Progressive-Addition Lenses versus Single-Vision Lenses for Slowing Progression of Myopia in Children with High Accommodative Lag and Near Esophoria

Correction of Myopia Evaluation Trial 2 Study Group for the Pediatric Eye Disease Investigator Group[1]

PURPOSE. To determine whether progressive-addition lenses (PALs) relative to single-vision lenses (SVLs) slow the progression of low myopia in children with high accommodative lag and near esophoria.

METHODS. One hundred eighteen children 8 to <12 years of age with spherical equivalent refraction (SER) from −0.75 to −2.50 D and near esophoria ≥2 PD were enrolled in this double-masked multicenter randomized trial. A key additional eligibility criterion was high accommodative lag, initially defined as at least 0.50 D (accommodative response less than 2.50 D for a 3.00-D demand) and later restricted further to at least 1.00 D. One hundred four subjects had accommodative lag of at least 1.00 D, and 14 had lag between 0.50 and 0.99 D. The children were randomized to receive either PALs with a +2.00-D addition or standard SVLs. The clinicians performing the outcome testing, as well as the children and their families, were masked to treatment group. Follow-up visits occurred every 6 months for 3 years. At annual visits, refractive error was assessed in each eye by using cycloplegic autorefraction. The main outcome measure was change from baseline to 3 years in SER by cycloplegic autorefraction.

RESULTS. The mean change in SER between baseline and the 3-year primary outcome visit was −0.87 D in the PAL group and −1.15 D in the SVL group, for a difference of 0.28 D (95% confidence interval [CI], 0.01–0.55D).

CONCLUSIONS. The PALs used in this study were found to have a statistically but not clinically significant effect of slowing myopia progression in children with high accommodative lag and near esophoria. (ClinicalTrials.gov number, NCT00320593.) (*Invest Ophthalmol Vis Sci.* 2011;52:2749–2757) DOI: 10.1167/iovs.10-6631

Myopia is a highly prevalent refractive condition, affecting 34% of children in the United States[1] and a much higher percentage in some countries in Asia.[2,3] Evidence suggests that the prevalence may be increasing over time.[1,4,5] Even low degrees of myopia are associated with increased risk of ocular complications, such as retinal detachment and glaucoma.[6–9]

Single-vision spectacle lenses (SVLs) and contact lenses are commonly prescribed to correct myopia in children. Occasionally other types of spectacle lenses, such as bifocals or progressive-addition lenses (PALs), are prescribed clinically, and many studies have been conducted to evaluate these lenses for slowing the progression of myopia.[10–16] Evidence from most well-designed studies shows that these lens therapies for controlling myopia have modest treatment benefits, which are found in the first year and sustained at the same level over time.[17] Overall, the use of standard bifocals or PALs versus SVLs for slowing the progression of myopia has produced treatment effects ranging from 0.14 to 0.59 D over 1.5 to 3 years.[10–16] The largest treatment trial evaluating PALs versus SVLs was the Correction of Myopia Evaluation Trial (COMET), a multicenter randomized double-masked clinical trial.[13] The study's primary finding was that the PALs (Varilux Comfort, Essilor of America, St. Petersburg, FL) slowed 3-year myopia progression by 0.20 D, a result that was statistically significant but not clinically important. Treatment was found to interact significantly with accommodative response and severity of myopia.[14] Therefore, additional analyses were conducted that showed statistically significant and more clinically meaningful 3-year treatment effects in subgroups of children with higher lags of accommodation (underaccommodation to near targets) in combination with near esophoria (0.64 D) or lower baseline myopia (0.48 D).[14] These results suggest that PALs are a clinically viable spectacle treatment for slowing progression in myopic children with high accommodative lags in conjunction with near esophoria and lower amounts of myopia.

The purpose of the present study was to reinvestigate the effect of PALs relative to SVLs on the progression of myopia in children with low baseline myopia, high accommodative lag, and near esophoria.

METHODS

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and was conducted by the Pediatric Eye Disease Investigator Group (PEDIG) at eight clinical sites consisting of seven optometry colleges and schools and one community-based ophthalmology practice. The study was conducted according to the tenets of the Declaration of Helsinki. The protocol and Health Insurance Portability and Accountability Act (HIPAA)–compliant informed consent forms were approved by institutional review boards, and a parent or guardian (referred to subsequently as "parent") of each study subject gave written informed consent. Subjects gave assent when required by the local review board of the participating institutions. Study oversight was provided by an independent data and safety monitoring committee. The protocol,

Correspondence and reprint requests: Jane E. Gwiazda, Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647; pedig@jaeb.org.

which is available on the PEDIG website (www.pedig.net), is summarized in the following sections.

Eligibility Criteria

Major eligibility criteria included age 8 to <12 years and refractive error meeting all the following, obtained by cycloplegic autorefraction: spherical equivalent −0.75 to −2.50 D in both eyes, astigmatism ≤1.50 D in both eyes, and spherical equivalent anisometropia ≤1.00 D. Other major eligibility criteria included near esophoria ≥2 PD, by prism and alternate cover test (PACT) at 33 cm, and high accommodative lag, as assessed by noncycloplegic autorefraction. High accommodative lag was originally defined as lag of at least 0.50 D in response to a target providing an accommodative demand of 3.00 D (33 cm; accommodative response less than 2.50 D for a 3.00-D demand), but was changed 1 year into recruitment to a lag of at least 1.00 D (accommodative response less than 2.00 D for a 3.00-D demand). The more stringent criterion was adopted in light of the results of a pilot study (Gwiazda J, unpublished data, 2005) which showed that the Grand Seiko autorefractor (Binocular Auto Refractor/Keratometer WR-5100; Grand Seiko Co., Ltd., Hiroshima, Japan; also known as Shin-Nippon) used in the present study measured approximately 0.35 D more lag than the autorefractor used in the original COMET study (R-1; Canon, Lake Success, NY). Additional major eligibility criteria included no strabismus, best corrected distance visual acuity at least 20/20, and no current or prior use of PALs, bifocals, or contact lenses in either eye (prior or current use of SVLs was permitted).

Randomization

In a permuted block design stratified by site and by history of previous SVL wear, each subject was randomly assigned with equal probability to receive spectacles that were either PALs with a +2.00-D near addition or SVLs. The clinicians, subjects, and subjects' families were all masked to treatment group for the duration of the study.

Treatment

Each subject received a new pair of spectacles provided by the study. Distance correction was prescribed according to the endpoint of the noncycloplegic subjective refraction (i.e., the minimum minus for best distance visual acuity). Subjects assigned to the SVL group received standard SVLs, whereas the PAL group subjects received Varilux Ellipse lenses (Essilor of America, St. Petersburg, FL) with a +2.00-D near addition. All lenses were polycarbonate and were fabricated at a central laboratory. To help maintain masking of the subjects, both SVLs and PALs were fit by study-certified, unmasked opticians who used a standard PAL fitting protocol. In addition, wearing instructions were identical for both treatment groups: Subjects were encouraged to lower their eyes to read and to tip their chins down, if necessary, to view distant objects clearly. Spectacles were prescribed to be worn during all waking hours.

During follow-up, a change in the distance correction was required if the endpoint of the noncycloplegic subjective refraction differed from the current prescription by 0.50 D or more in spherical equivalent. Prescription changes could be made for smaller differences at investigator discretion if the new prescription improved the subject's visual acuity by at least one line over that in their current correction.

Follow-up Visits

Follow-up visits were conducted every 6 months (±2 weeks) for 3 years, with the 3-year visit specified as the primary outcome visit. At these protocol-specified follow-up visits, all testing procedures were performed by a study-certified optometrist or ophthalmologist who was masked to the subject's lens assignment. To maintain masking of the investigators, the subject saw an unmasked coordinator before the examination who collected the subject's spectacles and told the optometrist or ophthalmologist performing the eye examination what distance refractive correction to use in trial frames for the examination.

In addition, anytime a subject reported a problem (e.g., blurry vision or headaches), he or she was evaluated by an unmasked consulting clinician who was aware of the subject's lens assignment. The consulting clinician could update the refraction as needed, but did not perform any study-specific measurements.

At each follow-up visit, the coordinator discussed spectacle compliance with the subject and family and estimated how often the spectacles were being worn during school, after school, and on weekends, by using a five-point Likert scale (always, 5; often, 4; sometimes, 3; rarely, 2; never, 1) for each period.

Testing Procedures and Assessments

At annual visits, the primary outcome of cycloplegic refractive error was assessed in each eye with the Grand Seiko autorefractor 30 minutes after administration of 2 drops of 1% tropicamide. Five readings (sphere, cylinder, and axis) were taken in each eye, with the room lights out while the subject fixated a row of 20/100 letters on an ETDRS chart in a light box at 4 m.

Additional procedures performed at all protocol-specified visits consisted of subjective refraction of both eyes and an oculomotor assessment using the cover–uncover test and the PACT. Accommodative response was measured with the Grand Seiko autorefractor with the room lights off. The accommodative target was an illuminated row of 20/100 letters positioned 33 cm from the subject and calibrated for that distance. The subject's right eye viewed the target through a lens placed in a trial frame that was equal to the spherical equivalent of the endpoint of the subjective refraction, and the left eye was occluded. Five readings (sphere, cylinder, and axis) were taken. To determine the accommodative lag or accommodative lead, the accommodative measurement was added to the 3.00-D demand to result in the accommodative lag or lead. If the value was positive (i.e., underaccommodation), it indicated accommodative lag; if the number was negative (i.e., overaccommodation), it indicated accommodative lead. The median of the five baseline accommodative lag/lead readings for each subject was used in the analysis.

At one visit, the parental history of myopia was assessed by asking each subject's parents, "Are you nearsighted? In other words, do you (or did you ever) wear glasses or contact lenses primarily to see far away or that are equally important for seeing far away and up close?"

Statistical Methods

The sample size was computed to be 100 subjects overall (50 per treatment group) to reach a 90% power and a type 1 error rate of 5%, so that a difference in 3-year myopia progression between PAL and SVL treatment groups would be detected if the true difference was at least 0.60 D, assuming a standard deviation of 0.85 D in each treatment group and allowing for a 10% loss to follow-up.

The primary analysis was a comparison of treatment groups using an analysis of covariance (ANCOVA) model in which myopia at 3 years was adjusted for myopia at baseline and prior SVL wear (currently or in the past versus never). The primary outcome measure was a change in spherical equivalent refractive error (SER) in diopters from baseline to the 3-year visit, as assessed by cycloplegic autorefraction. Each autorefraction reading was converted to an SER, and the medians of the five SERs for each eye were averaged to produce a subject-level SER for analysis (Pearson correlation for SER between right and left eyes at 3 years = 0.89). All analyses followed the intent-to-treat principle. The Monte Carlo Markov Chain (MCMC)[18] method of multiple imputation was used to impute data for subjects who did not complete the 3-year visit. To evaluate the effect of imputation on the primary results, we also performed the primary analysis (1) using the last-observation-carried-forward method and (2) using only data from subjects who completed the 3-year visit. In addition, an adjusted analysis was performed by including in the ANCOVA model the following covariates, which are known to be related to myopia progression: age, sex, ethnicity, accommodative lag, and magnitude of near esophoria. Interaction between baseline factors and treatment effect was formally

assessed by including interaction terms in the ANCOVA model, although it is acknowledged that the statistical power is low for detecting such interactions. For the adjusted model and for models testing for interactions, the baseline factors of refractive error, age, accommodative lag, and near esophoria size were treated as continuous variables, unless there was evidence of nonlinear associations between the factor and the outcome (for adjusted models) or between the factor and the treatment effect (for interaction models).

Secondary analyses were conducted to assess the treatment effect on myopia at interim time points of 1 and 2 years, using the same method as was used in the primary analysis, except that only complete cases were included.

Secondary outcomes evaluated were main axis astigmatism (J_0, dioptric power of a Jackson cross cylinder with axis at 0°) and oblique astigmatism (J_{45}, dioptric power of a Jackson cross cylinder with axis at 45°) by using the power vector approach.[19] For J_0 and J_{45}, the average of the medians of the five autorefraction readings for each measure was used for analysis. Because oblique astigmatism is often mirror symmetric in the two eyes, the average J_{45} values were calculated by transforming the axis values between 91° and 180° to values between 0° and 90° for each eye, then averaging the median value between the two eyes. J_0 and J_{45} were compared between treatment groups at annual visits by using separate ANCOVA models in which the outcome was adjusted for their respective baseline values.

RESULTS

Between April 2005 and March 2007, 118 subjects were enrolled in the study at eight clinical centers. The number of subjects enrolled per site ranged from 6 to 25 (median = 15). As part of the screening for the randomized trial, 67 (57%) of the 118 subjects participated in an ancillary study that was an evaluation of the methods of measuring accommodation.[20] The average age of the 118 subjects was 10.1 (±1.1) years, 64 (54%) were girls, and 59 (50%) were white. One hundred four children had accommodative lags of 1.00 D or more (accommodative response less than 2.00 D for a 3.00-D demand), and 14 had lags between 0.50 and 0.99 D. The mean SER at baseline was −1.48 (±0.46) D. All baseline characteristics that were evaluated were well balanced between treatment groups (Table 1).

Study and Visit Completion

Of the 118 subjects enrolled in the study, 110 (93%) completed the 3-year visit. One (2%) SVL group subject and seven (12%) PAL group subjects withdrew from the study early and did not complete the 3-year visit (Fig. 1). Of the eight subjects who did not complete the study, three were lost to follow-up, one moved to another state, three withdrew, and one was withdrawn by the clinical site. Compared with the 110 subjects who completed the study, the eight subjects who did not had less baseline myopia (mean SER −1.20 D vs. −1.50 D) and less baseline accommodative lag (mean, 1.16 D vs. 1.46 D). Overall, the 3-year visits were completed within the ±2-week window in 74 (67%) of the subjects, 1 to 30 days early or late in 22 (20%), and more than 30 days early or late in 14 (13%).

Effect of Treatment on Change in Myopia

From baseline to the 3-year visit, the mean change in SER was −0.87 D in the PAL group versus −1.15 D in the SVL group, for a difference of 0.28 D (95% confidence interval [CI], 0.01–0.55 D; Table 2; Fig. 2). In a model further adjusted by including age, sex, ethnicity, baseline accommodative lag, and baseline near esophoria, in addition to baseline SER and prior SVL wear, the 3-year difference in progression between PAL and SVL subjects was 0.27 D (95% CI, 0.02–0.53 D). Table 2 also shows that the 3-year change in spherical equivalent myopia was at

TABLE 1. Baseline Characteristics According to Treatment Group

Characteristic	SVL ($n = 59$) n (%)	PAL ($n = 59$) n (%)
Sex, female	28 (47)	36 (61)
Race/ethnicity		
White	31 (53)	28 (47)
African American	10 (17)	14 (24)
Hispanic or Latino	12 (20)	10 (17)
Asian	4 (7)	5 (8)
Other	2 (3)	2 (3)
Age, y		
Mean (SD)	10.0 (1.1)	10.2 (1.1)
Range	8.1 to 12.0	8.0 to 11.9
8 to <9	14 (24)	8 (14)
9 to <10	17 (29)	15 (25)
10 to <11	14 (24)	18 (31)
11 to <12	14 (24)	18 (31)
Spectacle wear (SVLs)		
Currently	33 (56)	33 (56)
In past but not currently	2 (3)	4 (7)
Never	24 (41)	22 (37)
Average spherical equivalent between the eyes, D*		
Mean (SD)	−1.45 (0.47)	−1.50 (0.45)
Range	−0.75 to −2.40	−0.78 to −2.38
−0.75 to −0.99	12 (20)	8 (14)
−1.00 to −1.49	23 (39)	22 (37)
−1.50 to −1.99	14 (24)	18 (31)
−2.00 to −2.50	10 (17)	11 (19)
Average J_0 between the eyes, D*		
Mean (SD)	−0.02 (0.15)	−0.02 (0.18)
Range	−0.53 to 0.27	−0.47 to 0.54
Average J_{45} between the eyes, D*		
Mean (SD)	0.10 (0.07)	0.11 (0.07)
Range	0.00 to 0.27	0.00 to 0.33
Anisometropia, D		
Mean	0.21 (0.16)	0.22 (0.20)
Range	0.00 to 0.93	0.00 to 1.00
Near esophoria, PD		
Mean (SD)	5.9 (3.4)	5.8 (3.2)
Range	2–20	2–16
2 to 5	34 (58)	33 (56)
6 to 10	21 (36)	22 (37)
11 to 15	3 (5)	3 (5)
16 to 20	1 (2)	1 (2)
Accommodative lag, D†		
Mean (SD)	1.40 (0.48)	1.47 (0.53)
Range	0.6–3.7	0.5–2.9
0.50 to 0.99	6 (10)	8 (14)
1.00 to 1.49	33 (56)	26 (44)
1.50 to 1.99	16 (27)	13 (22)
2.00 or more	4 (7)	12 (20)
Parental history of myopia‡		
Neither parent	5 (14)	10 (23)
One parent	10 (29)	16 (36)
Both parents	20 (57)	18 (41)

$N = 118$. Rounded percentages may not sum to 100%.

* Spherical equivalent, J_0, and J_{45} are averages of the median values from the five readings of cycloplegic autorefraction in each eye.

† Accommodative lag is the average of the median accommodative lag of the five readings of the right eye.

‡ Thirty-nine subjects had missing data or unknown parental history of myopia for at least one parent—15 subjects had missing data for both parents, 1 subject had missing data for one parent and uncertain data for the other, 19 subjects had missing data for one parent and known data for the other, and 4 subjects had data for one parent and uncertain data for the other.

least −1.50 D in 13% ($n = 7$) of subjects in PALs versus 36% ($n = 21$) of subjects in SVLs.

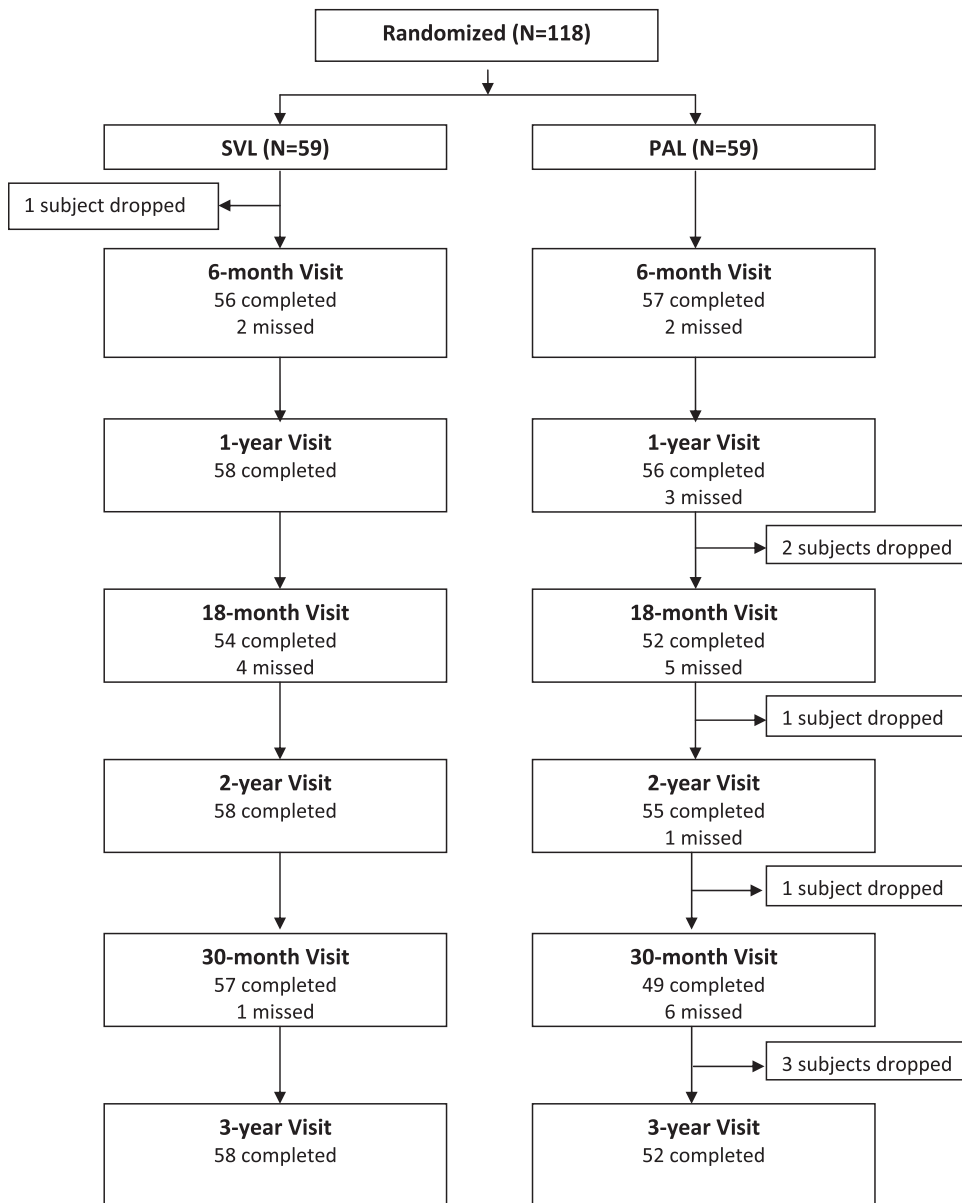The 3-year change in SER is shown stratified by baseline characteristics in Table 3. The treatment group difference

FIGURE 1. Flowchart of subjects throughout the study.

between PALs and SVLs was 0.35 D among subjects with baseline SER from −0.75 to −1.49 D and was 0.17 D among subjects with baseline SER from −11.50 to −2.50 D (*P* for continuous interaction = 0.24). In subjects with accommodative lag of 1.50 D or worse, the treatment effect was 0.41 D, and in subjects with lag from 0.50 to 1.49 D, it was 0.24 D (*P* for continuous interaction = 0.23). In subjects with no history of previous SVL wear, the treatment group difference was 0.42 D, whereas in subjects with previous SVL, wear it was 0.22 D (*P* for interaction = 0.48).

The mean change in SER from baseline to 1 year was −0.29 D in the PAL group versus −0.42 D in the SVL group (difference, 0.14; 95% CI, −0.005 to 0.28 D) and from baseline to 2 years was −0.58 D in the PAL group versus −0.80 D in the SVL group (difference, 0.23; 95% CI, 0.02–0.45 D; Table 2; Fig. 2).

Results of analyses (1) using the last-observation-carried-forward method, (2) using only data from subjects who completed the 3-year visit, and (3) limited to the 104 subjects with accommodative lag ≥1.00 D were similar to the results of the primary analysis.

Effect of Treatment on Change in Astigmatism

The change in astigmatism was small and did not differ by lens group. The mean change in J_0 (main axis astigmatism) from baseline to 3 years was 0.07 D in the PAL group versus 0.11 D in the SVL group (difference, −0.04 D; 95% CI, −0.11 to 0.03 D). The mean change in J_{45} (oblique astigmatism) from baseline to 3 years was 0.04 D in the PAL group versus 0.02 D in the SVL group (difference, 0.03 D; 95% CI, −0.006 to 0.06 D).

Treatment Compliance

As shown in Table 4, the percentages of PAL and SVL subjects estimated at every follow-up visit to have been wearing their study spectacles either always (score of 5) or often (score of 4), were 72% and 90% during school, 60% and 76% after school, and 60% and 71% on weekends, respectively. Treatment compliance appeared to be worse in the PAL group than in the SVL group, particularly among subjects with lower amounts of baseline myopia (−0.75 to −1.49 D; Table 4). There was no evidence that poor treatment compliance was related to increased progression (data not shown).

TABLE 2. Spherical Equivalent Refractive Error during Follow-up

	1 Year		2 Years		3 Years	
	SVL (n = 58) n (%)	PAL (n = 55) n (%)	SVL (n = 58) n (%)	PAL (n = 55) n (%)	SVL (n = 58) n (%)	PAL (n = 52) n (%)
Change in Spherical Equivalent Refractive Error from Baseline, D						
Mean (SD)	−0.42 (0.37)	−0.29 (0.39)	−0.80 (0.61)	−0.58 (0.55)	−1.15 (0.75)	−0.87 (0.72)
Range	−1.38 to 0.70	−1.56 to 0.82	−2.26 to 0.84	−2.16 to 0.78	−2.97 to 0.38	−3.13 to 0.22
>0.00 (less myopia)	6 (10)	6 (11)	5 (9)	5 (9)	3 (5)	6 (12)
0.00 to −0.49	27 (47)	35 (64)	11 (19)	18 (33)	8 (14)	11 (21)
−0.50 to −0.99	21 (36)	12 (22)	19 (33)	23 (42)	13 (23)	16 (31)
−1.00 to −1.49	4 (7)	1 (2)	17 (29)	5 (9)	13 (23)	12 (23)
≤−1.50 (more myopia)	0 (0)	1 (2)	6 (10)	4 (7)	21 (36)	7 (13)
Spherical Equivalent Refractive Error, D						
Mean (SD)	−1.88 (0.66)	−1.80 (0.63)	−2.26 (0.84)	−2.10 (0.81)	−2.60 (0.91)	−2.41 (0.95)
Range	−3.56 to −0.69	−3.75 to −0.72	−4.44 to 0.09	−4.19 to −0.75	−4.47 to −0.38	−5.13 to −0.72
Better than or equal to −0.49	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
−0.50 to −0.99	4 (7)	4 (7)	3 (5)	3 (5)	1 (2)	2 (4)
−1.00 to −1.99	30 (52)	34 (61)	18 (31)	25 (45)	14 (24)	18 (35)
−2.00 to −2.99	21 (36)	16 (29)	27 (47)	19 (35)	21 (36)	20 (38)
−3.00 to −3.99	3 (5)	2 (4)	7 (12)	6 (11)	17 (29)	8 (15)
Worse than or equal to −4.00	0 (0)	0 (0)	2 (3)	2 (4)	4 (7)	4 (8)

A negative value indicates that the myopia worsened over time; a positive value indicates that it improved over time. Rounded percentages may not sum to 100%.

* For baseline and each time point, a spherical equivalent was calculated for each eye for each of the five readings of cycloplegic autorefraction, and the median for each eye was averaged to obtain the spherical equivalent used for analysis. The change in average spherical equivalent was calculated by subtracting the spherical equivalent at baseline from each time point.

Two cases of treatment crossover are known. A PAL group subject wore SVLs for 6 months after SVLs were ordered by mistake when the distance correction was changed. This same subject later obtained contact lenses outside the study and wore them approximately 5 days a week for the last year of the study, although usually only for a few hours a day after school. Another PAL group subject reported having worn the PALs for 1.5 years before switching to wearing SVLs obtained outside the study for the remainder of the study.

FIGURE 2. Mean change in spherical equivalent refractive error during follow-up. The mean difference between treatment groups (SVL − PAL) in the change in spherical equivalent refractive error from baseline to 1 year was 0.14 D (95% CI, −0.005–0.30 D), from baseline to 2 years was 0.23 D (95% CI, 0.02–0.45), and from baseline to the 3 years was 0.28 D (95% CI, 0.01–0.55).

Adverse Events

No serious treatment-related adverse events were reported during the 3 years of follow-up. Of the three PAL group subjects seen by a consulting clinician for a problem, one reported distance blur and was prescribed a change in distance correction, one had conjunctivitis, and one reported dizziness, particularly during gymnastics (the subject was advised not to wear spectacles during this activity). Of the four SVL subjects seen by a consulting clinician for a problem, two had reduced visual acuity and were prescribed a change in distance correction, one reported eye pain in addition to reduced distance visual acuity and was prescribed a change in distance correction (the eye pain later resolved), and one had a floater and was referred to a retina specialist who detected a retinal hole not associated with the treatment.

DISCUSSION

In this randomized trial of 118 subjects aged 8 to <12 years with low myopia, high accommodative lag, and near esophoria, the PALs were found to slow the progression of myopia by 0.28 D (95% CI, 0.01–0.55 D) over 3 years. This result, while small in magnitude, is statistically significant and, combined with findings in other studies, suggests a true biological effect of slowed eye growth in children wearing PALs.[14]

The most prominent hypothesis for the development and progression of myopia is that children with insufficient accommodation when engaged in near work activities may experience retinal defocus that may lead to axial elongation and myopia.[21,22] Because PALs would be expected to provide clearer vision across a range of viewing distances, one would expect that they would reduce defocus and might lead to slower eye growth.

This hypothesis was in part the rationale for the original COMET and its exploratory analyses of accommodative lag,
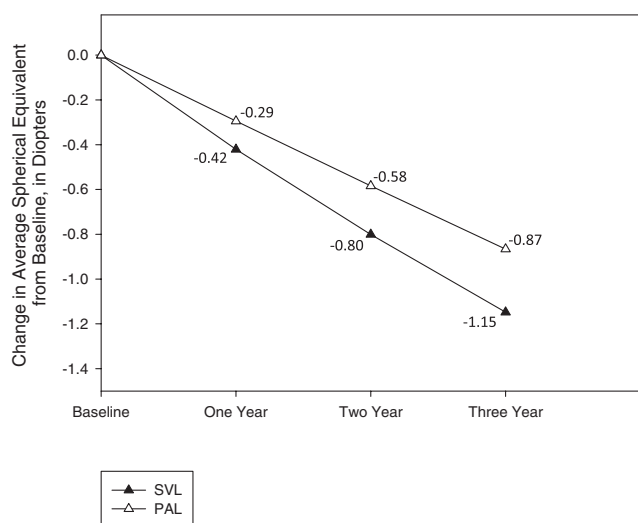
TABLE 3. Three-Year Change in Spherical Equivalent Refractive Error According to Baseline Characteristics

Baseline Characteristic	Change in Average Spherical Equivalent between Baseline and 3 Years (D)				Estimated Difference, Adjusted for Baseline Spherical Equivalent	*P* for Interaction
	SVL		PAL			
	n	Mean	*n*	Mean		
Age, y						0.92*
8 to <9	13	−1.39	8	−1.23	0.18	
9 to <10	17	−1.14	13	−1.11	0.11	
10 to <11	14	−1.19	15	−0.71	0.48	
11 to <12	14	−0.88	16	−0.64	0.26	
Sex						0.52
Male	31	−1.09	19	−0.95	0.20	
Female	27	−1.21	33	−0.82	0.39	
Race/Ethnicity						0.94
White	30	−1.10	26	−0.79	0.32	
Nonwhite	28	−1.19	26	−0.94	0.30	
Prior spectacle wear (SVLs)						0.48
Currently or in past	34	−1.10	31	−0.90	0.22	
Never	24	−1.22	21	−0.81	0.42	
Spherical equivalent, D						0.24/0.57†
−0.75 to −1.49	33	−1.20	25	−0.79	0.35	
−1.50 to −2.50	25	−1.08	27	−0.93	0.17	
Accommodative lag, D						0.23/0.55†
0.50 to 1.49	38	−1.12	28	−0.91	0.24	
1.50 or worse	20	−1.20	24	−0.81	0.41	
Near esophoria, PD						0.56
2 to 5	33	−1.13	30	−0.97	0.18	
6 to 10	21	−1.09	18	−0.66	0.46	
>10	4	−1.60	4	−1.01	0.63	
Parental history of myopia						0.43
Neither parent	5	−0.72	9	−0.83	−0.10	
One parent	10	−1.28	15	−0.73	0.57	
Both parents	20	−1.29	18	−0.99	0.30	

* Corresponds to the interaction between treatment and the continuous variable.

† The first *P* value tests for the interaction between treatment and age as a continuous variable; the second *P* value tests for the interaction between treatment and the two-level categorical variable.

which showed that the 3-year treatment benefit of PALs on progression of myopia was larger in subgroups of children with higher accommodative lag and near esophoria (0.64 D; 95% CI, 0.08–1.19 D; *n* = 76) and in children with higher accommodative lag and lower baseline myopia (0.48 D; 95% CI, 0.02–0.93 D; *n* = 104) than in the overall cohort (0.20 D; 95% CI,

TABLE 4. Spectacle Compliance*

Period	All Subjects		Baseline Spherical Equivalent −0.75 D to −1.49 D		Baseline Spherical Equivalent −1.50 D to −2.50 D	
	SVL (*n* = 58)	PAL (*n* = 58)	SVL (*n* = 33)	PAL (*n* = 30)	SVL (*n* = 25)	PAL (*n* = 28)
During school						
Mean compliance score	4.80	4.60	4.76	4.42	4.85	4.79
Excellent compliance, %†	90	72	88	60	92	86
After school						
Mean compliance score	4.61	4.37	4.49	4.10	4.76	4.65
Excellent compliance, %†	76	60	70	47	84	75
Weekends						
Mean compliance score	4.55	4.33	4.44	4.06	4.69	4.61
Excellent compliance, %†	71	60	63	50	80	71

* Compliance was assessed on a five-point Likert scale: always, 5; often, 4; sometimes, 3; rarely, 2; and never, 1.

† Excellent compliance indicates that for the specified period, spectacles were estimated at all visits to have been worn either always or often. Two subjects had no follow-up visits (one SVL, one PAL).

0.06–0.33 D; $n = 469$).[13,14] Analysis of data from a smaller subgroup of 35 COMET subjects meeting the COMET2 eligibility criteria for age, baseline myopia, accommodative lag, and near esophoria showed a 0.71-D (95% CI, 0.22–1.20 D) 3-year treatment effect of PALs (COMET, unpublished data, 1997–2001). The treatment effect found in COMET2 is not significantly different from that found in each of these three subgroup analyses from the original COMET study[14] ($P = 0.25$, 0.46, and 0.12 for Cochrane's Q tests for heterogeneity comparing COMET2 results versus the results in each COMET subgroup, respectively).

Two other recent clinical trials of spectacle lenses for myopia control also reported statistically significant treatment effects in subgroups of children with high accommodative lag.[15,16] Hasebe et al.,[15] in a study of myopic Japanese children randomized to PALs or SVLs for 18 months, reported that a subgroup of 36 children with accommodative lag of at least 1.80 D had an 18-month treatment effect of 0.61 D (95% CI, 0.30–0.92 D), with myopia in the PAL group progressing by 0.87 D and in the SVL group by 1.48 D. The use of standard bifocals versus SVLs in a study by Cheng et al.[16] of Chinese Canadian children with high rates of previous myopic progression significantly reduced progression over 2 years (by 0.88 D; 95% CI, 0.45–1.31 D) in a subgroup of 43 children with lags of accommodation of at least 1.00 D (progression in the standard bifocal group was 0.88 D and in the SVL group was 1.76 D). For comparison, in the present study the treatment effect of PALs was 0.17 D (95% CI, 0.02–0.32 D) at 18 months and 0.23 D (95% CI, 0.02–0.45 D) at 2 years. The treatment effect found in COMET2 is significantly smaller than those found in the subgroup analyses in Cheng et al.[16] and Hasebe et al.[15] at the same time points ($P = 0.01$ for Cochrane's Q tests for both comparisons).

Methodological differences among all the studies may have affected the results. First, the lens type used was different in each study: the Ellipse in the present study, the Varilux Comfort in COMET (Essilor of America),[13] the Sola MCLens (Sola International, San Diego, CA) in Hasebe et al.,[15] and Essilor Executive bifocals (Essilor of America) in Cheng et al.[16] While many details of the lens designs are proprietary, it is known that the Varilux Comfort lens has a wider distance and intermediate zone and more induced astigmatism than does the Ellipse lens.[23] In these lenses, the widths of the near zones vary greatly with fitting height; the Comfort's near zone is narrower than the Ellipse's for a fitting height of 14 mm, which is the minimum recommended for the Ellipse.[23] Also, the present study and the original COMET study[13] used a +2.00-D near addition, whereas Cheng et al.[16] and Hasebe et al.[15] used a +1.50-D addition. These lens variations may have produced differences in peripheral aberrations and in the power of the addition used for near work, both of which could affect progression.[24,25] Second, high accommodative lag was defined as 1.00 D or more in the current study and in Cheng et al.,[16] greater than 0.43 D in the original COMET study,[13] and 1.80 D or more in Hasebe et al.[15] Third, the other studies had higher rates of myopia progression, most likely because they included children who were younger[15] and/or Asian,[15,16] factors that are associated with increased progression.[26,27] Also, Cheng et al.[16] was limited to children who had previously demonstrated fast progression. It might be expected that treatments would work better when myopia is still progressing rather than when it is close to reaching a plateau.

We found no statistically significant associations between baseline factors and treatment effect; however, our study was underpowered to detect these types of associations unless they were very strong. Although not statistically significant, there may be some evidence in our data that children with lower myopia might benefit more from PALs. This finding is consistent with those in the COMET which showed greater treatment benefit among subjects with baseline myopia of −1.25 to −2.24 D compared with those with −2.25 to −4.50 D, both in the overall cohort and in the subgroup of subjects with higher accommodative lag.[14] In addition, although COMET2 enrolled only subjects with larger lags of accommodation, there is a suggestion that, within this group, the children with higher lag (≥ 1.50 D) had an increased treatment effect, consistent with the COMET study's finding that higher lag was associated with increased treatment effect across a wider range of lags.

Strengths of the present study include the use of a double-masked design with random assignment to treatment groups and training and certification of study investigators. In addition, missing data did not appear to influence the results. Another strength is an adequately powered sample size and a high rate of follow-up overall, although a limitation is that there was higher loss to follow-up in the PAL ($n = 7$) group than in the SVL ($n = 1$) group. Another limitation is that compliance with lens wear was reported to be worse in the PAL group, a factor that could have diluted the treatment effect of the PALs. However, this difference in compliance did not appear to affect progression. In the present study, as in other studies of PALs or bifocals for control of myopia,[15,16] we prescribed a consistent near addition power for all children, +2.00 D. It is possible that if this power were customized for individual children based on the level of myopia, near accommodative response, and phoria, then the treatment benefit of the lenses might be enhanced. In addition, although we collected estimates of compliance with spectacle wear, we do not have data on what part of the lens the children were actually looking through during near work, and so it is possible that the full benefit of the near addition was not realized.

The treatment effect in this study increased over the 3 years rather than maintaining the same level as found in the first year, the latter of which is a more typical finding with various lens treatments.[17] The pattern in the present study is similar to that in the subgroup of COMET subjects with higher lag,[13,14] but different from that in the overall COMET cohort.[13] Given the current result, a longer trial might find a greater treatment effect of PALs.

The consistent presence of an effect of PALs or bifocals in different studies suggests that the visual environment plays a definite, but perhaps modest, role in myopia progression, although it is not completely clear what in the environment is being manipulated with the lenses. COMET2 was designed to examine the effects of high accommodative lag and the resultant central hyperopic defocus. Recent work[28] indicates that an important additional mechanism may be peripheral hyperopic defocus, which was reduced in the lower visual field only with the PALs, in which case the effect might be stronger if defocus was reduced in the entire visual periphery. However, a recent study evaluating three different spectacle lens designs for reducing peripheral hyperopic defocus versus SVLs found no statistically significant differences in the 1-year progression of myopia.[29] These results suggest that there is much more to be learned about the mechanisms of eye growth. It is hoped that when the mechanisms are better understood, more powerful, clinically useful lens treatments for slowing the progression of myopia may be developed.

In conclusion, the PALs used in this study were found to have a statistically, but not clinically significant effect on slowing myopia progression in children with high accommodative lag and near esophoria.

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APPENDIX

The Correction of Myopia Evaluation Trial 2 (COMET2) Study Group

WRITING COMMITTEE: *Lead Authors*: Jane Gwiazda and Danielle L. Chandler. *Additional Authors*: Susan A. Cotter, Donald F. Everett, Leslie Hyman, Brett M. Kaminski, Marjean T. Kulp, Don W. Lyon, Ruth E. Manny, Wendy L. Marsh-Tootle, Noelle S. Matta, B. Michele Melia, Thomas T. Norton, Mitchell M. Scheiman, David I. Silbert, and Erik M. Weissberg.

Clinical Sites that Participated in the Protocol

Sites are listed in order by number of subjects enrolled in the study. Personnel are coded according their roles: I, Investigator; C, Coordinator; O, Optician; CC, Consulting Clinician.

University of Alabama at Birmingham School of Optometry, Birmingham, Alabama (25): Wendy L. Marsh-Tootle (I), Michelle L. Anderson (I), Marcela Frazier (I), Kristine T. Hopkins (I), Katherine K. Weise (I), Cathy Baldwin (C), and Michael Hill (I).

University of Houston College of Optometry, Houston, Texas (19): Ruth E. Manny (I), Heather A. Anderson (I), Soyung A. Kim (I), Karen D. Fern (CC), Gabynely Solis (C), and Andy Ketcham (O).

New England College of Optometry, Boston, Massachusetts (16): Erik M. Weissberg (I), Elise N. Harb (I), Sally Bittinger (C), and Robert Owens (C).

Family Eye Group, Lancaster, Pennsylvania (15): David I. Silbert (I), Don D. Blackburn (I), Troy J. Hosey (I), Eric L. Singman (I), Noelle S. Matta (C), Kourosh A. Dastgheib (CC), and Michael R. Pavlica (CC).

Indiana University School of Optometry, *Indianapolis, Indiana* (15): Don. W. Lyon (I), Kathryn Gray (I), Kristy Dunlap (C), Sara Long (C), Julia Wilhite (C), and Danielle F. Warren (CC).

Pennsylvania College of Optometry, Philadelphia, Pennsylvania (13): Mitchell M. Scheiman (I), Karen Pollack (C), and Brandy J. Scombordi (CC).

The Ohio State University, Columbus, Ohio (9): Marjean T. Kulp (I), Mark A. Bullimore (I), Jeffrey J. Walline (I), Nancy Stevens (C), Gilbert E. Pierce (CC), and Freda Dallas (O).

Southern California College of Optometry, Fullerton, California (6): Susan A. Cotter (I), Carmen N. Barnhardt (I), Kristine Huang (I), Monique M. Nguyen (I), Catherine Heyman (C), Sue M. Parker (C), and Michael W. Rouse (CC).

PEDIG Coordinating Center

Raymond T. Kraker, Roy W. Beck, Danielle L. Chandler, Elise R. Diamond, Quayleen Donahue, Heidi Gillespie, Brett M. Kaminski, Stephanie V. Lee, B. Michele Melia, and Pamela S. Moke.