
			76	N/A	Single vision spectacles	-3.28 (0.13)	24.62 (0.10)	-1.40 (0.09) D/year	0.59 (0.04) mm/year
Chua, WH. et al, 2006 (ATOM1 study)[4]	Singapore	24	400	6 to12		-1.0 D to -6.0 D			
			200	9.2	1 % Atropine treated	-3.36 (1.38)	24.80 (0.83)	-0.28 (0.92) D/2year	-0.02 (0.35) D/2year
					1 % Atropine untreated	-3.40 (1.35)	24.81 (0.84)		
			200	9.2	Placebo treated	-3.58 (1.17)	24.80 (0.84)	-1.20 (0.69) D/2year	0.38 (0.38) D/2year
					Placebo untreated	-3.55 (1.21)	24.76 (0.86)		
Liang, CK. et al, 2008[5]	Taiwan	8.28 ± 2.48	71	6 to 15		-0.5 D or less			
			23	10.91 (2.43)	0.5 % Atropine	-2.17 (1.48)	24.11 (0.89)	-0.15 (0.15) D/year	NA
			22	9.91 (2.11)	0.25 % Atropine	-2.09 (1.68)	24.24 (0.53)	-0.38 (0.32) D/year	NA
			26	10.23 (1.66)	0.25 % Atropine+acupoints	-1.91 (1.20)	23.95 (0.77)	-0.21 (0.23) D/year	NA
Chia, A. et al, 2012 (ATOM2 study)[6]	Singapore	24	400	6 to 12		-2.0 D or less			
			161	9.70 (1.5)	0.5 % Atropine	-4.7 (1.8)	25.2 (0.9)	-0.30 (0.60) D/2year	0.27 (0.25) mm/2year
			155	9.70 (1.6)	0.1 % Atropine	-4.8 (1.5)	25.2 (0.8)	-0.38 (0.60) D/2year	0.28 (0.28)

									mm/2year
			84	9.50 (1.5)	0.01 % Atropine	-4.5 (1.5)	25.1 (1.0)	-0.49 (0.63) D/2year	0.41 (0.32) mm/2year
Yi, S. et al, 2015[7]	China	12	132	7 to 12		-0.5 to -2.0 D			
			68	9.91 (1.36)	1 % Atropine	-1.23 (0.32)	23.75 (0.10)	0.32 (0.22) D/year	-0.03 (0.07) mm/year
			64	9.72 (1.40)	Placebo	-1.15 (0.30)	23.72 (0.12)	-0.85 (0.31) D/year	0.32 (0.15) mm/year
Wang, YR. et al, 2017[8]	China	12	126	5 to 10		-0.5 to -2.0 D			
			63	9.1 (1.4)	0.5 % Atropine	-1.3 (0.4)	24.1 (1.0)	-0.8 D/year	23.0 mm at 1 year
			63	8.7 (1.5)	Placebo	-1.2 (0.3)	23.8 (0.9)	-2.0 D/year	24.3 mm at 1 year
Yam, JC. et al, 2019 (LAMP study)[9]	Hong Kong	12	438	4 to 12		-1.0 D or less			
			109	8.45 (1.81)	0.05% Atropine	-3.98 (1.69)	24.85 (0.90)	-0.27 (0.61) D/year	0.20 (0.25) mm/year
			108	8.54 (1.71)	0.025% Atropine	-3.71 (1.85)	24.86 (0.95)	-0.46 (0.45) D/year	0.29 (0.20) mm/year
			110	8.23 (1.83)	0.01% Atropine	-3.77 (1.85)	24.70 (0.99)	-0.59 (0.61) D/year	0.36 (0.29) mm/year
			111	8.42 (1.72)	Placebo	-3.85 (1.95)	24.82 (0.97)	-0.81 (0.53) D/year	0.41 (0.22) mm/year
Fu, A. et al, 2020[10]	China	12	336	6-14		−1.25 to −6.00D			
			117	9.40 (1.80)	0.02% Atropine	-2.76 (1.47)	24.60 (0.72)	-0.38 (0.35)	0.30 (0.21)
			119	9.30 (1.90)	0.01% Atropine	-2.70 (1.64)	24.58 (0.74)	-0.47 (0.45)	0.37 (0.22)
			100	9.50 (1.40)	Control group	-2.68 (1.42)	24.55 (0.71)	-0.70 (0.60)	0.46 (0.35)
Kinoshita, N. et al, 2020[11]	Japan	24	73	8-12		-1.0 D to -6.0 D			
			38	10.33 (1.59)	OK and 0.01% atropine ophthalmic solution	-2.60 (1.29)	24.69 (0.58)	NA	0.29 (0.20)
			35	10.37 (1.65)	OK	-2.72 (1.31)	24.86 (0.81)	NA	0.40 (0.23)
Tan, Q. et al, 2020[12]	Hong Kong	12	59	6-11		-1.0 D to -4.0 D			
			29	9.0 (1.2)	0.01% Atropine with ortho-k (AOK)	-2.65 (0.92)	24.43 (0.62)	2.95 (1.00)	0.07 (0.16)
			30	9.0 (1.2)	Ortho-k alone (OK)	-2.84 (0.96)	24.43 (0.81)	2.87 (0.97)	0.16 (0.15)
Wei, S.et al, 2020[13]	China	12	220	6-12		-1.0 D to -6.0 D			
			110	9.44 (1.80)	0.01% Atropine	-2.52 (1.33)	24.50 (0.76)	-0.49 (0.42)	0.32 (0.19)
			110	9.84 (1.53)	Placebo	-2.64 (1.46)	24.69 (0.97)	-0.76 (0.50)	0.41 (0.19)

Ye, L.et al, 2020[14]	China	6	185	6-12		-1.0 D to -3.0 D			
			98	8.94 (1.55)	1% Atropine	-2.12 (1.09)	24.34 (0.82)	0.28 (0.37)	−0.03 (0.12)
			87	8.84 (1.65)	0.01% Atropine	-2.16 (1.10)	24.27 (0.74)	-0.27 (0.34)	0.19 (0.12)
Zhao, Q.et al, 2021[15]	China	12	80	5-14		-1.0 D to -3.0 D			
			20	9.7 (1.49)	Spectacles	-1.93 (0.74)	24.28 (0.83)	-1.30 (0.44)	0.72 (0.21)
			20	9.65 (1.53)	Spectacles with 0.01% atropine	-1.98 (0.45)	24.17 (0.68)	-0.34 (0.16)	0.24 (0.12)
			20	11.00 (1.17)	Orthokeratology	-2.75 (0.46)	24.42 (0.48)	-0.33 (0.16)	0.29 (0.11)
			20	10.9 (1.29)	Orthokeratology with 0.01% atropine	-2.85 (0.45)	24.56 (0.39)	-0.15 (0.08)	0.14 (0.08)
Moriche-Carretero, M.et al, 2021[16]	Spain	24	339	5-11		-1.0 D to -4.0 D			
			168	7.24 (1.77)	Control	-2.16 (0.62)	24.26 (0.91)	-0.76 (0.37)	0.37 (0.27)
			171	7.37 (1.54)	0.01% Atropine	-2.13 (0.63)	24.22 (0.66)	-0.51 (0.39)	0.20 (0.20)
Saxena, R.et al, 2021[17]	India	12	102	6-14		-0.5D to -6.0 D			
			47	10.6 (2.2)	0.01% Atropine	-3.45 (1.3)	24.62 (0.98)	-0.16 (0.38)	0.22 (0.20)
			45	10.8 (2.2)	Placebo	-3.68 (1.3)	24.70 (0.74)	-0.35 (0.4)	0.28 (0.28)
Hieda, O.et al, 2021[18]	Japan	24	168	6-12		-1.0 D to -6.0 D			
			84	8.99 (1.44)	0.01% Atropine	-2.91	24.43	-1.26	0.63
			84	8.98 (1.50)	Placebo	-2.98	24.51	-1.48	0.77
Zhao, Q.et al, 2021[19]	China	12	120	8-10		At least -1.0 D			
					Spectacles and 0.01% atropine	-5.82 (0.76)	27.03 (0.58)	-0.38 (0.09)	0.29 (0.08)
					Orthokeratology	-5.97 (0.72)	27.12 (0.57)	-0.35 (0.10)	0.24 (0.08)
Hao, Q.et al, 2021[20]	China	12	75	8-12		-1.0 D to -6.0 D			
			22		Spectacles and 0.01% atropine	-3.62 (0.57)	24.91 (0.61)	NA	0.20 (0.03)
			24		OK	-3.66 (0.60)	25.17 (0.52)	NA	0.28 (0.03)
			21		OK and 0.01% atropine	-4.07 (0.74)	25.29 (0.56)	NA	0.14 (0.03)
Cui, C.et al, 2021[21]	China	24	300	6-14		-1.25D to -6.00 D			
			105		0.02% Atropine	-2.81 (1.47)	24.61 (0.69)	-0.03	0.03
			106		0.01% Atropine	-2.76 (1.56)	24.60 (0.72)	-0.04	0.03
			89		Single-vision spectacles	-2.66 (1.39)	24.54 (0.69)	-0.06	0.04
Lee, SS.et al, 2022[22]	Australia	24	153	9-14		Less than -1.50 D			
			49	12.2 (2.5)	Placebo	-3.56	24.7	-0.78	0.38
			104	11.2 (2.7)	Atropine 0.01%	-3.13	24.6	-0.64	0.34

Jethani, J.et al, 2022[23]	India	24	60	4-12		Less than +1.0 D			
			30		0.01% Atropine	NA	20.8 (0.6)	-0.31 (0.3)	0.12 (0.1)
			30		Control	NA	21.0 (0.5)	-0.76 (0.4)	0.21 (0.2)
Chan, HHL.et al, 2022[24]	Hong Kong	18	61	7-10		-0.5 D to -5.0 D			
					0.01% Atropine	-1.88 (1.08)	24.17 (0.79)	-0.70 (0.39)	0.32 (0.16)
					Placebo	-1.74 (0.71)	24.09 (0.74)	-0.66 (0.41)	0.30 (0.22)
Sen, S.et al, 2022[25]	India	24	145	5-15		More than -2.0 D			
			72		Atropine 0.01%	-4.26	24.61	0.33	0.12
			73		Placebo	-4.98	24.86	0.89	0.31
Chen, Y.et al, 2022[26]	China	12	62	7-15		At least -1.0 D			
			31		Repeated low-level red light	-2.60 (1.17)	24.48 (0.79)	-0.03	0.08
			31		0.01% Atropine eye drops	-2.59 (1.24)	24.67 (0.98)	-0.60	0.33
Yu, S.et al, 2022[27]	China	12	53	8-12		-1.0 D to -4.0 D			
			27		OK and 0.01% atropine eye drops	-2.81 (0.92)	24.79 (0.72)	NA	0.10 (0.14)
			26		OK and placebo	-2.81 (0.97)	24.64 (0.79)	NA	0.20 (0.15)

Mean (SD) showed in this Table. Abbreviations: OK, Orthokeratology; NA, not available.

eAppendix Table 2. Summary of Ongoing Randomized Controlled Trials (RCTs) in Atropine for Myopia Control [a]

Investigator (s), year	Area	Follow-up, months	Sample Size	Age, years	Arms and Interventions
Repka, X. et al, 2017	USA	30	187	5-12	
					1. 0.01% Atropine eyedrops
					2. Placebo
Chia, A.et al, 2017	Singapore	40	571	5-9	
					1. Premyopia Group: Active Comparator: Atropine 2. 0.01%/Placebo Comparator: Placebo
					3. Low myopia Group: Active Comparator: Atropine 4. 0.01%/Placebo Comparator: Placebo
Ganesh, A.et al, 2018	Oman	36	150	6-15	
					1. Atropine Sulfate 0.01% Eye Drops
					2. Control
Zhu, JF.et al, 2019	China	12	222	7-12	
					1. Atropine Sulfate 1 % Ophthalmic 2. Ointment and Atropine Sulfate 3. 0.01% Eye Drop
					4. Atropine 0.01% eye drop
Azuara-Blanco, A.et al, 2019	UK	24	289	6-12	
			193		1. Atropine 0.01%
			96		2. Placebo
Sankaridurg, P.et al, 2019	Vietnam	24	112	6-13	
					1. BHVI1 (atropine) eye drops
					2. BHVI2 (atropine) eye drops
					3. Combination of BHVI1 and BHVI2 eye drops
					4. Non-randomized control: single-vision spectacles
Kessel, L.et al, 2019	Denmark	36	97	6-12	
					1. 0.1% Atropine and 0.01% atropine
					2. 0.01% Atropine
					3. 0.9% Sodium-chloride
Sydnexis, Inc. 2019	USA	36	852	3-14	
					1. SYD-101 (atropine) Dose 1
					2. SYD-101 (atropine) Dose 2
					3. Placebo
Donatello, D.et al, 2019	USA	36	420	3-12	
					1. Atropine 0.1% Ophthalmic Solution

					2. Atropine 0.01% Ophthalmic Solution
					3. Placebo Ophthalmic Solution
Sauer, A.et al, 2020	France	12	160	4-12	
					1. Atropine 0.01%
					2. Placebo
Zhu, JF.et al, 2021	China	24	186	8-15	
			62		1. Atropine Sulfate 0.01% Eye Drop
			62		2. Atropine Sulfate 0.04% Eye Drop
			62		3. Orthokeratology
Xu, X.et al, 2021	China	36	357	6-12	
					1. 0.01% Atropine
					2. 0.04% Atropine
					3. 0.1% Atropine
Martin, G.et al, 2021	France	24	242	4-14	
					1. Defocus Incorporated Multiple Segments® lenses
					3. Atropine 0.05% eyedrops and Monofocal lenses
Lagrèze, W.et al, 2021	Germany	36	300	8-12	
					Year 1: Intervention: atropine 0.02% Control: placebo Year 2: Intervention: atropine 0.02% Control: atropine 0.01% Year 3: Intervention: placebo Control: atropine 0.01%
Lane, K.et al, 2021	USA	48	678	3-15	
					1. Atropine Sulfate 0.01% Ophthalmic Solution through year 4
					2. Atropine Sulfate 0.01% Ophthalmic Solution through year 3 followed by placebo for 1 year
					3. Placebo (Investigational Product minus active ingredient) through year 4
Xu, Y.et al, 2022	China	12	192	6-12	
					1% Atropine “5+3”
					1% Atropine weekly
Zhou, P.et al, 2022	China	12	100	8-18	
					Low-dose(0.01% and 0.02%) atropine eye drops
					Orthokeratology
Huang, JN.et	China	12	104	6-12	

al, 2022					Repeated Low-Level Red-Light Therapy
					0.01% Atropine
Oh, SY.et al, 2022	Korea	12	472	5-12	
					Atropine sulfate 01 ophthalmic solution
					Atropine sulfate 02 ophthalmic solution
					Atropine sulfate 03 ophthalmic solution
					Placebo ophthalmic solution
Revell, T.et al, 2022	Australia	28 days	82	18-36	
					0.025% eyedrop aqueous solution (Active Comparator)
					CBT-009 vehicle formulation (Vehicle)
					CBT-009 low dose formulation
					CBT-009 mid dose formulation
					CBT-009 high dose formulation
Zhao, C.et al, 2022	China	12	334	5-14	
					0.01% Atropine eye drops
					Placebo eye drops (0.9% preservative free sodium chloride)
Xu, Y.et al, 2022	China	7 days	144	6-12	
					1% Atropine eye drops
					Tropicamide eye drops

a. All data extracted from ClinicalTrials.gov (https://clinicaltrials.gov/)

eAppendix References

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eTable 1. Outdoor Time and Near Work over Two Years

	0.05% Atropine			0.01% Atropine			Placebo			*P* value [c]		
	Baseline	First-year	Second year	Baseline	First-year	Second year	Baseline	First-year	Second year	Baseline	First year	Second year
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
Outdoor activity, hours per day [a]	1.48 (0.51)	1.49 (0.53)	1.45 (0.56)	1.50 (0.48)	1.42 (0.63)	1.38 (0.58)	1.46 (0.48)	1.32 (0.50)	1.39 (0.51)	0.81	0.07	0.61
Near work, diopter hours per day [b]	10.55 (3.55)	11.79 (3.82)	12.75 (3.99)	10.20 (3.64)	12.83 (4.28)	13.32 (3.92)	10.54 (3.69)	11.90 (3.39)	12.77 (3.74)	0.71	0.08	0.53

a. Outdoor activity = outdoor exercise + outdoor leisure activity.
b. Near work = 3*(homework + reading + playing cell phone) + 2*(using computer + playing video game) + 1*(watching TV).
c. *P* values were generated by the analysis of variance (ANOVA) test.

eTable 2. Baseline Demographics and Clinical Characteristics in 0.05% Atropine, 0.01% Atropine and Placebo Groups for Those Who Completed 2 Years versus Those Who Did Not Complete 2 Years of Treatment

	Completed 2 years (n=353)			Did not complete 2 years (n=121)		
	0.05% Atropine (n=116)	0.01% Atropine (n=122)	Placebo (n=115)	0.05% Atropine (n=44)	0.01% Atropine (n=37)	Placebo (n=40)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Age, years	6.73 (1.46)	6.86 (1.30)	6.77 (1.23)	7.22 (1.25)	6.94 (1.52)	6.68 (1.40)
Sex, No. (%)						
Male	59 (50.9%)	59 (48.4%)	60 (52.2%)	22 (50.0%)	19 (51.4%)	18 (45.0%)
Female	57 (49.1%)	63 (51.6%)	55 (47.8%)	22 (50.0%)	18 (48.6%)	22 (55.0%)
BMI, kg/m^2	15.76 (2.79)	15.62 (2.06)	15.37 (1.94)	15.39 (2.01)	15.48 (2.24)	15.82 (2.18)
Spherical equivalent, D	0.50 (0.32)	0.51 (0.33)	0.54 (0.32)	0.50 (0.33)	0.50 (0.35)	0.50 (0.30)
Axial length, mm	22.80 (0.72)	22.93 (0.71)	22.80 (0.64)	22.90 (0.75)	22.79 (0.68)	22.78 (0.67)
Central corneal thickness, um	555.43 (31.19)	557.18 (33.35)	554.15 (32.60)	557.74 (35.00)	551.76 (25.95)	550.27 (29.46)
IOP, mmHg	16.02 (2.07)	15.91 (2.10)	15.85 (1.93)	15.57 (1.83)	15.66 (1.68)	16.30 (1.86)
Photopic pupil size, mm	3.52 (0.56)	3.55 (0.60)	3.66 (0.63)	3.64 (0.59)	3.63 (0.64)	3.75 (0.91)
Mesopic pupil size, mm	6.37 (0.64)	6.33 (0.77)	6.53 (0.75)	6.34 (0.77)	6.39 (0.65)	6.53 (0.75)
Accommodation amplitude, D	13.48 (2.94)	13.59 (2.51)	13.29 (2.75)	12.97 (1.86)	13.66 (3.19)	13.44 (2.75)
Distance VA, logMAR	0.03 (0.09)	0.02 (0.08)	0.02 (0.07)	0.02 (0.12)	0.03 (0.11)	0.02 (0.07)
Near VA, logMAR	0.04 (0.10)	0.03 (0.10)	0.03 (0.09)	0.03 (0.09)	0.04 (0.13)	0.01 (0.10)
Outdoor activity, hours per day [a]	1.46 (0.52)	1.50 (0.48)	1.46 (0.48)	1.52 (0.52)	1.50 (0.52)	1.44 (0.48)
Near work, diopter hours per day [b]	10.62 (3.42)	10.58 (3.60)	10.56 (3.77)	10.19 (4.00)	8.94 (3.52)	10.47 (3.51)
No. of Parental myopia						
1	41 (35.3%)	49 (40.2%)	36 (31.3%)	25 (56.8%)	13 (35.1%)	22 (55.0%)
2	75 (64.7%)	73 (59.8%)	79 (68.7%)	19 (43.2%)	24 (64.9%)	18 (45.0%)
Baseline visit before the COVID-19 pandemic	64 (55.2%)	77 (63.1%)	72 (62.6%)	30 (68.2%)	25 (67.6%)	20 (50.0%)

Abbreviations: VA = visual acuity; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; D = diopter.

a. Outdoor activity = outdoor exercise + outdoor leisure activity.

b. Near work = 3*(homework + reading + playing cell phone) + 2*(using computer + playing video game) + 1*(watching TV).

eTable 3. Dropout Rate and Compliance over Two Years

	0.05% Atropine	0.01% Atropine	Placebo	*P* value [a]
Dropout rate in the 1st year	24 (15.0%)	20 (12.6%)	27 (17.4%)	0.49
Dropout rate in 2 years	44 (27.5%)	37 (23.3%)	40 (25.8%)	0.68
>75% Compliance in the 1st year	126 (92.7%)	131 (94.2%)	123 (96.1%)	0.48
>75% Compliance in the 2nd year	105 (90.5%)	114 (93.4%)	110 (95.7%)	0.30

a. *P* values were generated by Pearson's Chi-square test.

eTable 4. Association between Dropout and Baseline Characteristics

Baseline Characteristics	Dependent variable: Dropout over two years (no as reference)		Dependent variable: Dropout during the second year (no as reference)		Dependent variable: Dropout during the first year (no as reference)	
Treatment	OR (95%CI)	*P* value [a]	OR (95%CI) [a]	*P* value [a]	OR (95%CI) [a]	*P* value [a]
Placebo	Reference		Reference		Reference	
0.01% Atropine	0.87 (0.52-1.46)	0.60	1.23 (0.57-2.65)	0.59	0.68 (0.37-1.28)	0.23
0.05% Atropine	1.09 (0.66-1.80)	0.73	1.53 (0.73-3.21)	0.27	0.84 (0.46-1.53)	0.56
Age, years	1.09 (0.93-1.27)	0.28	1.35 (1.08-1.68)	0.009 [c]	0.90 (0.75-1.09)	0.29
Sex, male as reference	1.07 (0.71-1.62)	0.75	1.02 (0.56-1.84)	0.96	1.11 (0.67-1.83)	0.70
Spherical equivalent, D	0.88 (0.46-1.66)	0.68	0.60 (0.24-1.52)	0.28	1.21 (0.55-2.65)	0.63
Outdoor activity, hours per day	1.19 (0.72-1.97)	0.51	0.95 (0.49-1.86)	0.89	1.52 (0.77-2.99)	0.23
Near work, diopter hours per day	0.94 (0.87-1.01)	0.10	0.94 (0.85-1.03)	0.20	0.95 (0.86-1.05)	0.27
No. of Parental myopia	0.54 (0.36-0.82)	0.004 [b]	1.41 (0.73-2.71)	0.30	0.27 (0.16-0.46)	<0.001 [d]

a. *P* values were calculated by univariate logistic regression.
b. There was no significant interaction between treatment and parental myopia on the dropout over two years.
c. There was no significant interaction between treatment and age on the dropout during the second year.
d. There was no significant interaction between treatment and parental myopia on the dropout during the first year.

eTable 5. Comparison of Baseline and First Year Outcomes between Those Discontinued after the First Year and Those Completed Two Years

	Completed 2 years (n=353)			Discontinued after the first year (n=50)		
	0.05% Atropine (n=116)	0.01% Atropine (n=122)	Placebo (n=115)	0.05% Atropine (n=20)	0.01% Atropine (n=17)	Placebo (n=13)
Baseline spherical equivalent, D	0.50 (0.44 to 0.56)	0.51 (0.45 to 0.57)	0.54 (0.48 to 0.59)	0.46 (0.30 to 0.61)	0.43 (0.28 to 0.58)	0.51 (0.33 to 0.69)
Baseline axial length, mm	22.80 (22.67 to 22.94)	22.93 (22.80 to 23.06)	22.80 (22.69 to 22.92)	22.85 (22.46 to 23.23)	22.72 (22.35 to 23.09)	22.56 (22.19 to 22.93)
Spherical equivalent change during 1st year, D	-0.10 (-0.17 to -0.03)	-0.35 (-0.44 to -0.27)	-0.53 (-0.63 to -0.43)	-0.16 (-0.45 to 0.12)	-0.58 (-0.86 to -0.30)	-0.68 (-1.12 to -0.25)
Axial length change during 1st year, mm	0.24 (0.21 to 0.27)	0.33 (0.30 to 0.37)	0.39 (0.35 to 0.44)	0.26 (0.15 to 0.37)	0.38 (0.25 to 0.51)	0.49 (0.30 to 0.68)
Cumulative myopia incidence in 1st year [a]	10/116 (8.6%) (4.8% to 15.6%)	29/122 (23.8%) (17.3% to 32.7%)	35/115 (30.4%) (23.1% to 40.1%)	3/20 (15.0%) (5.3% to 42.6%)	6/17 (35.3%) (18.5% to 67.2%)	4/13 (30.8%) (13.6% to 69.5%)
Proportion with fast myopic shift in 1st year [b]	33/116 (28.4%) (21.3% to 38.0%)	58/122 (47.5%) (39.5% to 57.3%)	73/115 (63.5%) (55.3% to 72.9%)	6/20 (30.0%) (15.4% to 58.6%)	10/17 (58.8%) (39.5% to 87.6%)	8/13 (61.5%) (40.0% to 94.6%)

a. Myopia was defined as spherical equivalent less or equal than -0.50D in at least one eye.
b. Fast myopic shift was defined as spherical equivalent myopic shift equal or more than 0.50D over 1st year in at least one eye.

eTable 6. Myopia Incidence over Two Years Using Different Cut-off Points to Define Myopia

	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [a]	Adjusted *P* for trend [b]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [c] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
Cumulative myopia incidence (defined as spherical equivalent ≤-0.75D)											
4 months	1/138 (0.7%)	3/127 (2.4%)	5/130 (3.8%)	0.10	0.13	1.6 (-1.9 to 6.1)	3.1 (-0.6 to 8.1)	1.5 (-3.3 to 6.6)	0.27	0.08	0.49
8 months	3/132 (2.3%)	9/131 (6.9%)	14/120 (11.7%)	0.005	0.001	4.6 (-0.5 to 10.6)	9.4 (3.5 to 16.6)	4.8 (-2.4 to 12.6)	0.07	0.003	0.19
12 months	6/136 (4.4%)	20/139 (14.4%)	30/128 (23.4%)	<0.001	<0.001	10.0 (3.3 to 17.3)	19.0 (11.2 to 27.6)	9.0 (0.0 to 18.6)	0.005	<0.001	0.06
16 months	14/124 (11.3%)	34/132 (25.8%)	38/124 (30.6%)	<0.001	<0.001	14.5 (5.1 to 23.9)	19.4 (9.5 to 29.2)	4.9 (-6.1 to 15.9)	0.003	<0.001	0.38
20 months	18/95 (18.9%)	30/92 (32.6%)	32/88 (36.4%)	0.01	0.005	13.7 (11.5 to 26.0)	17.4 (4.5 to 30.0)	3.8 (-10.1 to 17.5)	0.03	0.008	0.60
24 months	31/116 (26.7%)	45/122 (36.9%)	52/115 (45.2%)	0.004	0.007	10.2 (-1.7 to 21.7)	18.5 (6.2 to 30.3)	8.3 (-4.2 to 20.6)	0.09	0.003	0.19
Cumulative myopia incidence (defined as spherical equivalent ≤-1.00D)											
4 months	0/138 (0.0%)	1/127 (0.8%)	1/130 (0.8%)	0.40	0.37	0.8 (-1.9 to 4.3)	0.8 (-1.9 to 4.2)	0.0 (-3.6 to 3.5)	0.30	0.30	0.99
8 months	1/132 (0.8%)	7/131 (5.3%)	11/120 (9.2%)	0.004	0.001	4.6 (0.6 to 10.0)	8.4 (3.7 to 15.0)	3.8 (-2.7 to 11.0)	0.03	0.002	0.24
12 months	3/136 (2.2%)	14/139 (10.1%)	20/128 (15.6%)	<0.001	<0.001	7.9 (2.4 to 14.3)	13.4 (7.1 to 21.0)	5.6 (-2.5 to 14.0)	0.007	<0.001	0.17
16 months	8/124 (6.5%)	25/132 (18.9%)	27/124 (21.8%)	0.001	<0.001	12.5 (4.5 to 20.8)	15.3 (7.0 to 24.2)	2.8 (-7.1 to 12.8)	0.003	<0.001	0.57
20 months	12/95 (12.6%)	25/92 (27.2%)	27/88 (30.7%)	0.004	0.002	14.5 (3.2 to 26.0)	18.1 (6.3 to 29.9)	3.5 (-9.7 to 16.7)	0.01	0.003	0.60
24 months	19/116 (16.4%)	38/122 (31.1%)	44/115 (38.3%)	<0.001	<0.001	14.8 (4.0 to 25.3)	21.9 (10.6 to 32.9)	7.1 (-5.0 to 19.1)	0.008	<0.001	0.25

a. *P* values for trends were calculated via logistic regression without adjustment

b. Adjusted *P* values for trends were calculated via logistic regression with adjustment of baseline age, sex, baseline spherical equivalent, outdoor time, near work, and parental myopia.

c. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 7. Myopia Incidence over Two Years (Including Those Who Had Become Myopic before Discontinuing Treatment) [a]

Cumulative myopia incidence (defined as spherical equivalent≤-0.50D)											
	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [b]	Adjusted *P* for trend [c]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [d] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
4 months	1/138 (0.7%)	4/127 (3.1%)	8/130 (6.2%)	0.02	0.01	2.4 (-1.2 to 7.2)	5.4 (1.4 to 11.0)	3.0 (-2.5 to 8.9)	0.15	0.01	0.25
8 months	8/132 (6.1%)	20/131 (15.3%)	22/121 (18.2%)	0.005	0.001	9.2 (1.8 to 17.1)	12.1 (4.3 to 20.6)	2.9 (-6.4 to 12.4)	0.02	0.003	0.54
12 months	13/136 (9.6%)	36/140 (25.7%)	43/132 (32.6%)	<0.001	<0.001	16.2 (7.4 to 25.1)	23.0 (13.6 to 32.5)	6.9 (-3.9 to 17.6)	<0.001	<0.001	0.21
16 months	23/124 (18.5%)	45/134 (33.6%)	51/131 (38.9%)	0.001	<0.001	15.0 (4.3 to 25.4)	20.4 (9.4 to 31.0)	5.3 (-6.2 to 16.8)	0.006	<0.001	0.37
20 months	28/97 (28.9%)	41/97 (42.3%)	47/97 (48.5%)	0.006	0.001	13.4 (-0.1 to 26.4)	19.6 (5.9 to 32.6)	6.2 (-7.8 to 19.9)	0.05	0.005	0.39
24 months	36/119 (30.3%)	64/130 (49.2%)	71/125 (56.8%)	<0.001	<0.001	19.0 (6.8 to 30.5)	26.5 (14.2 to 38.0)	7.6 (-4.7 to 19.6)	0.002	<0.001	0.23

a. Those who became myopic before dropping out were included in the myopia incidence calculation because the onset of myopia is irreversible.
b. *P* values for trend were calculated via logistic regression without adjustment.
c. Adjusted *P* values for trend were calculated via logistic regression with adjustment of baseline age, sex, baseline spherical equivalent, outdoor time, near work, and parental myopia.
d. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 8. Myopia Incidence over Two Years (Including the Missing Data for Those Who Had Missed the Follow-up Visit before 24-month but Had Completed Two Years) [a]

Cumulative myopia incidence (defined as spherical equivalent≤-0.50D)											
	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [b]	Adjusted *P* for trend [c]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [d] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
4 months	1/142 (0.7%)	4/140 (2.9%)	8/136 (5.9%)	0.02	0.02	2.2 (-1.3 to 6.5)	5.2 (1.3 to 10.6)	3.0 (-2.0 to 8.7)	0.17	0.01	0.22
8 months	8/139 (5.8%)	20/138 (14.5%)	21/131 (16.0%)	0.01	0.004	8.7 (1.7 to 16.3)	10.3 (3.0 to 18.2)	1.5 (-7.2 to 10.4)	0.02	0.006	0.73
12 months	13/136 (9.6%)	35/139 (25.2%)	39/128 (30.5%)	<0.001	<0.001	15.6 (6.9 to 24.5)	20.9 (11.6 to 30.4)	5.3 (-5.4 to 16.0)	<0.001	<0.001	0.33
16 months	23/129 (17.8%)	43/134 (32.1%)	44/125 (35.2%)	0.002	0.001	14.3 (3.8 to 24.5)	17.4 (6.6 to 27.9)	3.1 (-8.4 to 14.6)	0.008	0.002	0.60
20 months	26/122 (21.3%)	46/123 (37.4%)	50/118 (42.4%)	0.001	<0.001	16.1 (4.7 to 27.1)	21.1 (9.4 to 32.3)	5.0 (-7.4 to 17.2)	0.006	<0.001	0.43
24 months	33/116 (28.4%)	56/122 (45.9%)	61/115 (53.0%)	<0.001	<0.001	17.5 (5.2 to 29.2)	24.6 (12.0 to 36.4)	7.1 (-5.6 to 19.6)	0.005	<0.001	0.27

a. The missing data was included if 1) participants in both pre and post visit were non-myopic, included as non-myopic. 2) participants in both pre and post visit were myopic, included as myopic.
b. *P* values for trend were calculated via logistic regression without adjustment.
c. Adjusted *P* values for trend were calculated via logistic regression with adjustment of baseline age, sex, baseline spherical equivalent, outdoor time, near work, and parental myopia.
d. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 9. Myopia Incidence over Two Years (Including the Missing Data for Those Who Missed the Follow-up or Discontinued Treatment)

Cumulative myopia incidence (defined as spherical equivalent ≤-0.50D), and it was assumed that all missing data were non-myopic.											
	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [a]	Adjusted *P* for trend [b]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [c] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
4 months	1/160 (0.6%)	4/159 (2.5%)	8/155 (5.2%)	0.02	0.02	1.9 (-1.2 to 5.7)	4.5 (1.1 to 9.3)	2.6 (-1.8 to 7.7)	0.17	0.02	0.22
8 months	8/160 (5.0%)	20/159 (12.6%)	21/155 (13.5%)	0.01	0.009	7.6 (1.4 to 14.2)	8.5 (2.3 to 15.4)	1.0 (-6.6 to 8.6)	0.02	0.009	0.80
12 months	13/160 (8.1%)	35/159 (22.0%)	39/155 (25.2%)	<0.001	<0.001	13.9 (6.2 to 21.8)	17.0 (9.1 to 25.3)	3.1 (-6.3 to 12.6)	<0.001	<0.001	0.51
16 months	23/160 (14.4%)	43/159 (27.0%)	44/155 (28.4%)	0.003	0.004	12.7 (3.8 to 21.5)	14.0 (5.0 to 23.0)	1.3 (-8.6 to 11.2)	0.005	0.002	0.79
20 months	26/160 (16.3%)	36/159 (22.6%)	38/155 (24.5%)	0.07	0.09	6.4 (-2.3 to 15.1)	8.3 (-0.6 to 17.2)	1.9 (-7.5 to 11.3)	0.15	0.07	0.70
24 months	33/160 (20.6%)	56/159 (35.2%)	61/155 (39.4%)	<0.001	0.001	14.6 (4.8 to 24.2)	18.7 (8.7 to 28.5)	4.1 (-6.5 to 14.7)	0.004	<0.001	0.45
Cumulative myopia incidence (defined as spherical equivalent ≤-0.50D), and it was assumed that all missing data was myopic.											
4 months	23/160 (14.4%)	36/159 (22.6%)	33/155 (21.3%)	0.12	0.14	8.3 (-0.3 to 16.8)	6.9 (-1.6 to 15.5)	-1.4 (-10.5 to 7.9)	0.06	0.11	0.77
8 months	36/160 (22.5%)	48/159 (30.2%)	56/155 (36.1%)	0.008	0.002	7.7 (-2.0 to 17.3)	13.6 (3.6 to 23.5)	5.9 (-4.5 to 16.3)	0.12	0.008	0.26
12 months	37/160 (23.1%)	55/159 (34.6%)	66/155 (42.6%)	<0.001	0.001	11.5 (1.5 to 21.2)	19.5 (9.2 to 29.4)	8.0 (-2.8 to 18.6)	0.02	<0.001	0.15
16 months	59/160 (36.9%)	70/159 (44.0%)	75/155 (48.4%)	0.04	0.02	7.2 (-3.6 to 17.8)	11.5 (0.6 to 22.2)	4.4 (-6.6 to 15.3)	0.19	0.04	0.44
20 months	91/160 (56.9%)	103/159 (64.8%)	105/155 (67.7%)	0.05	0.08	7.9 (-2.8 to 18.4)	10.9 (0.2 to 21.3)	3.0 (-7.5 to 13.3)	0.15	0.05	0.58
24 months	77/160 (48.1%)	93/159 (58.5%)	101/155 (65.2%)	0.002	0.002	10.4 (-0.6 to 21.1)	17.0 (6.1 to 27.6)	6.7 (-4.1 to 17.3)	0.06	0.002	0.22

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, outdoor time, near work, and parental myopia.
c. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 10. Proportion with Fast Myopic Shift over Two Years Using Different Cut-off Points to Define Fast Myopic Shift

Proportion with fast myopic shift (defined as spherical equivalent myopic shift ≥0.75D over the first 12 months; and ≥1.50D over 24 months)											
	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [a]	Adjusted *P* for trend [b]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [c] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
12 months	14/136 (10.3%)	42/139 (30.2%)	50/128 (39.1%)	<0.001	<0.001	19.9 (10.7 to 29.2)	28.8 (18.8 to 38.6)	8.8 (-2.6 to 20.1)	<0.001	<0.001	0.13
24 months	14/116 (12.1%)	38/122 (31.1%)	43/115 (37.4%)	<0.001	<0.001	19.1 (8.8 to 29.2)	25.3 (14.5 to 35.9)	6.2 (-5.8 to 18.2)	<0.001	<0.001	0.31
Proportion with fast myopic shift (defined as spherical equivalent myopic shift ≥1.00D over the first 12 months; and ≥2.00D over 24 months)											
12 months	9/136 (6.6%)	22/139 (15.8%)	35/128 (27.3%)	<0.001	<0.001	9.2 (1.8 to 17.0)	20.7 (12.1 to 29.8)	11.5 (1.7 to 21.4)	0.02	<0.001	0.02
24 months	9/116 (7.8%)	17/122 (13.9%)	23/115 (20.0%)	0.008	0.02	6.2 (-1.9 to 14.4)	12.2 (3.5 to 21.4)	6.1 (-3.5 to 15.9)	0.13	0.007	0.21

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, outdoor time, near work, and parental myopia.
c. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 11. Proportion with Fast Myopic Shift over Two Years (Including the Missing Data for Those Who Missed the Follow-up or Discontinued Treatment)

Proportion with fast myopic shift (defined as spherical equivalent myopic shift ≥0.50D over the first 12 months; and ≥1.00D over 24 months), and it was assumed that all missing data were not fast myopic shift.												
	(2) 0.05% Atropine	(1) 0.01% Atropine	(0) Placebo	*P* for trend [a]	Adjusted *P* for trend [b]	Difference, % (95%CI) (2) vs. (1), (2) vs. (0), (1) vs. (0)			*P* value [c] (2) vs. (1), (2) vs. (0), (1) vs. (0)		
12 months	39/160 (24.4%)	68/159 (42.8%)	81/155 (52.3%)	<0.001	<0.001	18.4 (8.1 to 28.4)	27.9 (17.3 to 37.8)	9.5 (-1.6 to 20.3)	<0.001	<0.001	0.09
24 months	29/160 (18.1%)	55/159 (34.6%)	62/155 (40.0%)	<0.001	<0.001	16.5 (6.9 to 25.9)	21.9 (12.0 to 31.5)	5.4 (-5.3 to 16.0)	<0.001	<0.001	0.32
Proportion with fast myopic shift (defined as spherical equivalent myopic shift ≥0.50D over the first 12 months; and ≥1.00D over 24 months), and it was assumed that all missing data was fast myopic shift.												
12 months	63/160 (39.4%)	88/159 (55.3%)	108/155 (69.7%)	<0.001	<0.001	16.0 (5.0 to 26.5)	30.3 (19.5 to 40.4)	14.3 (3.6 to 24.7)	0.004	<0.001	0.009
24 months	73/160 (45.6%)	92/159 (57.9%)	102/155 (65.8%)	<0.001	<0.001	12.2 (1.3 to 22.9)	20.2 (9.3 to 30.6)	7.9 (-2.8 to 18.5)	0.03	<0.001	0.15

a. *P* values for trend were calculated via logistic regression without adjustment.

b. Adjusted *P* value for trend were calculated via logistic regression with adjustment of baseline age, sex, baseline spherical equivalent, outdoor time, near work, and parental myopia.

c. *P* values were calculated by exact unconditional methods based on the Farrington-Manning score statistic.

eTable 12. Spherical Equivalent and Axial Length at Follow-Up Visits over Two years

	(2) 0.05% Atropine		(1) 0.01% Atropine		(0) Placebo		Overall *P* value [b]	*P* value, pairwise comparisons (2) vs. (1), (2) vs. (0), (1) vs. (0)		
	n	mean (SD) [a]	n	mean (SD) [a]	n	mean (SD) [a]				
Spherical equivalent, D										
0 month	160	0.50 (0.33)	159	0.51 (0.33)	155	0.53 (0.31)	0.85	0.93	0.59	0.66
2 weeks	143	0.69 (0.39)	138	0.58 (0.41)	136	0.56 (0.34)	<0.001	0.01	<0.001	0.003
4 months	138	0.66 (0.43)	127	0.50 (0.48)	130	0.38 (0.45)	<0.001	<0.001	<0.001	0.001
8 months	132	0.50 (0.47)	131	0.25 (0.56)	120	0.20 (0.58)	<0.001	<0.001	<0.001	0.03
12 months	136	0.39 (0.51)	139	0.12 (0.62)	128	-0.01 (0.65)	<0.001	<0.001	<0.001	0.03
16 months	124	0.25 (0.65)	132	-0.06 (0.75)	124	-0.15 (0.73)	<0.001	<0.001	<0.001	0.07
20 months	95	0.10 (0.76)	92	-0.19 (0.82)	88	-0.28 (0.82)	<0.001	0.002	<0.001	0.36
24 months	116	0.05 (0.76)	122	-0.33 (0.92)	115	-0.46 (0.90)	<0.001	<0.001	<0.001	0.18
Axial length, mm										
0 month	158	22.82 (0.72)	157	22.89 (0.70)	155	22.80 (0.64)	0.88	0.85	0.75	0.62
2 weeks	142	22.82 (0.73)	136	22.90 (0.71)	136	22.84 (0.66)	0.002	0.38	0.001	0.005
4 months	138	22.90 (0.73)	126	22.99 (0.73)	129	22.94 (0.65)	<0.001	0.05	<0.001	0.01
8 months	132	22.95 (0.73)	131	23.15 (0.70)	119	23.05 (0.68)	<0.001	<0.001	<0.001	0.04
12 months	136	23.05 (0.73)	139	23.24 (0.71)	126	23.19 (0.69)	<0.001	<0.001	<0.001	0.09
16 months	124	23.10 (0.71)	132	23.36 (0.76)	123	23.28 (0.69)	<0.001	<0.001	<0.001	0.20
20 months	95	23.20 (0.71)	92	23.47 (0.82)	98	23.38 (0.67)	<0.001	0.001	0.001	0.75
24 months	115	23.25 (0.71)	121	23.55 (0.81)	114	23.51 (0.73)	<0.001	<0.001	<0.001	0.33

a. Mean and SD were calculated with data from both eyes.

b. *P* values were generated by the generalized estimating equation model. Baseline spherical equivalent/axial length was compared with adjustment of baseline age, sex, outdoor time, near work, and parental myopia; spherical equivalent/axial length in other follow-up visits was compared with adjustment of baseline age, sex, baseline spherical equivalent/axial length, outdoor time, near work and parental myopia.

eTable 13. Changes in Spherical Equivalent and Axial Length over Two Years Using the Right or Left Eyes

Using data from right eyes										
Changes in	(2) 0.05% Atropine		(1) 0.01% Atropine		(0) Placebo		*P* for trend [a]	*P* value [a], pairwise comparisons (2) vs. (1), (2) vs. (0), (1) vs. (0)		
Spherical equivalent, D	n	mean (95%CI)	n	mean (95%CI)	n	mean (95%CI)				
2 weeks	143	0.18 (0.14 to 0.23)	138	0.07 (0.03 to 0.11)	136	0.01 (-0.03 to 0.05)	<0.001	0.004	<0.001	0.03
4 months	138	0.16 (0.11 to 0.22)	127	-0.02 (-0.08 to 0.04)	130	-0.15 (-0.21 to -0.09)	<0.001	0.001	<0.001	0.002
8 months	132	-0.01 (-0.08 to 0.06)	131	-0.25 (-0.33 to 0.18)	120	-0.39 (-0.48 to -0.31)	<0.001	0.001	<0.001	0.008
12 months	136	-0.12 (-0.20 to -0.04)	139	-0.40 (-0.49 to -0.31)	128	-0.55 (-0.65 to -0.45)	<0.001	<0.001	<0.001	0.04
16 months	124	-0.25 (-0.36 to -0.14)	132	-0.57 (-0.69 to -0.46)	124	-0.71 (-0.82 to -0.60)	<0.001	0.001	<0.001	0.11
20 months	95	-0.36 (-0.51 to -0.21)	92	-0.73 (-0.89 to -0.57)	88	-0.86 (-1.01 to -0.70)	<0.001	0.006	<0.001	0.41
24 months	116	-0.46 (-0.59 to -0.33)	122	-0.82 (-0.97 to -0.68)	115	-1.03 (-1.17 to -0.88)	<0.001	0.002	<0.001	0.09
Axial length, mm										
2 weeks	140	0.01 (0.00 to 0.02)	136	0.02 (0.01 to 0.03)	135	0.04 (0.03 to 0.06)	<0.001	0.56	<0.001	0.001
4 months	137	0.07 (0.06 to 0.09)	125	0.12 (0.10 to 0.13)	129	0.16 (0.14 to 0.18)	<0.001	0.06	<0.001	0.007
8 months	131	0.17 (0.14 to 0.19)	129	0.24 (0.21 to 0.27)	120	0.31 (0.27 to 0.34)	<0.001	0.006	<0.001	0.02
12 months	135	0.25 (0.22 to 0.28)	137	0.34 (0.31 to 0.38)	127	0.41 (0.37 to 0.45)	<0.001	0.002	<0.001	0.07
16 months	123	0.34 (0.29 to 0.38)	130	0.47 (0.42 to 0.52)	123	0.52 (0.47 to 0.56)	<0.001	0.001	<0.001	0.23
20 months	94	0.42 (0.36 to 0.48)	92	0.57 (0.50 to 0.63)	87	0.61 (0.55 to 0.67)	0.001	0.004	0.001	0.61
24 months	114	0.47 (0.42 to 0.53)	120	0.63 (0.57 to 0.69)	115	0.71 (0.64 to 0.77)	<0.001	0.002	<0.001	0.19
Using data from left eyes										
Spherical equivalent, D										
2 weeks	143	0.16 (0.12 to 0.21)	138	0.10 (0.07 to 0.14)	136	0.01 (-0.02 to 0.05)	<0.001	0.08	<0.001	0.009

4 months	138	0.17 (0.11 to 0.22)	127	0.00 (-0.06 to 0.05)	130	-0.16 (-0.21 to -0.10)	<0.001	<0.001	<0.001	0.003
8 months	132	0.04 (-0.03 to 0.11)	131	-0.23 (-0.30 to -0.16)	120	-0.34 (-0.44 to -0.25)	<0.001	<0.001	<0.001	0.09
12 months	136	-0.10 (-0.17 to -0.02)	139	-0.36 (-0.44 to -0.28)	128	-0.54 (-0.65 to -0.44)	<0.001	<0.001	<0.001	0.02
16 months	124	-0.25 (-0.35 to -0.15)	132	-0.54 (-0.65 to -0.44)	124	-0.68 (-0.79 to -0.56)	<0.001	0.002	<0.001	0.09
20 months	95	-0.39 (-0.53 to -0.25)	92	-0.68 (-0.83 to -0.54)	88	-0.81 (-0.96 to -0.66)	<0.001	0.009	<0.001	0.37
24 months	116	-0.45 (-0.58 to -0.33)	122	-0.85 (-1.00 to -0.70)	115	-0.99 (-1.14 to -0.84)	<0.001	<0.001	<0.001	0.39
Axial length, mm										
2 weeks	140	0.01 (0.00 to 0.02)	136	0.02 (0.01 to 0.02)	135	0.04 (0.03 to 0.05)	0.001	0.50	0.001	0.007
4 months	137	0.08 (0.06 to 0.11)	125	0.11 (0.09 to 0.13)	129	0.15 (0.13 to 0.18)	<0.001	0.16	<0.001	0.05
8 months	131	0.16 (0.14 to 0.19)	129	0.24 (0.21 to 0.27)	120	0.30 (0.26 to 0.34)	<0.001	0.003	<0.001	0.04
12 months	135	0.24 (0.21 to 0.27)	137	0.34 (0.30 to 0.37)	127	0.40 (0.35 to 0.44)	<0.001	0.002	<0.001	0.11
16 months	123	0.33 (0.29 to 0.37)	130	0.45 (0.41 to 0.50)	123	0.51 (0.46 to 0.56)	<0.001	0.001	<0.001	0.18
20 months	94	0.42 (0.36 to 0.48)	92	0.56 (0.50 to 0.63)	87	0.59 (0.52 to 0.66)	0.002	0.002	0.002	0.94
24 months	114	0.48 (0.42 to 0.54)	120	0.64 (0.57 to 0.70)	115	0.69 (0.62 to 0.76)	<0.001	0.001	<0.001	0.54

a. *P* values were generated by the linear regression model with the adjustment of baseline age, sex, baseline SE/AL, outdoor time, near work, and parental myopia.

eTable 14. Changes in Accommodation, Pupil Diameter, and Visual Acuity over Two Years

Change in Accommodation amplitude, D	(2) 0.05% Atropine mean (95%CI) [a]	(1) 0.01% Atropine mean (95%CI) [a]	(0) Placebo mean (95%CI) [a]	*P* for trend [b]	Overall *P* value [b]	*P* value, pairwise comparisons (2) vs. (1), (2) vs. (0), (1) vs. (0)		
2 weeks	-3.61 (-4.03 to -3.19)	-1.63 (-2.01 to -1.25)	-0.69 (-1.08 to -0.30)	<0.001	<0.001	<0.001	<0.001	0.02
4 months	-1.97 (-2.39 to -1.55)	-1.43 (-1.83 to -1.04)	-0.69 (-1.08 to -0.29)	0.001	0.006	0.15	0.001	0.07
8 months	-1.99 (-2.39 to -1.60)	-1.68 (-2.09 to -1.27)	-0.94 (-1.40 to -0.48)	0.01	0.05	0.34	0.01	0.13
12 months	-2.00 (-2.49 to -1.52)	-1.52 (-1.94 to -1.09)	-1.29 (-1.80 to -0.78)	0.15	0.30	0.21	0.15	0.75
16 months	-2.60 (-3.07 to -2.13)	-1.78 (-2.27 to -1.30)	-1.43 (-1.96 to -0.90)	0.02	0.04	0.07	0.02	0.52
20 months	-3.46 (-4.00 to -2.91)	-1.53 (-2.04 to -1.01)	-1.65 (-2.28 to -1.03)	0.002	<0.001	<0.001	0.002	0.79
24 months	-3.17 (-3.72 to -2.62)	-2.26 (-2.74 to -1.77)	-2.12 (-2.64 to -1.60)	0.03	0.05	0.03	0.03	0.87
Photopic pupil size, mm								
2 weeks	1.39 (1.26 to 1.52)	0.56 (0.46 to 0.67)	-0.13 (-0.23 to -0.02)	<0.001	<0.001	<0.001	<0.001	<0.001
4 months	1.32 (1.19 to 1.46)	0.54 (0.42 to 0.66)	0.00 (-0.11 to 0.11)	<0.001	<0.001	<0.001	<0.001	<0.001
8 months	1.15 (1.02 to 1.28)	0.47 (0.35 to 0.58)	0.01 (-0.12 to 0.13)	<0.001	<0.001	<0.001	<0.001	<0.001
12 months	1.16 (1.03 to 1.29)	0.39 (0.29 to 0.50)	0.17 (0.04 to 0.30)	<0.001	<0.001	<0.001	<0.001	0.03
16 months	1.10 (0.97 to 1.24)	0.39 (0.28 to 0.50)	0.08 (-0.04 to 0.20)	<0.001	<0.001	<0.001	<0.001	0.004
20 months	1.26 (1.11 to 1.41)	0.51 (0.38 to 0.65)	0.14 (-0.01 to 0.29)	<0.001	<0.001	<0.001	<0.001	0.003
24 months	1.12 (0.99 to 1.25)	0.47 (0.36 to 0.59)	0.06 (-0.07 to 0.19)	<0.001	<0.001	<0.001	<0.001	<0.001
Mesopic pupil size, mm								
2 weeks	0.75 (0.68 to 0.83)	0.40 (0.32 to 0.48)	0.04 (-0.03 to 0.12)	<0.001	<0.001	<0.001	<0.001	<0.001
4 months	0.79 (0.71 to 0.87)	0.43 (0.34 to 0.52)	0.12 (0.05 to 0.19)	<0.001	<0.001	<0.001	<0.001	<0.001
8 months	0.74 (0.66 to 0.82)	0.42 (0.34 to 0.50)	0.14 (0.06 to 0.22)	<0.001	<0.001	<0.001	<0.001	<0.001
12 months	0.78 (0.70 to 0.86)	0.44 (0.35 to 0.52)	0.18 (0.11 to 0.24)	<0.001	<0.001	<0.001	<0.001	<0.001
16 months	0.79 (0.71 to 0.88)	0.40 (0.32 to 0.48)	0.13 (0.06 to 0.21)	<0.001	<0.001	<0.001	<0.001	<0.001
20 months	0.81 (0.72 to 0.91)	0.40 (0.30 to 0.51)	0.12 (0.03 to 0.21)	<0.001	<0.001	<0.001	<0.001	0.001
24 months	0.77 (0.69 to 0.86)	0.42 (0.34 to 0.51)	0.13 (0.05 to 0.21)	<0.001	<0.001	<0.001	<0.001	<0.001
Distance VA, logMAR								
2 weeks	0.00 (0.00 to 0.01)	0.00 (-0.01 to 0.00)	-0.01 (-0.01 to 0.00)	0.17	0.38	0.36	0.17	0.81
4 months	0.00 (-0.01 to 0.00)	-0.01 (-0.02 to 0.00)	-0.01 (-0.01 to 0.00)	0.48	0.71	0.45	0.51	0.82
8 months	-0.01 (-0.02 to 0.00)	-0.01 (-0.02 to 0.00)	-0.02 (-0.02 to -0.01)	0.73	0.79	0.82	0.68	0.51
12 months	-0.02 (-0.03 to -0.01)	-0.02 (-0.03 to -0.01)	-0.03 (-0.04 to -0.02)	0.49	0.76	0.90	0.48	0.56
16 months	-0.04 (-0.04 to -0.03)	-0.04 (-0.04 to -0.03)	-0.04 (-0.05 to -0.03)	0.32	0.49	0.99	0.31	0.31
20 months	-0.04 (-0.05 to -0.03)	-0.04 (-0.05 to -0.03)	-0.05 (-0.06 to -0.04)	0.15	0.35	0.63	0.15	0.40
24 months	-0.05 (-0.06 to -0.04)	-0.05 (-0.07 to -0.04)	-0.05 (-0.06 to -0.04)	0.85	0.97	0.80	0.86	0.94
Near VA, logMAR								
2 weeks	0.01 (0.00 to 0.02)	0.00 (-0.01 to 0.01)	0.00 (-0.01 to 0.01)	0.70	0.35	0.18	0.70	0.30

4 months	-0.01 (-0.02 to 0.00)	-0.02 (-0.03 to -0.01)	-0.01 (-0.02 to 0.00)	0.82	0.83	0.68	0.81	0.55
8 months	-0.02 (-0.03 to 0.00)	-0.02 (-0.03 to -0.01)	-0.01 (-0.02 to 0.00)	0.50	0.40	0.48	0.48	0.18
12 months	-0.02 (-0.04 to -0.01)	-0.03 (-0.04 to -0.02)	-0.02 (-0.04 to -0.01)	0.21	0.23	0.66	0.20	0.09
16 months	-0.03 (-0.04 to -0.01)	-0.03 (-0.04 to -0.02)	-0.02 (-0.04 to -0.01)	0.50	0.60	0.78	0.50	0.32
20 months	-0.03 (-0.05 to -0.02)	-0.04 (-0.06 to -0.03)	-0.03 (-0.04 to -0.01)	0.55	0.42	0.40	0.53	0.19
24 months	-0.03 (-0.05 to -0.02)	-0.04 (-0.05 to -0.03)	-0.03 (-0.04 to -0.01)	0.46	0.45	0.57	0.46	0.21

a. Mean and 95%CI were calculated with data from both eyes.

b. *P* values were generated by the generalized estimating equation model with the adjustment of baseline age and sex.

eTable 15. Accommodation, Pupil Diameter, and Visual Acuity at Follow-Up Visits over Two years

Accommodation amplitude, D	(2) 0.05% Atropine mean (SD) [a]	(1) 0.01% Atropine mean (SD) [a]	(0) Placebo mean (SD) [a]	Overall *P* value [b]	*P* value, pairwise comparisons (2) vs. (1), (2) vs. (0), (1) vs. (0)		
0 month	13.34 (2.69)	13.60 (2.67)	13.33 (2.74)	0.59	0.39	0.95	0.36
2 weeks	9.66 (3.03)	11.96 (2.78)	12.63 (2.96)	<0.001	<0.001	<0.001	0.03
4 months	11.31 (2.92)	12.29 (2.89)	12.58 (2.74)	0.001	0.01	<0.001	0.26
8 months	11.34 (2.76)	11.89 (2.88)	12.45 (3.18)	0.02	0.11	0.004	0.19
12 months	11.36 (3.12)	12.15 (3.15)	12.01 (3.51)	0.08	0.03	0.12	0.76
16 months	10.75 (3.06)	11.95 (3.27)	11.93 (3.14)	0.002	0.002	0.004	0.91
20 months	10.17 (3.02)	11.94 (3.18)	11.68 (3.05)	<0.001	<0.001	0.001	0.61
24 months	10.28 (2.90)	11.28 (3.33)	11.15 (2.96)	0.005	0.003	0.01	0.71
Photopic pupil size, mm							
0 month	3.55 (0.57)	3.57 (0.61)	3.69 (0.72)	0.14	0.69	0.05	0.13
2 weeks	4.95 (1.02)	4.18 (0.72)	3.50 (0.53)	<0.001	<0.001	<0.001	<0.001
4 months	4.91 (0.96)	4.10 (0.75)	3.66 (0.69)	<0.001	<0.001	<0.001	<0.001
8 months	4.71 (0.90)	4.04 (0.69)	3.64 (0.69)	<0.001	<0.001	<0.001	<0.001
12 months	4.67 (0.91)	3.98 (0.62)	3.77 (0.76)	<0.001	<0.001	<0.001	0.04
16 months	4.66 (0.86)	3.96 (0.65)	3.71 (0.76)	<0.001	<0.001	<0.001	0.01
20 months	4.80 (0.86)	4.05 (0.69)	3.72 (0.79)	<0.001	<0.001	<0.001	0.007
24 months	4.62 (0.84)	4.05 (0.72)	3.72 (0.82)	<0.001	<0.001	<0.001	0.001
Mesopic pupil size, mm							
0 month	6.36 (0.68)	6.34 (0.74)	6.53 (0.74)	0.04	0.76	0.04	0.02
2 weeks	7.13 (0.65)	6.76 (0.57)	6.53 (0.64)	<0.001	<0.001	<0.001	<0.001
4 months	7.17 (0.63)	6.70 (0.57)	6.66 (0.71)	<0.001	<0.001	<0.001	0.003
8 months	7.10 (0.63)	6.76 (0.52)	6.65 (0.65)	<0.001	<0.001	<0.001	0.001
12 months	7.14 (0.68)	6.75 (0.55)	6.70 (0.65)	<0.001	<0.001	<0.001	0.003
16 months	7.16 (0.61)	6.73 (0.53)	6.64 (0.65)	<0.001	<0.001	<0.001	0.001
20 months	7.21 (0.58)	6.68 (0.60)	6.69 (0.72)	<0.001	<0.001	<0.001	0.07
24 months	7.15 (0.61)	6.74 (0.53)	6.64 (0.71)	<0.001	<0.001	<0.001	0.002
Distance VA, logMAR							
0 month	0.03 (0.10)	0.02 (0.09)	0.02 (0.07)	0.37	0.29	0.17	0.88
2 weeks	0.03 (0.07)	0.02 (0.09)	0.02 (0.07)	0.08	0.15	0.03	0.72
4 months	0.03 (0.08)	0.01 (0.08)	0.02 (0.07)	0.21	0.12	0.14	0.78
8 months	0.02 (0.08)	0.01 (0.07)	0.01 (0.07)	0.63	0.61	0.34	0.65
12 months	0.01 (0.08)	0.00 (0.07)	0.00 (0.07)	0.37	0.31	0.18	0.70
16 months	0.00 (0.07)	-0.02 (0.08)	-0.01 (0.07)	0.23	0.41	0.09	0.39

20 months	-0.01 (0.07)	-0.01 (0.08)	-0.02 (0.06)	0.19	0.68	0.07	0.22
24 months	-0.02 (0.08)	-0.03 (0.08)	-0.03 (0.07)	0.56	0.29	0.51	0.68
Near VA, logMAR							
0 month	0.04 (0.10)	0.03 (0.10)	0.02 (0.09)	0.07	0.40	0.02	0.16
2 weeks	0.05 (0.08)	0.02 (0.09)	0.03 (0.09)	0.07	0.03	0.07	0.60
4 months	0.03 (0.10)	0.01 (0.09)	0.02 (0.08)	0.31	0.16	0.24	0.82
8 months	0.04 (0.08)	0.01 (0.07)	0.02 (0.08)	0.07	0.02	0.47	0.21
12 months	0.02 (0.07)	0.00 (0.07)	0.01 (0.07)	0.20	0.14	0.94	0.13
16 months	0.02 (0.09)	0.00 (0.07)	0.01 (0.07)	0.48	0.28	0.83	0.33
20 months	0.01 (0.07)	-0.01 (0.07)	0.00 (0.09)	0.56	0.31	0.96	0.43
24 months	0.01 (0.08)	0.00 (0.07)	0.00 (0.06)	0.28	0.12	0.53	0.31

a. Mean and SD were calculated with data from both eyes.

b. *P* values were generated by the generalized estimating equation model. The baseline variable was compared with adjustment of baseline age and sex; Variables in other follow-up visits were compared with adjustment of baseline age, sex, and corresponding baseline factor.

eTable 16. Adverse Events over Two Years

	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%)

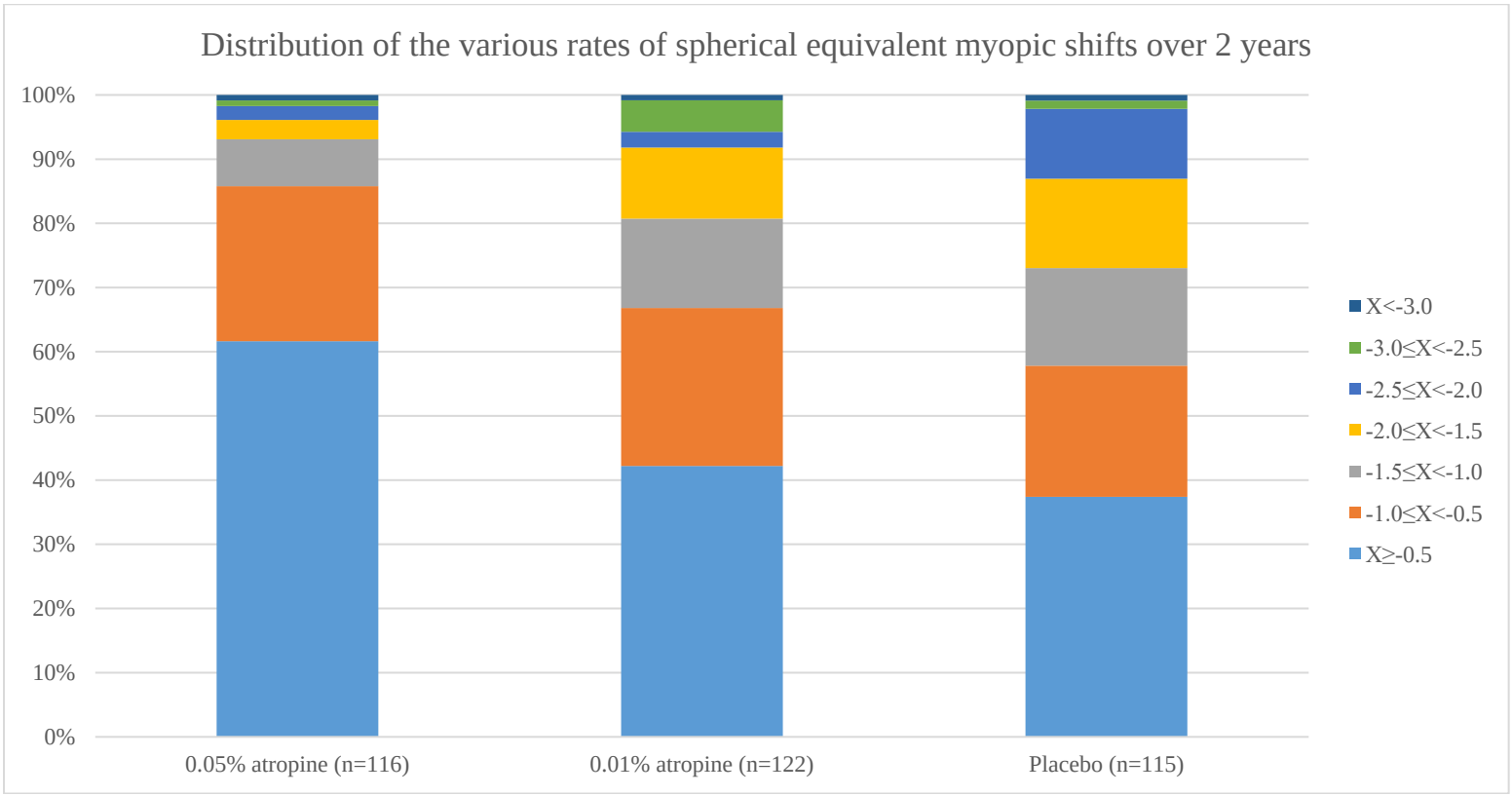
a. Hospitalization was not related to the medication. In the 0.05% atropine group, there were 2 cases of respiratory infections, 1 case of pneumonias, 1 case of fever, 1 case of sore throat, and 1 case of COVID-19. In the 0.01% atropine group, there were 4 cases of fever, 1 case of a sprain, 1 case of bone fractures, and 1 case of respiratory infection. In the placebo group, there was 1 case of fever, 1 case of gastroenteritis, and 1 case of asthma.

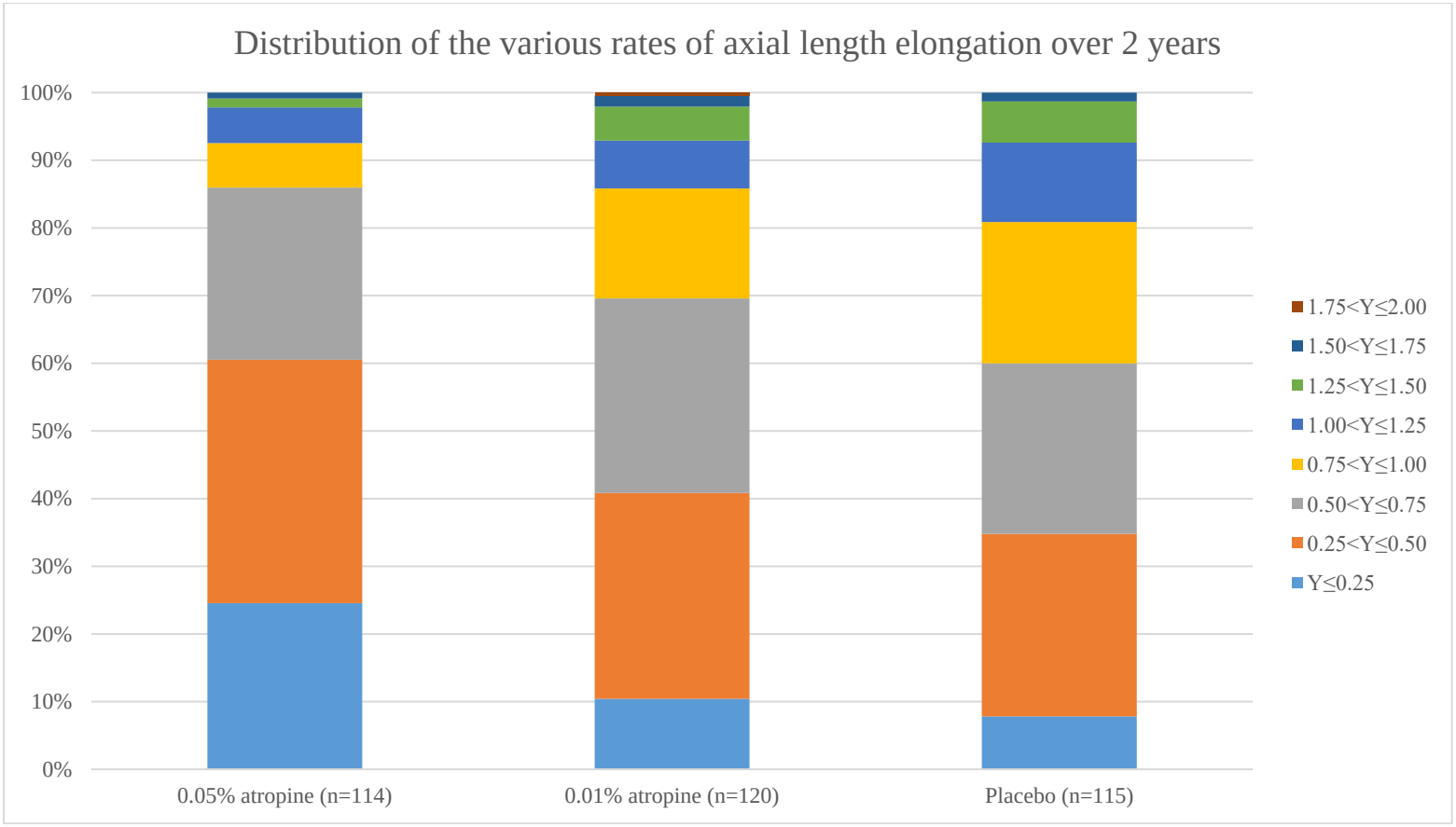
eTable 17. Visual Function Questionnaire Scores over Two Years

	0.05% Atropine			0.01% Atropine			Placebo			*P* value [a]		
	Baseline	First-year	Second year	Baseline	First-year	Second year	Baseline	First-year	Second year	Baseline	First year	Second year
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
General health	78.60 (13.57)	80.02 (12.90)	79.14 (13.63)	77.65 (15.29)	76.03 (14.49)	77.95 (12.73)	77.71 (14.32)	78.62 (15.24)	76.92 (15.91)	0.82	0.07	0.52
General vision	84.83 (9.77)	85.88 (9.50)	84.10 (10.51)	83.75 (11.37)	83.36 (10.14)	83.54 (9.95)	85.11 (11.16)	83.70 (10.91)	84.31 (11.94)	0.52	0.10	0.87
Ocular pain	92.42 (12.53)	91.89 (13.12)	92.45 (11.50)	92.19 (13.09)	90.65 (12.70)	91.98 (13.79)	90.58 (14.60)	92.42 (11.78)	92.25 (13.72)	0.45	0.51	0.97
Near activities	96.53 (8.77)	96.85 (7.77)	97.09 (7.61)	96.03 (8.65)	96.38 (8.05)	96.54 (7.77)	96.28 (7.48)	97.09 (6.92)	96.30 (7.22)	0.87	0.75	0.73
Distance activities	97.11 (8.58)	97.07 (7.71)	98.11 (5.99)	95.45 (9.04)	96.76 (6.41)	96.62 (6.47)	96.24 (7.79)	97.38 (7.01)	96.06 (7.23)	0.24	0.78	0.07
Social functioning	99.08 (5.24)	98.86 (5.68)	99.06 (5.63)	98.03 (7.06)	98.86 (4.50)	99.65 (2.70)	98.24 (6.59)	98.13 (7.22)	98.73 (4.49)	0.31	0.53	0.31
Mental health	92.92 (12.24)	92.70 (11.56)	92.14 (10.01)	92.64 (12.40)	93.08 (7.94)	91.69 (9.80)	92.25 (11.53)	92.18 (10.25)	92.65 (8.93)	0.90	0.77	0.76
Role difficulties	94.42 (14.74)	94.47 (15.79)	93.33 (15.76)	93.67 (16.96)	95.90 (9.72)	96.23 (10.06)	93.05 (17.07)	94.19 (15.14)	95.02 (11.43)	0.77	0.57	0.25
Dependency	96.94 (13.77)	96.69 (12.41)	96.35 (12.62)	97.26 (10.88)	97.65 (8.89)	95.99 (10.90)	97.30 (12.85)	97.18 (10.90)	97.92 (8.28)	0.97	0.78	0.38
Color vision	99.16 (5.37)	98.84 (9.28)	99.29 (5.42)	98.51 (6.60)	98.62 (6.52)	99.52 (3.43)	98.57 (7.20)	98.76 (7.79)	99.30 (4.14)	0.63	0.98	0.91
Peripheral vision	98.17 (8.24)	98.47 (6.75)	98.35 (7.11)	97.04 (9.51)	96.76 (8.42)	98.10 (7.49)	97.54 (8.05)	98.03 (7.44)	98.61 (6.68)	0.53	0.17	0.87
VFQ-25 composite	93.65 (7.18)	93.78 (6.47)	93.57 (6.65)	92.93 (7.75)	93.06 (5.37)	93.43 (5.63)	92.97 (7.14)	93.40 (6.70)	93.45 (5.66)	0.64	0.64	0.98

a. *P* values were generated by the analysis of variance (ANOVA) test.

eFigure 1. Bar Graph Showing the Distribution of the Various Rates of Spherical Equivalent Myopic Shifts over Two Years in the 0.05% Atropine, 0.01% Atropine and Placebo Groups





The analyses were based on the participants who completed the 2-year follow-up.
X represents the change in spherical equivalent (D) over 2-year follow-up; Y represents the change in axial length (mm) over 2-year follow-up.