A Randomized Trial Using Progressive Addition Lenses to Evaluate Theories of Myopia Progression in Children with a High Lag of Accommodation

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Purpose. To compare the effect of wearing, then ceasing to wear, progressive addition lenses (PALs) versus single vision lenses (SVLs) on myopia progression in children with high accommodative lag to evaluate accommodative lag and mechanical tension as theories of myopia progression.

Methods. Eighty-five children (age range, 6–11 years) with spherical equivalent (SE) cycloplegic autorefraction between −0.75 D and −4.50 D were randomly assigned to wear SVLs or PALs for 1 year; all children wore SVLs a second year. Children had high accommodative lag and also had near esophoria if their myopia was greater than −2.25 D SE. The primary outcome after each year was the previous year's change in SE.

Results. When the children were randomly assigned to SVLs or PALs, the adjusted 1-year changes in SE were −0.52 D (SVL group) and −0.35 D (PAL group; treatment effect = 0.18 D; $P = 0.01$). When all children wore SVLs the second year, there was no difference in myopia progression between SVL and former PAL wearers (0.06 D; $P = 0.50$). Accommodative lag was not associated with myopia progression.

Conclusions. The statistically significant, but clinically small, PAL effect suggests that treatments aimed at reducing foveal defocus may not be as effective as previously thought in myopic children with high accommodative lag. Finding no evidence of treatment loss after discontinuing PAL wear supports hyperopic defocus-based theories such as accommodative lag; however, not finding an association between accommodative lag and myopia progression is inconsistent with the PAL effect being due to decreased foveal blur during near work. (ClinicalTrials.gov number, NCT00335049.) (*Invest Ophthalmol Vis Sci.* 2012;53:640–649) DOI:10.1167/iovs.11-7769

The prevalence of myopia in the United States may be increasing[1]; one-third of US adults are myopic.[2] Elucidation of the mechanism underlying the progression of myopia in children could yield more effective treatments. Although progressive addition lenses (PALs) have generally yielded modest reductions in myopia progression that were not clinically meaningful,[3–8] subgroup analyses from a previous large, well-executed clinical trial found that PALs may be more effective in children with high lag of accommodation.[9] Positive results from PAL treatment in children with high lag of accommodation could provide insight into the mechanism responsible for juvenile-onset myopia progression.

The Study of Theories about Myopia Progression (STAMP) is a 2-year clinical trial designed to evaluate two theories of myopia progression using the previously reported PAL treatment effect. The first theory hypothesizes that high accommodative lag during near work produces hyperopic retinal blur that causes accelerated axial eye growth.[10–13] The ability of hyperopic retinal blur to accelerate eye growth is well documented in animals.[14–17] The effect of hyperopic retinal blur may be greatest in the fovea because constant, full-field hyperopic defocus can alter eye shape to create relative peripheral hyperopia (a more prolate eye shape) in monkeys.[18] However, the effect of hyperopic retinal blur is completely negated by short periods of clear vision.[19–21] The potent effect of clear vision calls into question whether transient hyperopic retinal blur during periods of near work can cause juvenile-onset myopia progression. Although the Correction of Myopia Evaluation Trial (COMET) reported a 3-year reduction in myopia progression of 0.20 D for myopic children wearing PALs,[6] subgroup analyses found a greater treatment effect when children had high accommodative lag and either near esophoria or low myopia.[9] Two other PAL trials have also reported that myopic children with high accommodative lag had a greater treatment effect than children with lower accommodative lag, with strong statistical support in one of the trials ($P < 0.05$; Hasebe et al.[7]) but marginal statistical evidence in the other ($P = 0.09$; Cheng et al.[22]). There is, however, controversy over whether an elevation in accommodative lag exists before myopia onset[23,24] and whether an association between accommodative lag and myopia progression exists.[25–28]

A second theory is based on longitudinal ocular growth data from emmetropic and myopic children and hypothesizes that mechanical tension created by the crystalline lens or ciliary body restricts equatorial ocular expansion, thereby causing accelerated axial elongation.[29,30] The mechanical tension theory hypothesizes that ciliary-choroidal tension in the anterior portion of the globe reaches a point at which proportional globe expansion during eye growth is no longer possible in children with larger than normal eyes. The restriction of equatorial growth results in accelerated axial elongation because the crystalline lens can no longer decrease in power by thinning and stretching.[29,30] The ciliary-choroidal tension is hypothesized to result in an increase in the effort required to accommodate, thereby increasing accommodative lag[23] and the AC/A ratio[31] in myopic children. In this theory, high accommodative lag is a consequence rather than a cause of myopia,[23] consistent with data in marmosets.[32] An added consequence to increased ciliary-choroidal tension in this model is the significant increase in relative peripheral hyperopia (devel-

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opment of a relatively more prolate globe shape) before[33–35] and after[36–39] the onset of myopia.

Myopic children with high lag of accommodation in STAMP were randomly assigned to wear either PALs or single vision lenses (SVLs) for 1 year. Randomized treatment ended after 1 year, and all children wore SVLs for a second year to determine whether myopia progression was similar in both groups (maintained treatment effect) or whether there was a treatment effect "rebound" (faster myopia progression in former PAL-wearing children resulting in a loss of treatment effect). This article presents the STAMP primary outcome data (change in refractive error) after the first and second years of the study.

SUBJECTS AND METHODS

Subjects participated in STAMP at The Ohio State University College of Optometry (Columbus, OH). Full details of the study design, hypotheses, eligibility criteria, and methods have been reported previously[40] and are briefly summarized here. The protocol was approved by the Biomedical Sciences Institutional Review Board at The Ohio State University and followed the tenets of the Declaration of Helsinki. Parents provided informed consent, and children provided verbal assent.

Enrolled children were 6 to 11 years of age at baseline. Children had between −0.75 D and −4.50 D of myopia in each meridian of each eye, <2.00 D astigmatism, and <2.00 D anisometropia as measured by cycloplegic autorefraction. Enrolled children had no history of bifocal or contact lens wear, strabismus, or diabetes mellitus. All children had best-corrected Snellen visual acuity of at least 20/30 in each eye and weighed at least 1250 g at birth by parental report. Eligible children had a lag of accommodation of at least 1.30 D to a 4-D Badal letter stimulus (before correction for lens effectivity). The lag value of 1.30 D was chosen based on a median split of data from myopic children in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study because the CLEERE protocol for measuring lag was used in STAMP.[23] If a child's spherical equivalent refractive error was more myopic than −2.25 D, he or she had to be esophoric at near while wearing full correction, as determined using the modified Thorington technique. These criteria were chosen because myopic children with both high accommodative lag and near esophoria had the greatest 1- and 3-year treatment effects in COMET when wearing PALs with a +2.00-D add (0.39 and 0.64 D, respectively).[9] Children with high accommodative lag and low myopia (spherical equivalent myopia of −2.25 D or less) also had significant 1- and 3-year treatment effects in COMET of 0.28 and 0.48 D, respectively.[9] Children with these same characteristics were enrolled to increase our ability to attempt to replicate and confirm a significant treatment effect after 1 year of wearing PALs with a +2.00-D add while maximizing the generalizability of the results to myopic children.

Spectacle Lenses

During the first year, children wore either SVLs or PALs with a +2.00-D add (Varilux Ellipse; Essilor of America, Dallas, TX). During the second year, all children wore SVLs. The Ellipse is a short-corridor PAL with a minimum fitting height of 14 mm, making it ideal for use in children's frames. The short-corridor PAL design decreases how far the eyes must be lowered to achieve the full add power, and the design still allows for a wide field of clear vision at distance. All frames selected in the study were required to have a minimum B dimension (vertical dimension) of 25 mm. PALs were fitted at least 2 mm higher than normal to encourage the child to use the near add while ensuring that the full near corridor was included and that adequate lens area remained for clear distance vision. During the fitting process, study opticians used the same protocol for making spectacle measurements regardless of the treatment group to which the child was assigned to preserve subject masking. During dispensing, all children were instructed to look down through the bottom portion of the spectacle lens when viewing near objects and to drop their chins if needed to view distant objects. All parents were given the same printed sheet detailing these instructions for properly using the study spectacles. All children demonstrated proper near fixation through the bottom of the spectacle lenses to the dispensing optician before leaving with the study spectacles. Proper lens use was reiterated at follow-up visits. Children were instructed to wear their spectacles at all times while awake.

A standardized subjective refraction procedure was used to determine the most plus (least minus) spectacle prescription that provided the child with his or her best visual acuity. At the 6- and 18-month visits, a power change was made if the child's prescription changed by an amount equal to or more minus than −0.50 D or if a change was necessary to improve the child's visual acuity to 20/20.

Randomization

Confirmation of eligibility and randomization of children to either SVLs or PALs was administered through a Web portal. A child's group assignment could not be accessed until all required baseline visit data were entered. Randomization was stratified by whether children were esophoric at near. The randomization sequence used random, even block sizes and was generated by the Optometry Coordinating Center at The Ohio State University.

Procedures

All measurements in STAMP were made on the right eye every 6 months. The primary outcome for each year of the study was the previous year's change in central spherical equivalent refractive error as measured by cycloplegic autorefraction (Grand Seiko WV-500 autorefractor; Grand Seiko Co., Hiroshima, Japan). Measurements were made 30 minutes after instillation of 0.5% proparacaine and the first of two drops of 1% tropicamide, separated by 5 minutes. The 1-year change in refractive error after the first study year evaluated the effect of PALs on myopia progression. During the second study year, when all children wore SVLs, the 1-year change in refractive error evaluated whether there was a rebound effect. A rebound effect in year 2 was defined as an increased rate of myopia progression in the former PAL group after the switch to SVLs compared with myopia progression in the SVL-only control group (i.e., a loss of the year 1 treatment effect after discontinuing PAL wear). Measurements were made while subjects viewed a reduced Snellen acuity chart through a Badal lens to ensure that any residual accommodation after cycloplegia was completely relaxed. Ten autorefractor readings were averaged using the power vector method described by Thibos et al.[41]

An optical biometer (IOLMaster; Carl Zeiss Meditec, Dublin, CA) was used to measure axial length. A-scan ultrasonography (model 820; Humphrey Instruments, San Leandro, CA) was used to measure anterior chamber depth and crystalline lens thickness. Both procedures were performed with cycloplegia, and five measurements were made with each instrument and averaged.

Before cycloplegic agents were instilled, near phoria was assessed using the modified Thorington technique with the child's best correction in place. Accommodative response (lag of accommodation) was measured monocularly (right eye) using an autorefractor (Grand Seiko WV-500; Grand Seiko Co.) through the child's habitual correction (sphere and cylinder) at three stimulus levels: 0.00 D, 2.00 D, and 4.00 D. Five readings were made at each accommodative demand. During the measurements, the child fixated a letter target (4 × 4 letter grid; 20/155 Snellen equivalent) viewed through a Badal lens while the left eye was occluded with an infrared filter. An accessory camera simultaneously measured the position of the left eye and recorded the positions of Purkinje images I and IV as a measure of eye position. The AC/A ratio was determined as the change in eye position per unit change in accommodative response. A 10° calibration eye movement performed by the child was used to relate the change in Purkinje image position to the change in eye position. Additional accommodative response measurements to a 4.00-D stimulus were also made at each visit. The baseline visit included measurements through the manifest refraction, and the 6-month and 12-month visits included measurements through the child's habitual correction with and without a +2.00-D add. Loose lenses in a trial frame were used when making all measurements to preserve masking of the examiner.

Simulated keratometry values (flat and steep keratometric readings) were obtained from a corneal topography system (Humphrey Atlas; Carl Zeiss Meditec). Corneal thickness was measured using an anterior segment optical coherence tomography system (Visante; Carl Zeiss Meditec). Intraocular pressure was measured using an applanation tonometer (Tono-Pen XL; Reichert, Depew, NY) after instilling 0.5% proparacaine.

Central and peripheral aberrations were measured under cycloplegia using an open-field aberrometer (Complete Ophthalmic Analysis System for Vision Research; AMO WaveFront Sciences, Albuquerque, NM). Nine measurements of the right eye were made in the following locations: centrally (along the line of sight); 30° nasally, temporally, and superiorly on the retina from the line of sight; and 20° inferiorly on the retina from the line of sight. Relative peripheral refraction (RPR) was calculated for the four peripheral retinal locations as the difference between the peripheral and central spherical equivalent refractive errors obtained from the aberrometer.[42]

Video phakometry was performed using a custom system after cycloplegia.[43] Video recordings of Purkinje images I, III, and IV were used to calculate the radii of curvature of the crystalline lens and an individual equivalent index of refraction for the crystalline lens.

Each child's near work and outdoor activity outside of school were assessed using a survey completed by the child's parent or guardian.[40] A composite variable (diopter hours) that weights each activity by its assumed accommodative demand was calculated as follows: 3 × (hours studying + hours reading for pleasure + hours playing handheld electronic games) + 2 × (hours playing video games + computer hours) + (hours watching television).

Parents and children also completed surveys at each visit (originally developed for COMET)[6] to determine the child's compliance with wearing the study spectacles. Parents and children were both asked how often the child wore his or her STAMP glasses after school and on weekends, holidays, or vacations. Children were also asked how often they wore their STAMP glasses at school. For each question, the options to choose from were: none of the time, some of the time, about half of the time, most of the time, or all of the time.

Masking

All outcome data were collected by an examiner masked to the treatment assignment. At each visit, subjects were reminded not to talk about their spectacles or vision when the examiner was in the room. The child's spectacles were removed and hidden from view before the examiner entered the room.

Sample Size

A sample size of 84 children (42 children per group) provided 80% power (with $\alpha = 0.05$) to detect a 1-year treatment effect of at least 0.25 D. This sample size was also adequate to detect a loss of any year 1 treatment effect of at least 0.25 D in the year after PAL treatment ceased because of potentially increased myopia progression when children previously assigned to wear PALs were switched to SVLs. The sample size was based on an average progression rate of −0.69 D ± 0.37 D per year, which was calculated for the subgroups of children in COMET who wore SVLs and had high accommodative lag with either low myopia or moderate myopia with esophoria at near.[9] The SD of 0.37 D was estimated from reports of annual myopia progression[44–46] and data from the Contact Lens and Myopia Progression (CLAMP) Study (J. Walline and L. Jones-Jordan, personal communication, 2005). The sample size also allowed for a loss to follow-up of up to 15%.

Statistical Analysis

Data were dual-entered by the Optometry Coordinating Center at The Ohio State University. Analyses were performed using two programs (SAS 9.2 [SAS Institute Inc., Cary, NC] and STATA 11.1 [STATA Corp. LP, College Station, TX]). The primary outcome was the 1-year change in the spherical equivalent refractive error of the right eye after the first and second study years. The 1-year change in axial length after each study year was evaluated as a secondary outcome. Intent-to-treat methods were applied to all analyses. Multiple linear regression was used to model the 1-year change in spherical equivalent refractive error and axial length. A control model was built evaluating potential covariates before adding treatment group to the final model. Covariates considered included baseline variables known to have an association with myopia progression: age, baseline refractive error, sex, near phoria, and ethnicity. Any baseline variables with significant between-group differences that occurred by chance, despite randomization, were included in all models. We also evaluated whether accommodative lag measured through the assigned near correction was associated with the 1-year change in refractive error during the first study year using an average of each child's 6-month and 12-month lag while wearing his or her assigned habitual near correction (habitual correction or habitual correction with +2.00-D add). During the second study year when all children wore SVLs, an average of each child's 18-month and 24-month lag measured with his or her habitual prescription was used to evaluate whether accommodative lag was associated with the previous year's change in refractive error.

RESULTS

One hundred ninety-two children were screened between December 2006 and May 2008. Of these children, 85 (44%) were eligible and enrolled, with 42 children randomly assigned to wear PALs and 43 to wear SVLs (Fig. 1). Fifty-four children (64%) were esophoric at near, with 28 assigned to SVLs and 26 to PALs. The mean age (± SD) of the children enrolled was

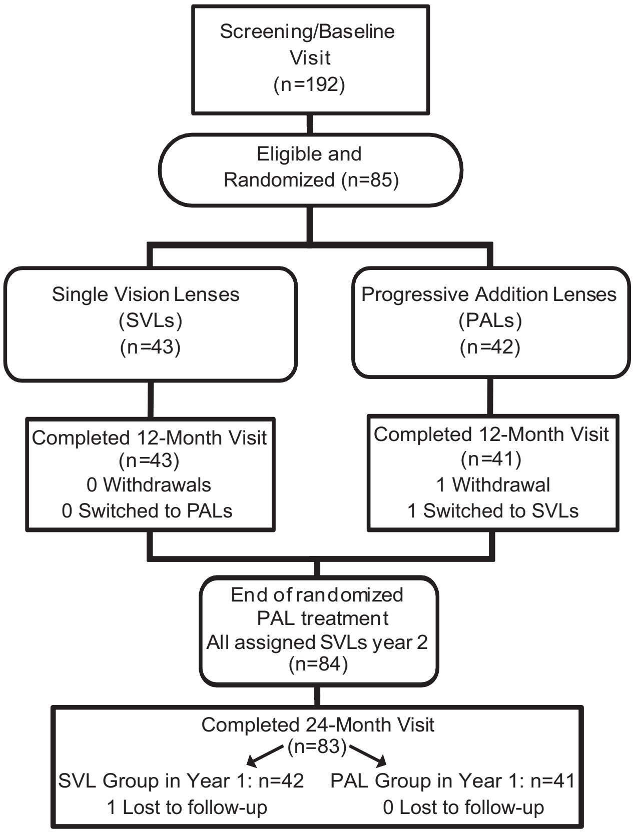

FIGURE 1. Flow diagram of subjects in STAMP. Data were analyzed using the intent-to-treat method.

Table 1. Race and Ethnicity Distribution of Children Enrolled in STAMP

	SVL		PAL		
	Hispanic		**Hispanic**		
	No	**Yes**	**No**	**Yes**	**Total**
African American	10	1	6	0	17
Asian	4	0	2	0	6
White	27	0	29	2	58
Other	1	0	1	2	4
Total	42	1	38	4	85

Table 3. Summary Statistics for Near Work and Outdoor Activity at Baseline

Hours per Week Outside School	SVL	PAL
Studies or reads for school	5.27 ± 6.01	6.86 ± 12.46
Reads for pleasure	4.33 ± 5.02	4.49 ± 3.93
Watches television	9.38 ± 7.84	9.24 ± 5.62
Uses a computer	4.49 ± 5.01	3.75 ± 2.90
Plays video games	2.66 ± 3.63	1.99 ± 2.95
Plays handheld electronic games	1.94 ± 2.70	1.87 ± 2.74
Engages in outdoor activities	7.57 ± 5.44	10.33 ± 7.07
Diopter hours (near work composite)	58.27 ± 38.89	60.38 ± 40.49

Values are mean ± SD. $n = 43$ for SVL and $n = 42$ for PAL.

9.8 ± 1.3 years; 44 (52%) were girls. Race and ethnicity distributions of the children are shown in Table 1. Because non-Hispanic white children made up the majority of the children enrolled (66%), children were grouped by whether they were non-Hispanic white for evaluating ethnicity in statistical models. Baseline characteristics are shown in Table 2. Baseline near work and outdoor activity survey results are shown in Table 3. Despite randomization, three baseline variables had appreciable between-group differences and were therefore included as covariates in all models (axial length, steep keratometry, and outdoor activity). On average, baseline axial length was 0.41 mm longer in the SVL group than in the PAL group, baseline steep keratometric corneal power was 0.72 D greater in the PAL group than in the SVL group, and the reported number of hours spent each week engaging in outdoor activities at baseline was 2.76 hours greater in the PAL group than in the SVL group.

Table 2. Summary Statistics by Treatment Group at Baseline

Characteristic	SVL	PAL
Age, y	10.1 ± 1.5	9.6 ± 1.2
OD M (SE), D	−2.03 ± 0.89	−1.88 ± 0.66
OD J_0, D	0.09 ± 0.20	0.07 ± 0.21
OD J_{45}, D	−0.13 ± 0.18	−0.15 ± 0.13
OS M (SE), D	−2.04 ± 0.91	−1.95 ± 0.64
OS J_0, D	0.13 ± 0.22	0.08 ± 0.18
OS J_{45}, D	−0.18 ± 0.16	−0.16 ± 0.19
Accommodative lag, D, (4-D stimulus with full manifest)	1.66 ± 0.34	1.77 ± 0.40
Axial length OD, mm	24.37 ± 0.88	23.96 ± 0.66
Near phoria, Δ; + = esophoria	0.86 ± 3.55	0.57 ± 4.86
AC/A ratio, Δ/D*	9.59 ± 3.79	8.10 ± 2.86
Flat meridian keratometry, D	43.13 ± 1.62	43.79 ± 1.55
Steep meridian keratometry, D	43.84 ± 1.66	44.56 ± 1.48
Intraocular pressure, mm Hg	16.9 ± 3.0	16.9 ± 2.8
Corneal thickness, μm	530.9 ± 33.5	541.8 ± 28.3
Crystalline lens		
Thickness, mm	3.36 ± 0.15	3.35 ± 0.14
Index of refraction†	1.429 ± 0.008	1.427 ± 0.008
Radius of curvature, mm		
Anterior lens†	12.27 ± 1.16	12.28 ± 1.19
Posterior lens†	6.51 ± 0.58	6.34 ± 0.48
Relative peripheral refraction, D		
30° Nasal retina	+0.56 ± 0.61	+0.56 ± 0.57
30° Temporal retina	+0.64 ± 0.74	+0.58 ± 0.80
30° Superior retina	−0.40 ± 0.92	−0.31 ± 0.93
20° Inferior retina	−0.45 ± 0.79	−0.52 ± 0.89

Values are mean ± SD. Unless otherwise noted, $n = 43$ for SVL and $n = 42$ for PAL.

* AC/A ratio values were censored if the accommodative response was <1 D for a 4-D stimulus and if the AC/A ratio was >20 Δ/D (SVL, $n = 34$; PAL, $n = 35$; data from 16 children censored).

† Phacometry data missing for two children (SVL, $n = 42$; PAL, $n = 41$).

Of the 85 children enrolled, 84 (99%) completed the 12-month visit and 83 (98%) completed the 24-month visit. One child in the PAL group withdrew from the study after the baseline visit and did not return for additional visits. During the first study year, one child in the PAL group switched to SVLs 4 months before the 12-month visit. There were no crossovers or withdrawals in the SVL group. During the second study year, one child in the original SVL group was lost to follow-up. Two children, both in the original SVL group, began wearing spherical soft contact lenses (one 8 months before the final visit and one 6 weeks before the final visit).

Treatment Compliance

Compliance with wearing the study spectacles was good (Table 4). At the 12-month visit, parents' reports that the children wore the study spectacles most of or all the time were the same after school as on weekends, holidays, or vacations (SVL children 98%, PAL children 93%). Nearly all children reported wearing their study spectacles most of or all the time at school. The percentage of children reporting that they wore their study spectacles most of or all the time after school (SVL children 93%, PAL children 88%) and on weekends, holidays, or vacations (SVL children 86%, PAL children 85%) was slightly lower than the percentage reported by parents.

Compliance was also good during the second study year, when all children wore SVLs. At the 24-month visit, parents' reports that the children wore the study spectacles most of or all the time were similar after school and on weekends, holidays, or vacations (all 90% or greater for both groups). Children's reports that they wore their study spectacles most of or

Table 4. Compliance Rates Wearing Study Spectacles as Reported by Parents and Children

	SVL Group (%)		PAL Group (%)	
Time of Day	**Parent**	**Child**	**Parent**	**Child**
12-Month Visit (SVLs vs. PALs)				
At school	—	95	—	98
After school	98	93	93	88
Weekends/holidays/vacations	98	86	93	85
24-Month Visit (All wear SVLs)				
At school	—	91	—	93
After school	93	93	90	93
Weekends/holidays/vacations	93	95	93	90

Values represent the percentages reporting that the child wore the study spectacles most of the time or all the time.

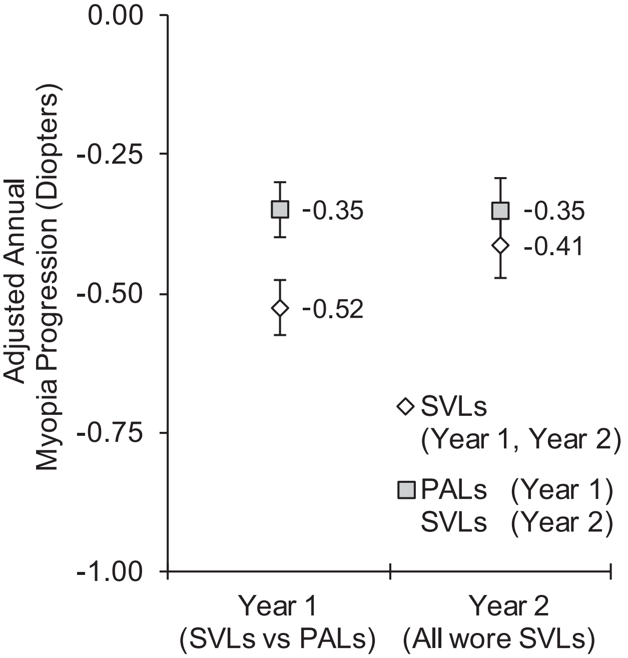

FIGURE 2. Mean 1-year change in spherical equivalent refractive error during year 1 (randomly assigned to PALs or SVLs) and during year 2 (all wore SVLs). Annual progression is adjusted for baseline refractive error, baseline age, sex, ethnicity, baseline axial length, baseline steep keratometry, and baseline outdoor activity. Error bars represent SE.

all the time were similar at school, after school, and on weekends, holidays, or vacations (all 90% or greater for both groups).

Primary Outcome

The primary outcome at the end of the first year (after randomization to either SVLs or PALs) and the second year (when all wore SVLs) was the previous year's change in cycloplegic spherical equivalent refractive error of the right eye. During the first year, the unadjusted 1-year change in spherical equivalent refractive error (mean ± SD) was −0.47 ± 0.38 D for SVL wearers ($n = 43$) and −0.40 ± 0.31 D for PAL wearers ($n = 41$). The unadjusted difference between PAL and SVL wearers of 0.07 D was not statistically significant ($P = 0.34$; 95% confidence interval [CI] = −0.08 to 0.23 D). After adjusting for baseline refractive error, age, sex, ethnicity, and the three covariates imbalanced at baseline (axial length, steep keratometry, and outdoor activity), children wearing PALs were found to have significantly less myopia progression than children wearing SVLs by 0.18 D ($P = 0.01$; 95% CI = 0.04 to 0.32 D; Fig. 2).

During the second study year when all children wore SVLs, the unadjusted 1-year change in spherical equivalent refractive error (mean ± SD) was −0.38 ± 0.40 D in the SVL group ($n = 42$) and −0.38 ± 0.43 D in the former PAL-wearing group ($n = 41$). The unadjusted difference between the groups was not statistically significant ($P = 0.95$; 95% CI = −0.19 to 0.17 D). After adjusting for the same covariates in the year 1 model, there was no difference in progression between groups ($P = 0.50$; 95% CI = −0.12 to 0.24 D; Fig. 2). Restating this result, there was no evidence that the small 1-year PAL treatment effect of 0.18 D was lost 1 year after discontinuing PALs because of a rebound effect.

Secondary Outcomes

Axial length was evaluated to determine whether the PAL treatment effect observed during the first year was due to decreased axial eye growth. The unadjusted 1-year change in axial length was 0.28 ± 0.17 mm for SVL wearers ($n = 43$) and 0.24 ± 0.15 mm for PAL wearers ($n = 41$). The unadjusted difference between PAL and SVL wearers of −0.04 mm was not statistically significant ($P = 0.22$; 95% CI = −0.11 to 0.03 mm). After adjusting for age, sex, ethnicity, and imbalanced baseline covariates, axial length in children wearing PALs increased significantly less than it did in children wearing SVLs by −0.08 mm ($P = 0.005$; 95% CI = −0.13 to −0.03 mm; Fig. 3).

During the second year when children wore SVLs, the unadjusted 1-year change in axial length (mean ± SD) was 0.23 ± 0.17 mm in the SVL group ($n = 42$) and 0.29 ± 0.16 mm in the former PAL-wearing group ($n = 41$). The unadjusted difference between the groups was not statistically significant ($P = 0.13$; 95% CI = −0.13 to 0.02 mm). After adjusting for the same covariates in the year-1 model, there was no difference in eye growth between the groups ($P = 0.43$; 95% CI = −0.04 to 0.09 mm; Fig. 3), which is consistent with the year-2 primary outcome finding of no difference in myopia progression between groups.

Baseline age, sex, and ethnicity each had a significant association with the 1-year change in refractive error during the first study year, when children were randomly assigned to PALs or SVLs; however, none of these covariates had a significant effect on the PAL treatment effect (all $P > 0.32$ in interactions with treatment; Table 5). Myopia progression in children younger than 10 years of age at baseline was roughly twice that of children older than 10 years of age ($P < 0.0001$). Myopia progression was greater in girls than in boys ($P = 0.0007$) and was significantly less in non-Hispanic white children than in children of other ethnicities ($P = 0.01$). There was no association between a child's baseline myopia and amount of myopia progression ($P = 0.32$), and the magnitude of the PAL treatment effect did not depend on a child's baseline amount of myopia ($P = 0.79$).

During the second year, when all children wore SVLs, the 1-year increase in myopia for younger children was greater than it was for older children ($P = 0.0003$). There was not a

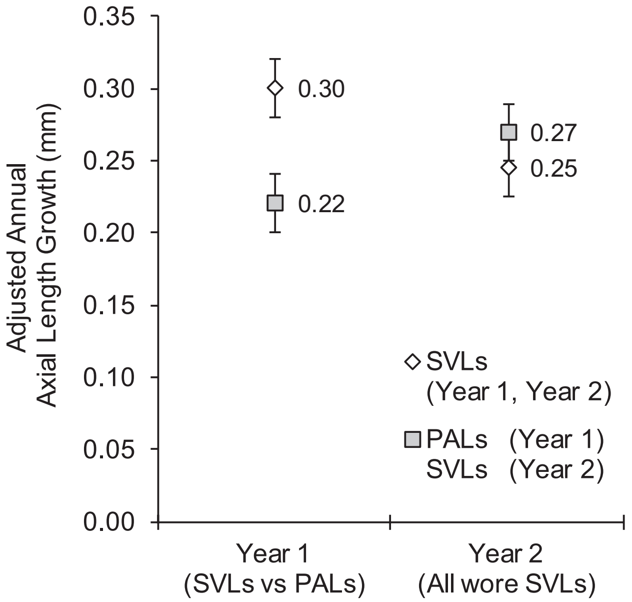

FIGURE 3. Mean 1-year change in axial length during year 1 (randomly assigned to PALs or SVLs) and during year 2 (all wore SVLs). Change in axial length is adjusted for baseline age, sex, ethnicity, baseline axial length, baseline steep keratometry, and baseline outdoor activity. Error bars represent SE.

TABLE 5. Adjusted Effect of Baseline Age, Sex, Ethnicity, and Baseline Myopia on the 1-Year Progression of Myopia (in diopters) by Treatment Group

Characteristic	Main Effect *P**	Treatment Group† Mean ± SE (*n*) SVLs	Treatment Group† Mean ± SE (*n*) PALs	Interaction *P*‡
Year 1 (SVLs vs. PALs)				
Age, y	<0.0001			
≤10.0		−0.73 ± 0.09 (15)	−0.46 ± 0.06 (27)	0.70 (0.32)§
>10.0		−0.36 ± 0.06 (28)	−0.25 ± 0.09 (14)	
Sex	0.0007			
Male		−0.42 ± 0.07 (22)	−0.18 ± 0.07 (19)	0.35
Female		−0.62 ± 0.07 (21)	−0.50 ± 0.07 (22)	
Ethnicity (non-Hispanic white)	0.01			
Yes		−0.45 ± 0.06 (27)	−0.31 ± 0.06 (28)	0.42
No		−0.67 ± 0.07 (16)	−0.42 ± 0.08 (13)	
Baseline myopia	0.32			
Less myopia (≥−1.70 D)		−0.56 ± 0.07 (20)	−0.37 ± 0.07 (22)	0.79 (0.72)§
More myopia (<−1.70 D)		−0.48 ± 0.07 (23)	−0.34 ± 0.07 (19)	
Year 2 (All wear SVLs)				
Age, y	0.0003			
≤10.0		−0.58 ± 0.11 (15)	−0.43 ± 0.08 (27)	0.92 (0.41)§
>10.0		−0.27 ± 0.08 (27)	−0.28 ± 0.11 (14)	
Sex	0.62			
Male		−0.40 ± 0.09 (22)	−0.31 ± 0.09 (19)	0.77
Female		−0.42 ± 0.09 (20)	−0.39 ± 0.09 (22)	
Ethnicity (non-Hispanic white)	0.43			
Yes		−0.44 ± 0.08 (27)	−0.36 ± 0.08 (28)	0.78
No		−0.35 ± 0.10 (15)	−0.32 ± 0.11 (13)	
Baseline myopia	0.41			
Less myopia (≥−1.70 D)		−0.34 ± 0.09 (19)	−0.38 ± 0.09 (22)	0.25 (0.20)§
More myopia (<−1.70 D)		−0.48 ± 0.09 (23)	−0.30 ± 0.09 (19)	

* *P* from the final model for the association between the indicated characteristic and the 1-year change in myopia (regardless of treatment group). Baseline age and baseline myopia were treated as continuous variables.

† All means adjusted for the factors present in the final model for the 1-year change in refractive error (baseline refractive error, age, axial length, steep keratometry power, outdoor activity, sex, and ethnicity) unless stratified by that factor.

‡ *P* for the interaction between treatment group and the variable indicated (i.e., whether any association between the characteristic and the 1-year change in myopia differed between the SVL and the PAL groups).

§ First *P* is for the interaction between treatment group and the indicated characteristic treated as a continuous variable. The *P* in parentheses is for the interaction between treatment effect and the indicated characteristic treated as a dichotomous variable split at its median.

significant association between the 1-year progression of myopia and sex ($P = 0.62$), ethnicity ($P = 0.43$), or baseline myopia ($P = 0.41$). As in the first year, none of the covariates had a significant effect on the progression of myopia by treatment group (all $P > 0.20$ in interaction with treatment group; Table 5).

Near phoria and near work (diopter-hours per week) at baseline were evaluated to determine whether either was associated with the 1-year change in refractive error during the first study year. Near phoria was evaluated as both a continuous variable and as a dichotomous variable with children classified as esophoric (near phoria >0) or non-esophoric (near phoria ≤0). A child's near phoria was not associated with the change in refractive error ($P = 0.56$ continuous; $P = 0.08$ dichotomous), and there was not a significant interaction between near phoria and the treatment effect ($P = 0.91$ continuous; $P = 0.83$ dichotomous). Baseline near work was not associated with the 1-year change in spherical equivalent refractive error ($P = 0.37$), and there was no interaction between a child's amount of near work and the PAL treatment effect ($P = 0.16$). Near phoria and near work were also not associated with the 1-year change in refractive error during the second year of the study, and there were no significant interactions with treatment group (all $P > 0.30$; data not shown).

Accommodative Lag and Myopia Progression

Accommodative lag measurements using the child's habitual prescription at the 6- through 24-month visits are shown in Table 6. A +2.00-D add reduced accommodative lag in children wearing PALs by 0.33 ± 0.34 D (mean ± SD) at the 6-month visit and by 0.42 ± 0.38 D at the 12-month visit. As expected, the mean of the 6-month and 12-month accommodative lags measured through the child's assigned near habitual correction (SVL group, habitual prescription or PAL group, habitual prescription +2.00 D) was significantly lower in children wearing PALs (0.33 ± 0.07 D; $P < 0.0001$), though the difference between groups was clinically small. During the first study year when children wore either SVLs or PALs, the mean habitual lag was not associated with the 1-year change in spherical equivalent refractive error ($\beta = 0.05$ D less myopia progression per diopter of lag; $P = 0.67$; 95% CI = −0.17 to 0.26 D change in refractive error per diopter of habitual lag), and there was no interaction between accommo-

TABLE 6. Accommodative Lag (in diopters) for a 4-D Badal Target when Children Were Measured with Their Habitual Prescription during Years 1 and 2 of the Study

	Treatment Group Mean Lag (±SD)	
	SVLs	**PALs**
Year 1 (SVLs vs. PALs)		
6-month visit	*n* = 43	*n* = 40
Habitual Rx (no add)	1.55 ± 0.45	1.55 ± 0.38
Habitual Rx with +2-D add	—	1.22 ± 0.25
Lag reduction with add	—	0.33 ± 0.34
12-month visit	*n* = 43	*n* = 41
Habitual Rx (no add)	1.54 ± 0.40	1.63 ± 0.41
Habitual Rx with +2-D add	—	1.21 ± 0.27
Lag reduction with add	—	0.42 ± 0.38
Mean lag experienced*	*n* = 43	*n* = 41
	1.55 ± 0.37	1.22 ± 0.21†
Year 2 (all wear SVLs)		
18-month visit	*n* = 41	*n* = 39
Habitual Rx (no add)	1.69 ± 0.62	1.67 ± 0.50
24-month visit	*n* = 42	*n* = 41
Habitual Rx (no add)	1.54 ± 0.35	1.70 ± 0.39
Mean lag experienced	*n* = 42	*n* = 41
	1.61 ± 0.40†	1.68 ± 0.40 †

Habitual prescription is defined as the prescription in the study spectacles worn to the visit.

* Mean of the 6-month and 12-month habitual lag values when wearing the assigned spectacle type (SVL [habitual Rx] or PAL [habitual Rx with +2-D add]).

† For children not seen at the 6-month or 18-month visit, the 12-month or 24-month lag value, respectively, was used as the child's mean value.

dative lag and the PAL treatment effect ($P = 0.34$). During the second study year when all children wore SVLs, the mean habitual lag from the 18- and 24-month visits was not associated with the 1-year change in refractive error ($\beta = 0.18$ D less myopia progression per diopter of lag; $P = 0.09$; 95% CI = −0.03 to 0.40 D change in refractive error per diopter of habitual lag), and there was again no interaction between accommodative lag and treatment group ($P = 0.18$).

DISCUSSION

In STAMP, PALs resulted in an adjusted reduction in myopia progression of 0.18 D (95% CI = 0.04 to 0.32) after 1 year in children with high accommodative lag. This effect size is similar to the 1- and 3-year effect sizes (0.18 D and 0.20 D, respectively) found by the largest PAL clinical trial in the United States (COMET).[6] Children in STAMP were specifically recruited to have high accommodative lag and low myopia (−2.25 D spherical equivalent myopia or less) and/or high accommodative lag and near esophoria. COMET reported that these subgroups of children had the greatest 1-year PAL treatment effects of 0.28 D (95% CI = 0.04 to 0.50) and 0.39 D (95% CI = 0.11 to 0.67), respectively.[9] After restricting enrollment to children with high accommodative lag, low myopia, and near esophoria to validate the COMET subgroup findings in a fully randomized sample, COMET2 reported a 1-year difference in progression for children wearing PALs versus SVLs of 0.14 D (95% CI = −0.005 to 0.28).[3] The upper limits of the 95% CI for the PAL treatment effect from these two randomized trials of children with high accommodative lag (COMET2 and STAMP) suggest that the greatest 1-year treatment effect that might be expected is between 0.28 and 0.32 D, which is less than previously suggested by COMET's original subgroup analysis.[9]

Both the accommodative lag theory and the mechanical tension theory of myopia progression are consistent with the 1-year PAL treatment effect in STAMP. Under the accommodative lag theory, PALs reduce accommodative lag during near work, thereby decreasing hyperopic foveal blur, axial elongation, and myopia progression.[10–12] If the reduction in accommodative lag due to PALs is consistent over time, this theory would predict that the treatment effect should continue to accumulate over time. COMET2 reported a continued increase in the PAL treatment effect of 0.09 D in year 2 of the study and 0.06 D in year 3, for a total 3-year effect of 0.28 D. Even in children with high accommodative lag, it appears that the treatment effect may be greatest in the first year of wear.

The mechanical tension theory also predicts a reduction in myopia progression when children wear PALs. Under the mechanical tension theory, PALs reduce the effort required to accommodate during near work activities, which in turn reduces axial elongation by decreasing ciliary-choroidal tension in the equatorial dimension of the globe. By reducing ciliary-choroidal tension, more proportional expansion of the globe might be possible, perhaps yielding less rapid axial elongation. The mechanical tension theory also predicts a limited period over which the treatment effect continues to accumulate because the additional equatorial expansion allowed by reducing accommodative effort ultimately results in ciliary-choroidal tension again reaching a critical point. At this point, PALs would no longer slow myopia progression, which could explain the previously reported finding of a PAL treatment effect limited to the first year of PAL wear.[6]

A previously unanswered question in the literature is whether the PAL treatment effect persists after children cease PAL wear. Assuming that accommodative lag returns to its baseline level once PALs are discontinued, the accommodative lag theory predicts equal progression between children who have always worn SVLs and previous PAL wearers who switch to wearing SVLs (maintained treatment effect). Under the mechanical tension theory, a rebound of the treatment effect (loss of the treatment effect) is predicted when children wearing PALs switch to wearing SVLs because of increased ciliary-choroidal tension. Once PAL wear ceases, more accommodative effort is necessary for former PAL-wearing children to achieve the same accommodative response as children who have worn only SVLs because of the additional equatorial expansion possible during PAL wear. The additional accommodative effort after switching from PALs to SVLs causes increased equatorial tension that would be hypothesized to result in more rapid axial elongation in year 2, negating any treatment effect in year 1.

There was no evidence that the small, 0.18-D treatment effect was lost 1 year after discontinuing PAL wear, which is consistent with the accommodative lag theory of hyperopic defocus causing myopia progression. The maintained treatment effect (lack of a rebound effect) is not consistent with the mechanical tension theory.

The smaller than expected year-1 PAL treatment effect might have made a rebound effect difficult to detect because the sample size was calculated to be able to find a clinically meaningful 1-year treatment and rebound effect of 0.25 D or more. Although the treatment effect was maintained for 1 year after ceasing PAL wear, it remains unclear whether the treatment effect is sustained indefinitely. Although COMET found a statistically significant 3-year PAL treatment effect of 0.20 D for all myopic children enrolled, the treatment effect after 5 years was no longer significant even though children continued wearing their original lens assignment (Gwiazda JE, et al. *IOVS* 2006;47:ARVO E-Abstract 1166).

Previous clinical trials have not reported the change in accommodative lag when children wear bifocals or PALs. Most studies in adults have reported that bifocal adds of +2.00 D or less either eliminate lag or result in a lead of accommodation[47–51]; however, this finding is not consistent in myopic children.[52–54] Cheng et al.[52] reported that an add in excess of +2.50 D was required to eliminate accommodative lag for a binocular, 3.00-D stimulus in children with progressing myopia. Sreenivasan et al.[54] reported that a +2.00-D bifocal add eliminated accommodative lag to a 3.00-D binocular stimulus in myopic children; however, their sample included no children with near esophoria. The study by Cheng et al.[52] and STAMP included myopic children with near esophoria, which has been previously associated with more rapid myopia progression.[5,9,55–57]

In STAMP, a +2.00-D add reduced accommodative lag to a 4.00-D stimulus by 0.33 D and 0.42 D at the 6- and 12-month visits, respectively. On average, 1.22 D of accommodative lag remained for children in the PAL group compared with 1.55 D of accommodative lag for children in the SVL group when viewing a 4.00-D Badal stimulus. As we previously reported,[53] a higher initial accommodative lag was associated with a greater reduction in lag with a +2.00-D bifocal; however, there was also a floor effect at roughly 1.00 D of lag where the +2.00-D add had no impact on lag. A higher add power might have resulted in a more pronounced reduction in accommodative lag in this study. Not finding an association between accommodative lag and myopia progression provides reason to consider whether any increase in the PAL treatment effect with a higher add power could be explained by a mechanism other than decreased hyperopic foveal blur.

Accommodative lag through the child's assigned near correction was not associated with the 1-year change in refractive error in year 1 of the study, and the size of the PAL treatment effect was not greater in children with higher lag of accommodation. The association between accommodative lag and the 1-year change in myopia approached statistical significance in year 2 of the study ($P = 0.09$); however, the positive sign of the slope coefficient suggests that accommodative lag would be protective against myopia progression had it been statistically significant, contrary to the effect predicted by a lag hypothesis. Not finding an association between accommodative lag and myopia progression is consistent with the negative results of the only studies that have evaluated this association in myopic children,[25,26] though studies in young adults have reported both positive and negative associations.[27,28] Although the results of this study support retinal blur-based hypotheses of myopia progression, they do not provide support for the theory that the PAL treatment effect is due to decreased foveal hyperopic defocus during near work.

Lag measured using the child's habitual correction was chosen for this analysis because we were interested in the amount of accommodative lag that best represented what the child experienced after adapting to his or her spectacles in each preceding 6-month period. We previously found that when accommodative lag was measured at baseline in STAMP children (when many children's vision was undercorrected or not corrected), using full manifest correction resulted in accommodative lag roughly 0.20 D greater on average than when measured with habitual correction.[53] We did not find a significant difference between accommodative lag values measured through a child's habitual and manifest correction once the child was enrolled in the study, had adapted to his or her spectacle prescription, and had lag measured after 6 months using both habitual correction and full manifest correction.[53] Although children with undercorrected vision experienced slightly increased accommodative lag when receiving their first pair of study spectacles after the baseline visit, a significant difference in lag measured with manifest versus habitual correction was not found during follow-up after all children wore their appropriate correction. Based on these results, the habitual lag measurements made at the follow-up visits are an accurate representation of the lag experienced by each child.

Near phoria has previously been an important factor in determining a child's response to PALs or bifocals; esophoric children have had greater treatment effects in subgroup analyses.[7–9] Although 64% of children in STAMP were esophoric at near, near phoria was not associated with myopia progression or the magnitude of the PAL treatment effect. Children eligible for STAMP were only required to be esophoric at near if their spherical equivalent myopia was greater than −2.25 D at enrollment, which could have potentially reduced the treatment effect. That said, of the children enrolled who had myopia less than −2.25 D, 53% were esophoric at near. It is noteworthy that the treatment effect in this study was consistent with that of COMET2, which enrolled only children with near esophoria.

Cross-sectional studies have reported that more time spent outdoors is associated with less myopic refractive errors in children,[58–60] and longitudinal data in children suggest that outdoor activity may be protective against myopia onset.[61] At baseline, children in STAMP assigned to the PAL group spent 2.76 more hours outdoors per week than children assigned to wear SVLs. One might wonder whether the treatment effect during the first year of STAMP was due to PAL-wearing children spending slightly more time outdoors than SVL-wearing children. We controlled for outdoor activity in the final model of myopia progression and did not find a significant association between outdoor activity and the 1-year change in myopia ($\beta = -0.01$ D refractive error change per hour spent outdoors each week; $P = 0.10$). We also did not find a significant interaction between outdoor activity and PAL treatment ($P = 0.62$). These analyses support the treatment effect being a PAL effect rather than an outdoor effect.

A study limitation is that we did not determine whether the treatment effect increases beyond the first year of PAL wear in these children with high accommodative lag. Recently published COMET2 results provided insight into this question and suggest the largest treatment effect occurs during the first year of wear, with perhaps modest additional treatment effect accumulation in subsequent years. This study also did not evaluate different add powers or customized add powers, which might have yielded a different treatment effect. Regardless of the add power used in previous clinical trials, the treatment effects reported have been relatively similar and clinically small (see Ref. 62 for review). It is possible that some children might have benefited more from a higher add power. Given the small effect sizes of multiple clinical trials combined with the previously reported diminishing benefit beyond the first year of bifocal wear, it is questionable whether different add powers would have resulted in a clinically meaningful and sustained increase in the treatment effect.

In contrast to foveal hyperopic blur, another recently proposed hypothesis is that peripheral hyperopic retinal blur causes myopia progression.[63–65] Under this theory, PALs decrease myopia progression by reducing hyperopic blur in the periphery. Because retinal regions have been shown to respond to local defocus signals in animal models,[66] it is possible that decreasing peripheral eye growth could result in a reduction in axial elongation. Because SVLs of greater myopic power have been reported to cause greater amounts of peripheral hyperopic blur than lenses of less myopic power,[65] this theory may also explain previously reported decreases in the PAL treatment effect over time as a child's myopia progresses. The influence of peripheral defocus on progression warrants further investigation.

In conclusion, these results confirm the presence of a small but statistically significant treatment effect when children with high accommodative lag wear PALs. Although these results provide additional evidence that PALs slightly reduce myopia progression, the 1-year effect of 0.18 D is not clinically meaningful. COMET2 and STAMP are the first two clinical trials to restrict enrollment and randomization to children with high lag of accommodation. The modest treatment effect from these two trials suggests that the expected reduction in myopia progression for children with high lag of accommodation may be smaller than previously thought. The absence of a rebound of the 0.18 D treatment effect after discontinuing PAL wear is not consistent with the mechanical tension theory. The lack of a rebound effect after discontinuing PAL wear supports the hyperopic defocus theory of myopia progression; however, not finding an association between accommodative lag and myopia progression in STAMP and in previous studies of myopic children is inconsistent with the PAL effect being due to decreased foveal blur during near work. The mechanism of the small PAL effect requires further study so it can be determined whether optical treatments can be optimized to be more effective.

References

1. Vitale S, Sperduto RD, Ferris FL 3rd. Increased prevalence of myopia in the United States between 1971–1972 and 1999–2004. *Arch Ophthalmol.* 2009;127:1632–1639.
2. Vitale S, Ellwein L, Cotch MF, Ferris FL 3rd, Sperduto R. Prevalence of refractive error in the United States: 1999–2004. *Arch Ophthalmol.* 2008;126:1111–1119.
3. Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group. Progressive-addition lenses versus single-vision lenses for slowing progression of myopia in children with high accommodative lag and near esophoria. *Invest Ophthalmol Vis Sci.* 2011;52:2749–2757.
4. Edwards MH, Li RW, Lam CS, Lew JK, Yu BS. The Hong Kong Progressive Lens Myopia Control Study: study design and main findings. *Invest Ophthalmol Vis Sci.* 2002;43:2852–2858.
5. Fulk GW, Cyert LA, Parker DE. A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. *Optom Vis Sci.* 2000;77:395–401.
6. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2003;44:1492–1500.
7. Hasebe S, Ohtsuki H, Nonaka T, et al. Effect of progressive addition lenses on myopia progression in Japanese children: a prospective, randomized, double-masked, crossover trial. *Invest Ophthalmol Vis Sci.* 2008;49:2781–2789.
8. Yang Z, Lan W, Ge J, et al. The effectiveness of progressive addition lenses on the progression of myopia in Chinese children. *Ophthalmic Physiol Opt.* 2009;29:41–48.
9. Gwiazda JE, Hyman L, Norton TT, et al. Accommodation and related risk factors associated with myopia progression and their interaction with treatment in COMET children. *Invest Ophthalmol Vis Sci.* 2004;45:2143–2151.
10. Charman WN. Near vision, lags of accommodation and myopia. *Ophthalmic Physiol Opt.* 1999;19:126–133.
11. Goss DA, Hampton MJ, Wickham MG. Selected review on genetic factors in myopia. *J Am Optom Assoc.* 1988;59:875–884.
12. Goss DA, Rainey BB. Relationship of accommodative response and nearpoint phoria in a sample of myopic children. *Optom Vis Sci.* 1999;76:292–294.
13. Gwiazda J, Thorn F, Bauer J, Held R. Myopic children show insufficient accommodative response to blur. *Invest Ophthalmol Vis Sci.* 1993;34:690–694.
14. Hung LF, Crawford ML, Smith EL. Spectacle lenses alter eye growth and the refractive status of young monkeys. *Nat Med.* 1995;1:761–765.
15. Schaeffel F, Glasser A, Howland HC. Accommodation, refractive error and eye growth in chickens. *Vision Res.* 1988;28:639–657.
16. Shaikh AW, Siegwart JT Jr, Norton TT. Effect of interrupted lens wear on compensation for a minus lens in tree shrews. *Optom Vis Sci.* 1999;76:308–315.
17. Wallman J, Winawer J. Homeostasis of eye growth and the question of myopia. *Neuron.* 2004;43:447–468.
18. Huang J, Hung LF, Smith EL. Changes in ocular shape and peripheral refractive errors in infant monkeys during recovery from experimentally induced myopia (Abstract). *Optom Vis Sci.* 2011; 88:110470.
19. Schmid KL, Wildsoet CF. Effects on the compensatory responses to positive and negative lenses of intermittent lens wear and ciliary nerve section in chicks. *Vision Res.* 1996;36:1023–1036.
20. Zhu X, Winawer JA, Wallman J. Potency of myopic defocus in spectacle lens compensation. *Invest Ophthalmol Vis Sci.* 2003;44: 2818–2827.
21. Norton TT, Siegwart JT Jr, Amedo AO. Effectiveness of hyperopic defocus, minimal defocus, or myopic defocus in competition with a myopiagenic stimulus in tree shrew eyes. *Invest Ophthalmol Vis Sci.* 2006;47:4687–4699.
22. Cheng D, Schmid KL, Woo GC, Drobe B. Randomized trial of effect of bifocal and prismatic bifocal spectacles on myopic progression: two-year results. *Arch Ophthalmol.* 2010;128:12–19.
23. Mutti DO, Mitchell GL, Hayes JR, et al. Accommodative lag before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2006; 47:837–846.
24. Gwiazda J, Thorn F, Held R. Accommodation, accommodative convergence, and response AC/A ratios before and at the onset of myopia in children. *Optom Vis Sci.* 2005;82:273–278.
25. Berntsen DA, Sinnott LT, Mutti DO, Zadnik K. Accommodative lag and juvenile-onset myopia progression in children wearing refractive correction. *Vision Res.* 2011;51:1039–1046.
26. Weizhong L, Zhikuan Y, Wen L, Xiang C, Jian G. A longitudinal study on the relationship between myopia development and near accommodation lag in myopic children. *Ophthalmic Physiol Opt.* 2008;28:57–61.
27. Allen PM, O'Leary DJ. Accommodation functions: co-dependency and relationship to refractive error. *Vision Res.* 2006;46:491–505.
28. Rosenfield M, Desai R, Portello JK. Do progressing myopes show reduced accommodative responses? *Optom Vis Sci.* 2002;79:268–273.
29. Mutti DO, Zadnik K, Fusaro RE, Friedman NE, Sholtz RI, Adams AJ. Optical and structural development of the crystalline lens in childhood. *Invest Ophthalmol Vis Sci.* 1998;39:120–133.
30. Zadnik K, Mutti DO, Fusaro RE, Adams AJ. Longitudinal evidence of crystalline lens thinning in children. *Invest Ophthalmol Vis Sci.* 1995;36:1581–1587.
31. Mutti DO, Jones LA, Moeschberger ML, Zadnik K. AC/A ratio, age, and refractive error in children. *Invest Ophthalmol Vis Sci.* 2000; 41:2469–2478.
32. Troilo D, Quinn N, Baker K. Accommodation and induced myopia in marmosets. *Vision Res.* 2007;47:1228–1244.
33. Hoogerheide J, Rempt F, Hoogenboom W. Acquired myopia in young pilots. *Ophthalmologica.* 1971;163:209–215.
34. Mutti DO, Hayes JR, Mitchell GL, et al. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2007;48:2510–2519.
35. Mutti DO, Sinnott LT, Mitchell GL, et al. Relative peripheral refractive error and the risk of onset and progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2011;52:199–205.
36. Atchison DA, Pritchard N, Schmid KL. Peripheral refraction along the horizontal and vertical visual fields in myopia. *Vision Res.* 2006;46:1450–1458.
37. Millodot M. Effect of ametropia on peripheral refraction. *Am J Optom Physiol Opt.* 1981;58:691–695.
38. Logan NS, Gilmartin B, Wildsoet CF, Dunne MC. Posterior retinal contour in adult human anisomyopia. *Invest Ophthalmol Vis Sci.* 2004;45:2152–2162.
39. Seidemann A, Schaeffel F, Guirao A, Lopez-Gil N, Artal P. Peripheral refractive errors in myopic, emmetropic, and hyperopic

young subjects. *J Opt Soc Am A Opt Image Sci Vis.* 2002;19:2363–2373.

40. Berntsen DA, Mutti DO, Zadnik K. Study of theories about myopia progression (STAMP) design and baseline data. *Optom Vis Sci.* 2010;87:823–832.
41. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci.* 1997;74:367–375.
42. Berntsen DA, Mutti DO, Zadnik K. Validation of aberrometry-based relative peripheral refraction measurements. *Ophthalmic Physiol Opt.* 2008;28:83–90.
43. Mutti DO, Zadnik K, Adams AJ. A video technique for phakometry of the human crystalline lens. *Invest Ophthalmol Vis Sci.* 1992;33:1771–1782.
44. Goss DA, Winkler RL. Progression of myopia in youth: age of cessation. *Am J Optom Physiol Opt.* 1983;60:651–658.
45. Goss DA, Cox VD. Trends in the change of clinical refractive error in myopes. *J Am Optom Assoc.* 1985;56:608–613.
46. Goss DA. Effect of bifocal lenses on the rate of childhood myopia progression. *Am J Optom Physiol Opt.* 1986;63:135–141.
47. Sreenivasan V, Irving EL, Bobier WR. Binocular adaptation to near addition lenses in emmetropic adults. *Vision Res.* 2008;48:1262–1269.
48. Shapiro JA, Kelly JE, Howland HC. Accommodative state of young adults using reading spectacles. *Vision Res.* 2005;45:233–245.
49. Rosenfield M, Carrel MF. Effect of near-vision addition lenses on the accuracy of the accommodative response. *Optometry.* 2001;72:19–24.
50. Jiang BC, Bussa S, Tea YC, Seger K. Optimal dioptric value of near addition lenses intended to slow myopic progression. *Optom Vis Sci.* 2008;85:1100–1105.
51. Seidemann A, Schaeffel F. An evaluation of the lag of accommodation using photorefraction. *Vision Res.* 2003;43:419–430.
52. Cheng D, Schmid KL, Woo GC. The effect of positive-lens addition and base-in prism on accommodation accuracy and near horizontal phoria in Chinese myopic children. *Ophthalmic Physiol Opt.* 2008;28:225–237.
53. Berntsen DA, Mutti DO, Zadnik K. The effect of bifocal add on accommodative lag in myopic children with high accommodative lag. *Invest Ophthalmol Vis Sci.* 2010;51:6104–6110.
54. Sreenivasan V, Irving EL, Bobier WR. Binocular adaptation to +2 D lenses in myopic and emmetropic children. *Optom Vis Sci.* 2009;86:731–740.
55. Fulk GW, Cyert LA, Parker DE. A randomized clinical trial of bifocal glasses for myopic children with esophoria: results after 54 months. *Optometry.* 2002;73:470–476.
56. Goss DA. Variables related to the rate of childhood myopia progression. *Optom Vis Sci.* 1990;67:631–636.
57. Goss DA, Jackson TW. Clinical findings before the onset of myopia in youth, 3: heterophoria. *Optom Vis Sci.* 1996;73:269–278.
58. Dirani M, Tong L, Gazzard G, et al. Outdoor activity and myopia in Singapore teenage children. *Br J Ophthalmol.* 2009;93:997–1000.
59. Rose KA, Morgan IG, Ip J, et al. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology.* 2008;115:1279–1285.
60. Onal S, Toker E, Akingol Z, et al. Refractive errors of medical students in Turkey: one year follow-up of refraction and biometry. *Optom Vis Sci.* 2007;84:175–180.
61. Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci.* 2007;48:3524–3532.
62. Cheng D, Woo GC, Schmid KL. Bifocal lens control of myopic progression in children. *Clin Exp Optom.* 2011;94:24–32.
63. Smith EL 3rd, Hung LF, Huang J. Relative peripheral hyperopic defocus alters central refractive development in infant monkeys. *Vision Res.* 2009;49:2386–2392.
64. Sankaridurg P, Donovan L, Varnas S, et al. Spectacle lenses designed to reduce progression of myopia: 12-month results. *Optom Vis Sci.* 2010;87:631–641.
65. Lin Z, Martinez A, Chen X, et al. Peripheral defocus with single-vision spectacle lenses in myopic children. *Optom Vis Sci.* 2010;87:4–9.
66. Smith EL 3rd, Hung LF, Huang J, Blasdel TL, Humbird TL, Bockhorst KH. Effects of optical defocus on refractive development in monkeys: evidence for local, regionally selective mechanisms. *Invest Ophthalmol Vis Sci.* 2010;51:3864–3873.

APPENDIX

Data and Safety Monitoring Committee: Mark A. Bullimore (chair, 2006-present), Leslie Hyman (2006-8/2011), and Melvin L. Moeschberger (2006-present).

Masked Examiners: Bradley Dougherty (2007–2010), Kerri McTigue (2008–2010), Donald O. Mutti (2008–2010), Kathryn Richdale (2007–2010), Eric Ritchey (2007–2010), and Aaron Zimmerman (2007–2008).

Opticians: Melissa Button (2007–2010), Aaron Chapman (2006–2007), Melissa Hill (2006–2008), Brandy Knight (2008–2010), Scott Motley (2007–2009), and Jeff Rohlf (2006–2010).

Optometry Coordinating Center: Lisa Jones-Jordan (director, 2005-present), G. Lynn Mitchell (biostatistician, 2005-present), Loraine Sinnott (biostatistician, 2005-present), Linda Barrett (data entry, 2005–2007), Austen Tanner (data entry, 2005–2010), Melanie Schray (database management, 2005–2010).