Supplement

eTable 1. Summary of Analysis Approaches for the 16-Week Primary Outcome

Analysis Approach [a]	Adjusted Treatment Group Difference (Line) [b] (Patching – Binocular Group)	Upper Limit of 95% CI (Line) [c]
Primary Analysis: Modified intent-to-treat analysis limited to participants with a 16-week exam completed within the analysis window (14 to <20 weeks after randomization). No imputation for missing data	0.31	0.53
Include multiple imputation for participants with a missing 16-week exam (n=15) or a 16-week exam outside the analysis window (n=7) based on baseline age and all available amblyopic-eye visual acuities from visits prior to 16 weeks	0.31	0.54
Include 16-week exams completed outside the analysis window (14 to 28 weeks after randomization, n=7)	0.33	0.56
Exclude 16-week exams completed outside the 16 ± 1 week protocol window (n=35)	0.30	0.53
Exclude 16-week exams from participants later found to be ineligible (n=7)	0.30	0.53
Exclude participants who received alternative treatment for ≥ 1 week during follow-up (n=4)	0.33	0.55

[a] For analyses other than the primary analysis, the modification to the primary analysis is specified.

[b] Treatment group difference (Patching – Binocular Group) in mean change in amblyopic-eye visual acuity from baseline to 16 weeks, adjusted for baseline covariates of age and amblyopic-eye visual acuity.

[c] Upper limit of the 1-sided 95% confidence interval computed on the treatment group difference (Patching – Binocular Group), adjusted for baseline covariates of age and amblyopic-eye visual acuity. The upper-limit of the 1-sided 95% confidence interval for all of the analysis approaches exceeded the pre-specified non-inferiority margin of 0.5 line, consistent with the primary analysis result.

eTable 2. Cross Tabulation of Baseline versus 16-Week Amblyopic-Eye Visual Acuity by Treatment Group

Binocular Group (N=177)	Distribution of Amblyopic-eye Visual Acuity at Baseline															
	20/40 (68-72 Letters)		20/50 (63-67 Letters)		20/63 (58-62 Letters)		20/80 (53-57 Letters)		20/100 (48-52 Letters)		20/125 (43-47 Letters)		20/160 (38-42 Letters)		20/200 (33-37 Letters)	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Distribution of Amblyopic-eye Visual Acuity at 16 Weeks																
20/200 (33-37 Letters)	0	0	0	0	0	0	0	0	1	6	0	0	0	0	1	20
20/160 (38-42 Letters)	0	0	0	0	0	0	0	0	0	0	0	0	1	17	1	20
20/125 (43-47 Letters)	0	0	0	0	0	0	1	3	2	13	1	13	4	67	2	40
20/100 (48-52 Letters)	0	0	1	2	0	0	2	7	4	25	3	38	1	17	1	20
20/80 (53-57 Letters)	0	0	1	2	3	9	7	24	5	31	2	25	0	0	0	0
20/63 (58-62 Letters)	1	4	7	13	6	19	7	24	3	19	1	13	0	0	0	0
20/50 (63-67 Letters)	2	8	13	24	8	25	6	21	1	6	0	0	0	0	0	0
20/40 (68-72 Letters)	8	31	12	22	8	25	4	14	0	0	0	0	0	0	0	0
20/32 (73-77 Letters)	10	38	16	29	6	19	1	3	0	0	0	0	0	0	0	0
20/25 (78-82 Letters)	3	12	3	5	0	0	1	3	0	0	1	13	0	0	0	0
20/20 (83-87 Letters)	1	4	2	4	0	0	0	0	0	0	0	0	0	0	0	0
20/16 (88-92 Letters)	1	4	0	0	1	3	0	0	0	0	0	0	0	0	0	0

eTable 2. (continued)

Patching Group (N=186) [a]	Distribution of Amblyopic-Eye Visual Acuity at Baseline [b]															
	20/40 (68-72 Letters)		20/50 (63-67 Letters)		20/63 (58-62 Letters)		20/80 (53-57 Letters)		20/100 (48-52 Letters)		20/125 (43-47 Letters)		20/160 (38-42 Letters)		20/200 (33-37 Letters)	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Distribution of Amblyopic-eye Visual Acuity at 16 Weeks																
20/200 (33-37 Letters)	0	0	0	0	0	0	0	0	0	0	0	0	1	14	0	0
20/160 (38-42 Letters)	0	0	0	0	0	0	0	0	0	0	0	0	2	29	1	33
20/125 (43-47 Letters)	0	0	0	0	0	0	0	0	0	0	1	25	1	14	0	0
20/100 (48-52 Letters)	0	0	0	0	0	0	1	4	3	25	0	0	2	29	1	33
20/80 (53-57 Letters)	0	0	0	0	2	4	7	29	3	25	3	75	1	14	1	33
20/63 (58-62 Letters)	1	2	2	4	8	18	8	33	3	25	0	0	0	0	0	0
20/50 (63-67 Letters)	5	12	14	28	14	31	3	13	2	17	0	0	0	0	0	0
20/40 (68-72 Letters)	7	17	15	30	10	22	4	17	1	8	0	0	0	0	0	0
20/32 (73-77 Letters)	9	22	8	16	9	20	1	4	0	0	0	0	0	0	0	0
20/25 (78-82 Letters)	14	34	6	12	2	4	0	0	0	0	0	0	0	0	0	0
20/20 (83-87 Letters)	5	12	5	10	0	0	0	0	0	0	0	0	0	0	0	0
20/16 (88-92 Letters)	0	0	0	0	0	0	0	0	0	0	0	0	1	14	0	0

[a] The distribution of visual acuity level at baseline and the 16-week visit was only tabulated for participants who completed the 16-week visit within the pre-defined analysis window (14 to <20 weeks after randomization).

[b] Percentages reflect the distribution of 16-week amblyopic-eye visual acuity scores within each level of visual acuity at baseline by treatment group.

eTable 3. Mean Change (LogMAR Line) in Amblyopic-Eye Visual Acuity from Baseline to 16 Weeks by Treatment Group according to Subgroups of Baseline Factors [a]

	Binocular Group (N=177)				Patching Group (N=186)				
	Baseline VA (logMAR)		16-Week VA Change (Line)		Baseline VA (logMAR)		16-Week VA Change (Line)		P-value (2-sided) [c]
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
Overall	**177**	**0.52 (0.17)**	**177**	**1.1 (1.5)**	**186**	**0.48 (0.16)**	**186**	**1.3 (1.3)**	
Gender									
Female	89	0.53 (0.19)	89	1.2 (1.5)	83	0.50 (0.17)	83	1.4 (1.2)	0.83
Male	88	0.50 (0.16)	88	1.0 (1.4)	103	0.47 (0.16)	103	1.3 (1.3)	
Race/Ethnicity [b]									
White/Non-Hispanic	122	0.51 (0.17)	122	1.0 (1.5)	139	0.49 (0.17)	139	1.3 (1.2)	0.54
Non-White or Hispanic	54	0.52 (0.17)	54	1.2 (1.5)	44	0.48 (0.14)	44	1.3 (1.4)	
Baseline Amblyopic-Eye Visual Acuity (Snellen)									
20/80 to 20/200	64	0.70 (0.13)	64	1.1 (1.6)	50	0.70 (0.13)	50	1.3 (1.3)	
20/63	32	0.49 (0.03)	32	1.3 (1.6)	45	0.50 (0.03)	45	1.4 (1.3)	0.99
20/50	55	0.41 (0.02)	55	1.0 (1.3)	50	0.40 (0.02)	50	1.3 (1.3)	
20/40	26	0.31 (0.03)	26	0.8 (1.2)	41	0.31 (0.02)	41	1.2 (1.2)	
Baseline Stereoacuity									
Nil	68	0.58 (0.18)	68	0.7 (1.3)	55	0.54 (0.18)	55	1.1 (1.1)	0.33
Better than Nil	109	0.47 (0.15)	109	1.3 (1.5)	131	0.46 (0.15)	131	1.4 (1.3)	
Presence of a Near Heterotropia at Baseline									
No	122	0.52 (0.17)	122	1.1 (1.3)	117	0.49 (0.17)	117	1.3 (1.2)	0.23
Yes	55	0.51 (0.17)	55	0.9 (1.7)	69	0.48 (0.15)	69	1.4 (1.3)	
Age at Baseline (Years)									
5 to <7	39	0.53 (0.19)	39	1.9 (1.8)	49	0.45 (0.13)	49	2.0 (1.4)	0.80
7 to <13	138	0.51 (0.17)	138	0.8 (1.2)	137	0.50 (0.17)	137	1.1 (1.1)	

		Binocular Group (N=177)				Patching Group (N=186)				
		Baseline VA (logMAR)		16-Week VA Change (Line)		Baseline VA (logMAR)		16-Week VA Change (Line)		P-value (2-sided) [c]
		N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
Prior Amblyopia Treatment										
No		41	0.51 (0.15)	41	1.9 (1.5)	39	0.51 (0.17)	39	2.2 (1.3)	0.87
Yes		136	0.52 (0.18)	136	0.8 (1.4)	147	0.48 (0.16)	147	1.1 (1.2)	
Prior Treatment within Age at Baseline (Years)										
5 to <7	No Prior Treatment	19	0.50 (0.16)	19	2.5 (1.5)	19	0.46 (0.13)	19	2.8 (0.8)	
	Prior Treatment	20	0.56 (0.21)	20	1.4 (1.9)	30	0.44 (0.13)	30	1.4 (1.4)	
7 to <13	No Prior Treatment	22	0.52 (0.14)	22	1.3 (1.2)	20	0.56 (0.19)	20	1.5 (1.3)	
	Prior Treatment	116	0.51 (0.17)	116	0.7 (1.2)	117	0.49 (0.17)	117	1.0 (1.1)	

VA = visual acuity, logMAR = logarithm of the minimum angle of resolution; SD = standard deviation

[a] Analyses were limited to participants who completed the 16-week visit within the pre-defined analysis window (14 to <20 weeks after randomization).

[b] Four participants (1 binocular group, 3 patching group) were excluded due to unknown/not reported race/ethnicity classification.

[c] P-value based on the addition of an interaction term between treatment group and each factor to the primary analysis model. Baseline factors of age and amblyopic-eye visual acuity were treated as continuous variables in the regression models. All of the subgroup factors were pre-specified except for baseline stereoacuity.

eTable 4. Randot Stereoacuity at Baseline and 16-Week Primary Outcome by Treatment Group

All Participants	Baseline				16-Week Visit			
	Binocular Group (N=190)		Patching Group (N=195)		Binocular Group (N=182)		Patching Group (N=188)	
	N	%	N	%	N	%	N	%
Randot Stereoacuity (Seconds of arc) [a]								
Missing/Not Done	0	0	0	0	1	<1	0	0
Nil	69	36	57	29	62	34	50	27
2000	28	15	37	19	32	18	32	17
800	18	9	26	13	19	10	28	15
400	17	9	19	10	14	8	17	9
200	23	12	18	9	15	8	27	14
100	23	12	23	12	17	9	19	10
60	10	5	9	5	10	5	11	6
40	2	1	6	3	12	7	4	2
Median	2000		800		2000		800	

Participants without Strabismus	Baseline				16-Week Visit			
	Binocular Group (N=107)		Patching Group (N=92)		Binocular Group (N=105)		Patching Group (N=90)	
	N	%	N	%	N	%	N	%
Randot Stereoacuity (Seconds of arc) [a]								
Missing/Not Done	0	0	0	0	1	<1	0	0
Nil	29	27	13	14	23	22	13	14
2000	14	13	17	18	14	13	12	13
800	8	7	11	12	12	11	14	16
400	10	9	10	11	10	10	10	11
200	18	17	12	13	12	11	17	19
100	19	18	17	18	14	13	15	17
60	7	7	7	8	9	9	6	7
40	2	2	5	5	10	10	3	3
Median	400		400		400		400	

[a] Results of the Randot Butterfly stereoacuity test were analyzed as 2000 seconds of arc (if correct response). Nil was defined as an incorrect response on the butterfly (n=67 and n=56 in binocular and patching groups at baseline, respectively; n=61 and n=50 in binocular and patching groups at 16 weeks, respectively), or on the 800 seconds of arc level of the Randot Preschool stereoacuity test if the butterfly was not attempted (n=2 and n=1 in binocular treatment and patching groups at baseline, respectively; n=1 and n=0 in the binocular and patching groups at 16 weeks, respectively).

eTable 4. (continued)

	All Participants [a]				Participants without Strabismus [a]			
	Binocular Group (N=181)		Patching Group (N=188)		Binocular Group (N=104)		Patching Group (N=90)	
	N	%	N	%	N	%	N	%
Change in Randot Stereoacuity from Baseline to 16 Weeks (Levels)[b]								
≥ 2 Levels Worse	19	11	24	13	12	12	14	16
Within 1 Level	130	72	122	65	67	64	58	64
≥ 2 Levels Better	32	18	42	22	25	24	18	20

[a] Excludes participants with 'Missing/Not Done' stereoacuity responses at either baseline and/or the 16-week primary outcome visit.

[b] P = 0.66 and P = 0.19 for the overall cohort and for participants without strabismus, respectively, from Wilcoxon rank-sum test for difference between treatment groups in distribution of levels of change from baseline to 16 weeks.

eTable 5. Median Change in Stereoacuity (Log Seconds of Arc) from Baseline to 16 Weeks by Treatment Group according to Subgroups of Baseline Factors [a]

		Binocular Group (N=177)				Patching Group (N=186)			
		Baseline Stereoacuity		Stereoacuity Change at 16 Weeks		Baseline Stereoacuity		Stereoacuity Change at 16 Weeks	
		N	Median[b]	N	Median[b]	N	Median[b]	N	Median[b]
Overall		**177**	**3.30**	**176**	**0**	**186**	**2.90**	**186**	**0**
Gender									
Female		89	3.30	89	0	83	2.90	83	0
Male		88	3.30	87	0	103	3.30	103	0
Race/Ethnicity[c]									
White/Non-Hispanic		122	3.30	122	0	139	3.30	139	0
Non-White or Hispanic		54	3.30	53	0	44	2.90	44	0
Baseline Amblyopic-Eye Visual Acuity (Snellen)									
20/80 to 20/200		64	3.60	63	0	50	3.30	50	0
20/63		32	3.30	32	0	45	2.90	45	0
20/50		55	2.90	55	0	50	2.90	50	0
20/40		26	2.30	26	0.11	41	2.60	41	0
Baseline Stereoacuity									
Nil		68	3.60	67	0	55	3.60	55	0
Better than Nil		109	2.60	109	0	131	2.60	131	0
Presence of a Near Heterotropia at Baseline									
No		122	2.90	121	0	117	2.60	117	0
Yes		55	3.60	55	0	69	3.30	69	0
Age at Baseline (Years)									
5 to <7		39	3.30	38	0	49	2.90	49	0
7 to <13		138	3.30	138	0	137	3.30	137	0
Prior Amblyopia Treatment									
No		41	2.30	41	0.22	39	2.30	39	0
Yes		136	3.30	135	0	147	3.30	147	0
Prior Treatment within Age at Baseline (Years)									
5 to <7	No Prior Treatment	19	2.30	19	0.22	19	2.30	19	0
	Prior Treatment	20	3.30	19	0	30	3.30	30	0
7 to <13	No Prior Treatment	22	2.30	22	0.20	20	2.45	20	0
	Prior Treatment	116	3.30	116	0	117	3.30	117	0

[a] Analyses were limited to participants who completed the 16-week visit within the pre-defined analysis window (14 to <20 weeks after randomization).

[b] Baseline stereoacuity was measured as log seconds of arc as follows: 1.60 (40'), 1.78 (60'), 2.00 (100'), 2.30 (200'), 2.60 (400'), 2.90 (800'), 3.30 (2000') and 3.60 (nil). Change in stereoacuity was calculated as the difference in the log seconds of arc (baseline - 16 weeks).

[c] Four participants (1 binocular group, 3 patching group) were excluded due to unknown/not reported race/ethnicity classification.

eTable 6. Change in Mean Fellow-Eye Visual Acuity from Baseline to 16 Weeks by Treatment Group

	Binocular Group (N=182)		Patching Group (N=188)	
	N	**%**	**N**	**%**
Visual Acuity Change				
2 lines (10-14 letters) better	6	3	2	1
1 line (5-9 letters) better	36	20	30	16
0 line (within 4 letters)	128	70	133	71
1 line (5-9 letters) worse	11	6	22	12
2 lines (10-14 letters) worse	1	<1	1	<1
Mean (SD) Lines	0.30 (0.74)		0.15 (0.71)	

SD = standard deviation

eTable 7. Distribution of Diplopia Frequency at 16 Weeks and Maximum Frequency of Diplopia across Follow-up according to Parent / Participant Responses by Treatment Group

	16-Week Visit [b]								Maximum Frequency of Reported Diplopia during Follow-up							
	Parent[a]				Participant				Parent[a]				Participant			
	Binocular Group (N=182)		Patching Group (N=187)		Binocular Group (N=182)		Patching Group (N=188)		Binocular Group (N=182)		Patching Group (N=188)		Binocular Group (N=182)		Patching Group (N=188)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Frequency of Diplopia																
Never	176	97	185	99	166	91	181	96	172	95	182	97	153	84	167	89
Less than once a week	5	3	0	0	5	3	3	2	6	3	4	2	6	3	10	5
Once a week	1	<1	2	1	5	3	3	2	2	1	1	<1	10	5	4	2
Once a day	0	0	0	0	2	1	1	<1	2	1	0	0	8	4	5	3
Up to 10 times a day	0	0	0	0	3	2	0	0	0	0	1	<1	3	2	2	1
>10 times a day	0	0	0	0	0	0	0	0	0	0	0	0	1	<1	0	0
All the time	0	0	0	0	1	<1	0	0	0	0	0	0	1	<1	0	0

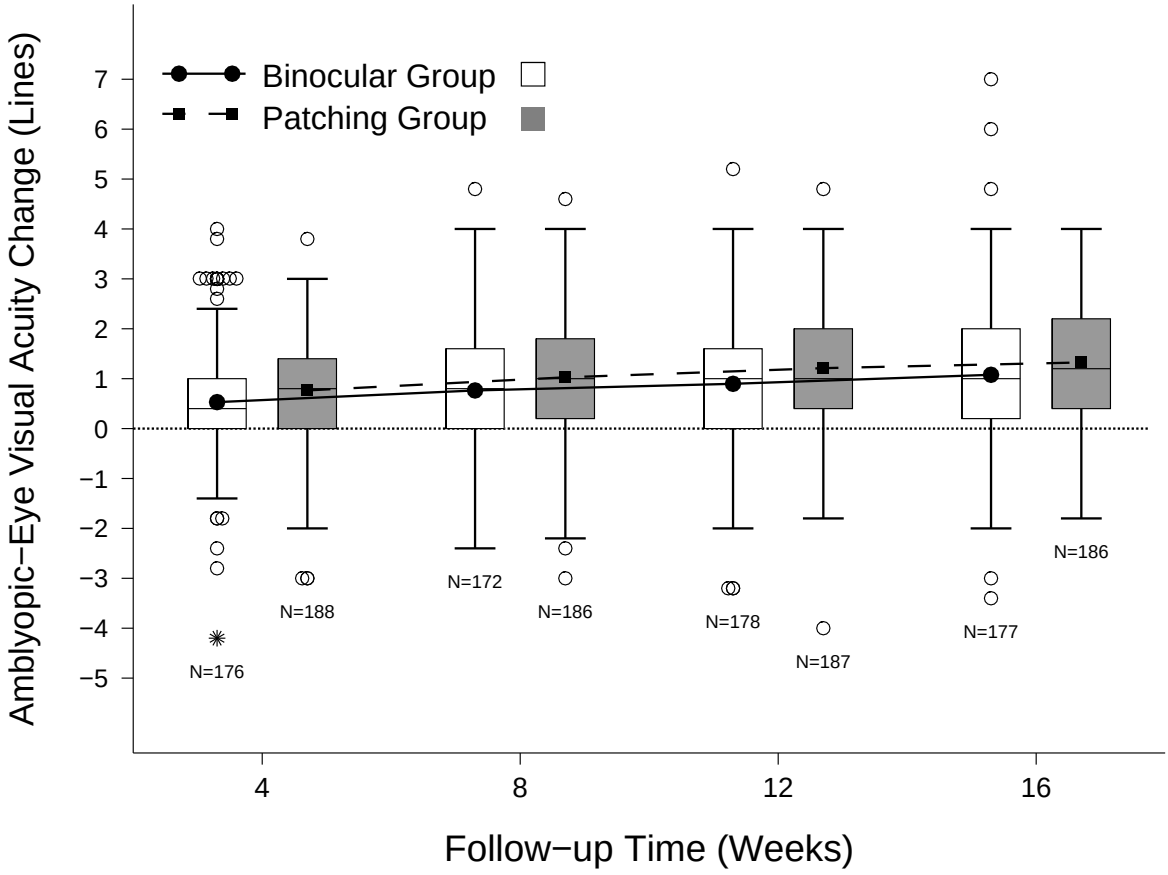
[a] The parental assessment may be missing if the parent was not available at the 16-week visit

[b] P=0.17 for the parental responses and P=0.05 for the participant responses on the diplopia assessment at the 16-week visit based on a Fisher exact test for the treatment group comparison of the presence (yes/no) of diplopia.

[b] P=0.48 for the parental responses and P=0.02 for the participant responses on the diplopia assessment at the 16-week visit based on a Cochran-Armitage trend test (exact) for the treatment group comparison of diplopia frequency.

[b] Two participants (1 per group) had monocular diplopia at the 16-week visit.

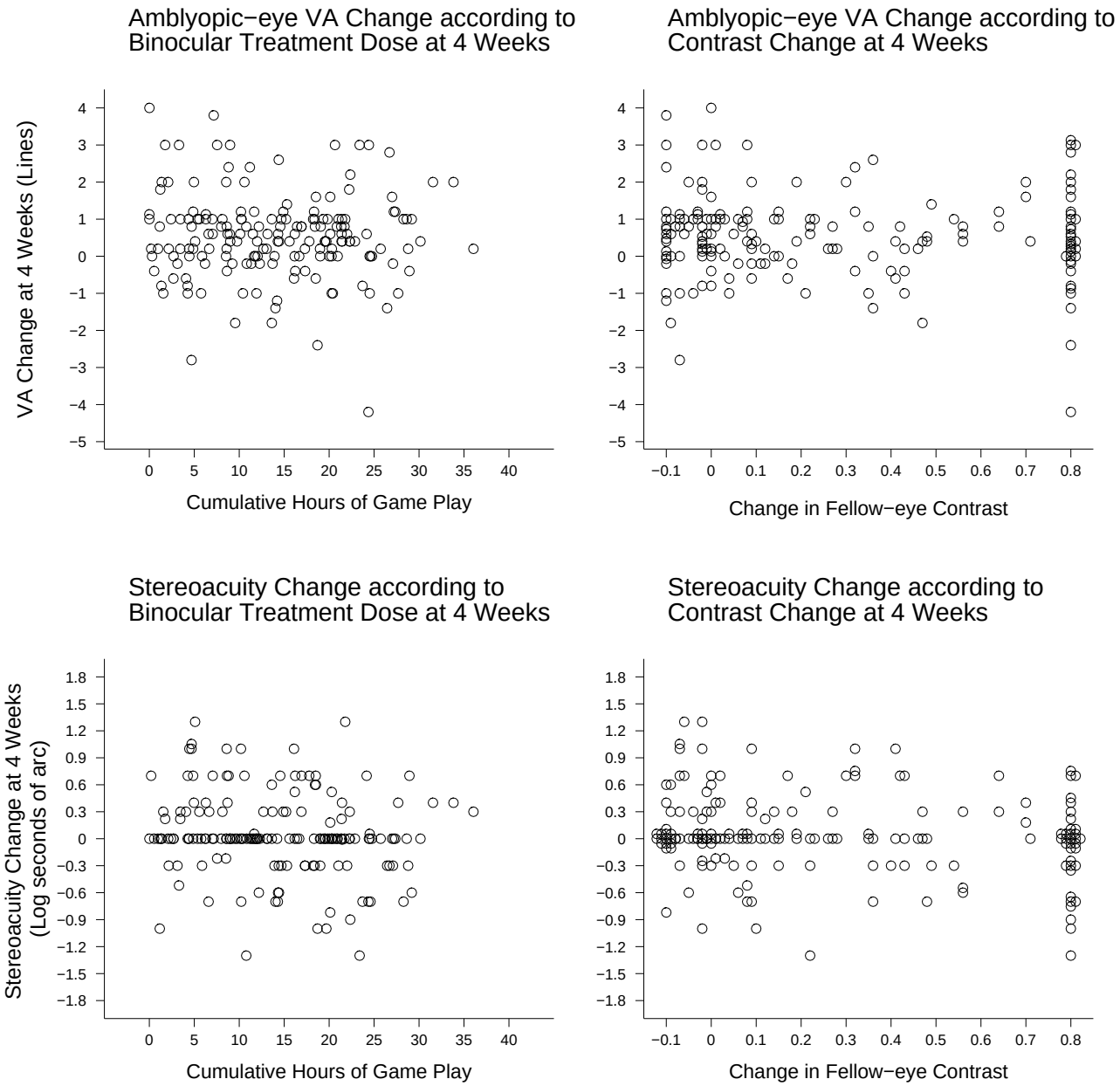
eFigure 1. Change in Amblyopic-Eye Visual Acuity from Baseline across Follow-up Visits



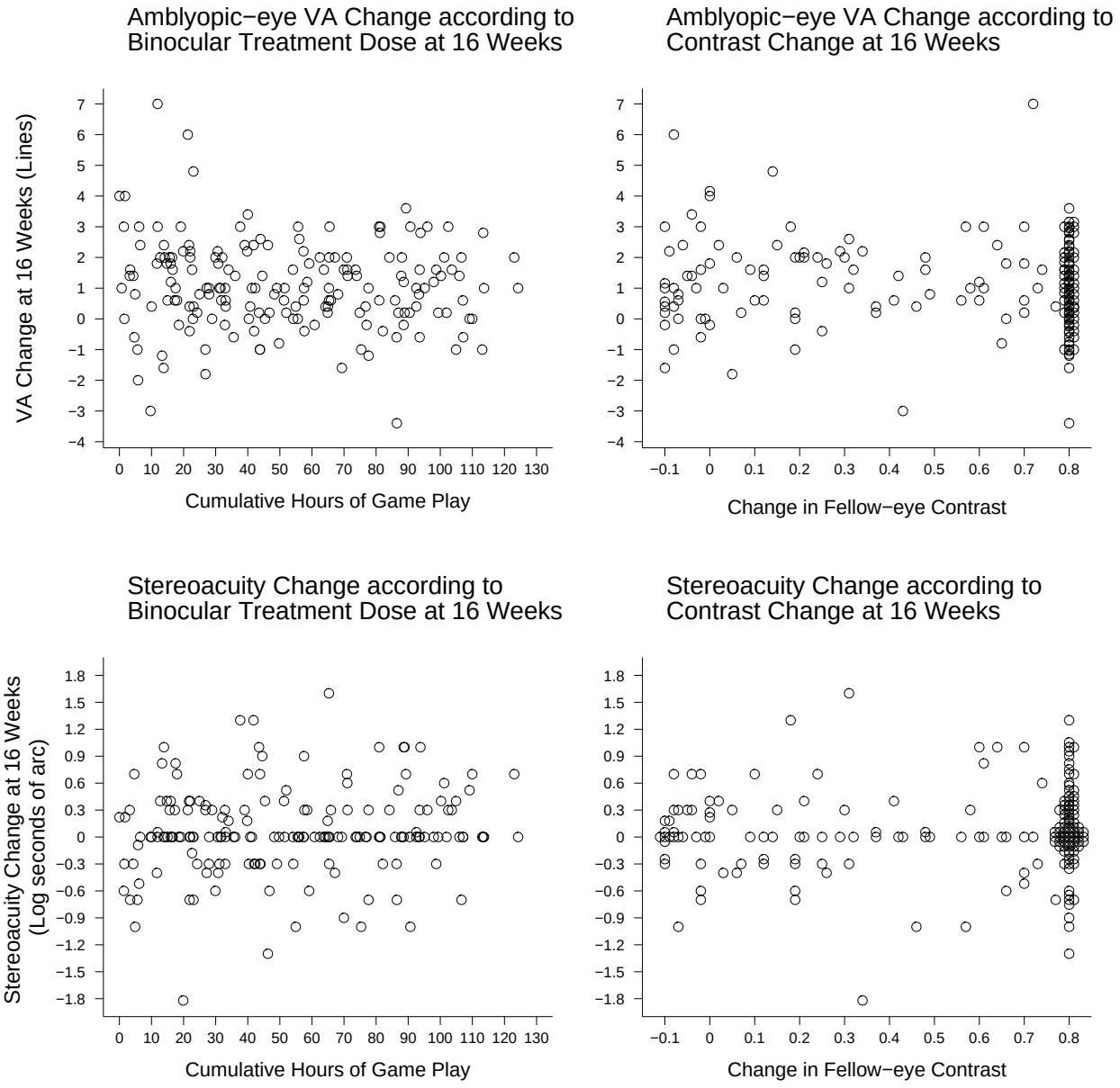
Mean Treatment Group Improvement in Amblyopic−Eye Visual Acuity at Follow−up Visits

Treatment Group:	4−Week Visit	8−Week Visit	12−Week Visit	16−Week Visit
Binocular Group	0.5 Line	0.8 Line	0.9 Line	1.1 Lines
Patching Group	0.8 Line	1.0 Lines	1.2 Lines	1.3 Lines

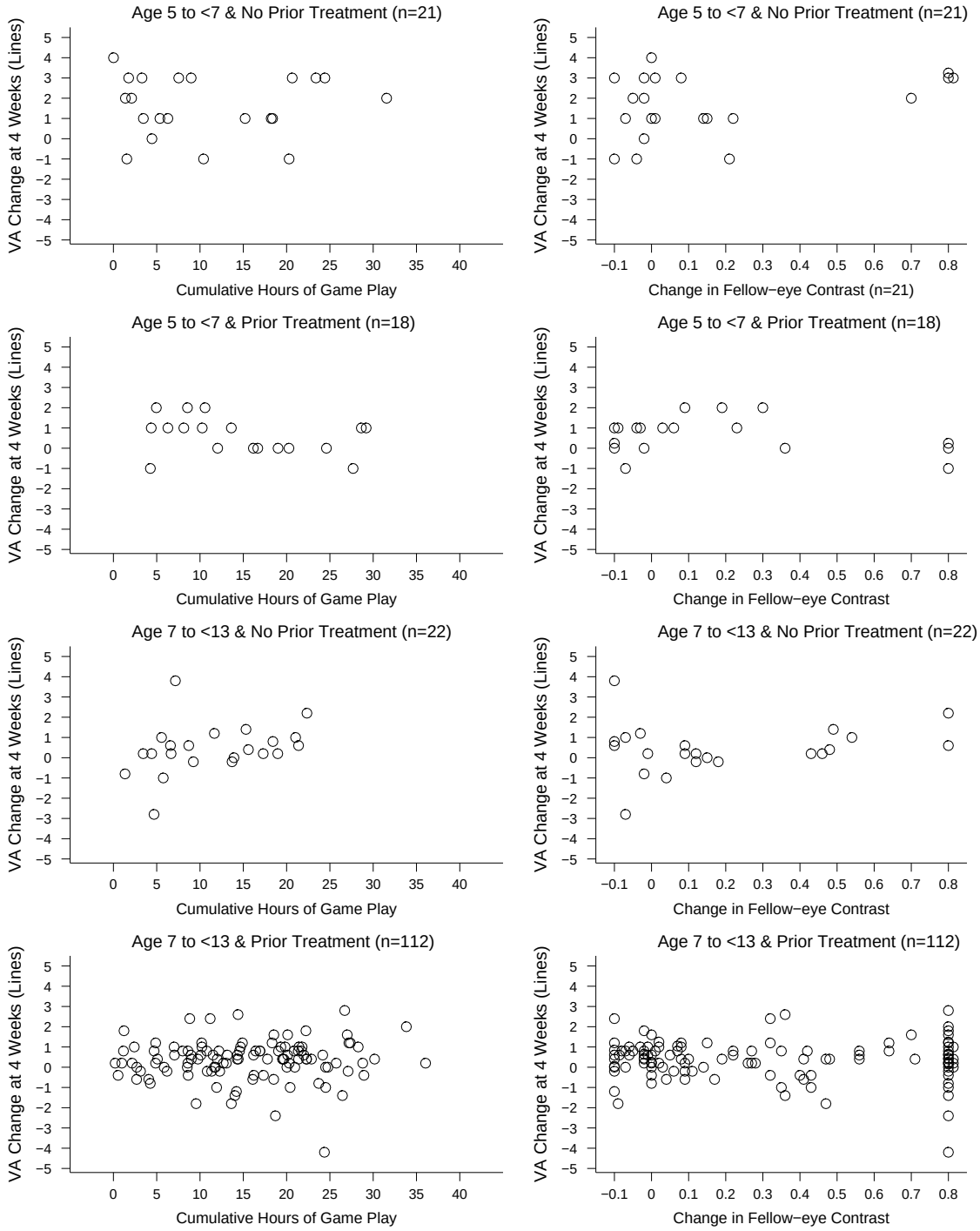
eFigure 2. Relationship between Change in 4-Week Outcomes and Objective Compliance Measures in the Binocular Group



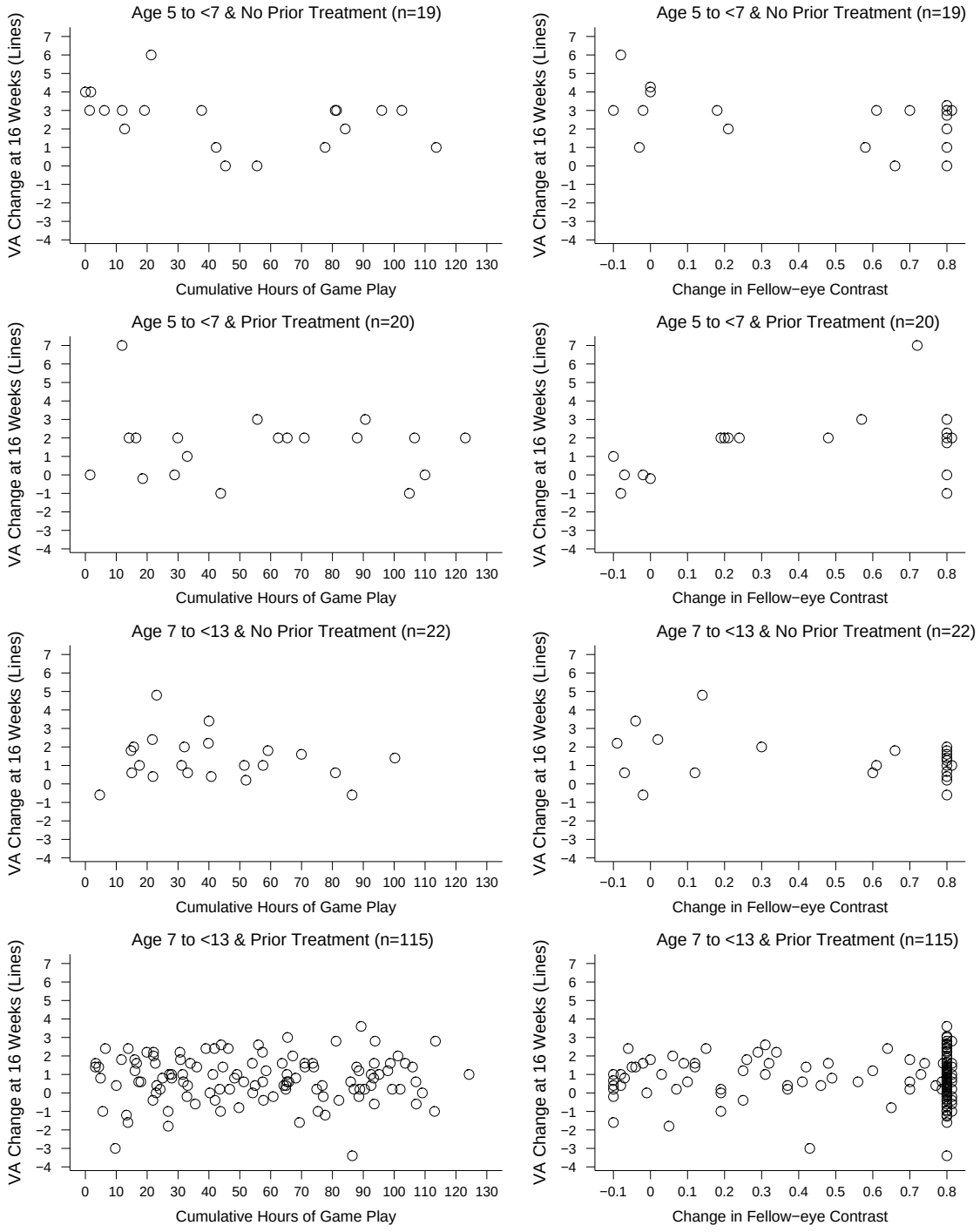
eFigure 3. Relationship between Change in 16-Week Outcomes and Objective Compliance Measures in the Binocular Group



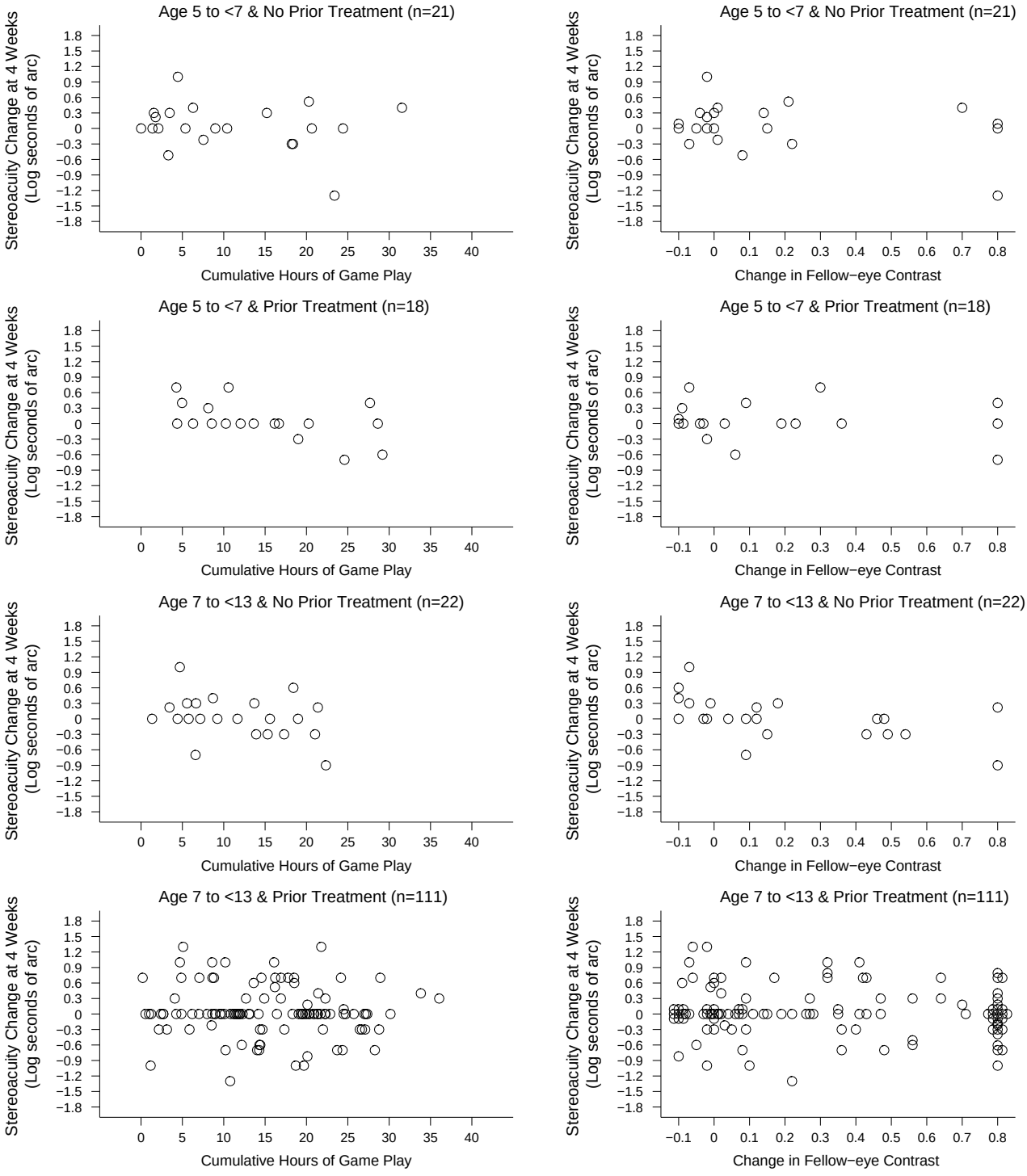
eFigure 4. Relationship between Change in Amblyopic-Eye VA from Baseline to 4 Weeks and Objective Compliance Measures in the Binocular Group at 4 Weeks according to Baseline Subgroups of Age with and without Prior Amblyopia Treatment



eFigure 5. Relationship between Change in Amblyopic-Eye VA from Baseline to 16 Weeks and Objective Compliance Measures in the Binocular Group at 16 Weeks according to Baseline Subgroups of Age with and without Prior Amblyopia Treatment



eFigure 6. Relationship between Change in Stereoacuity from Baseline to 4 Weeks and Objective Compliance Measures in the Binocular Group at 4 Weeks according to Baseline Subgroups of Age with and without Prior Amblyopia Treatment



eFigure 7. Relationship between Change in Stereoacuity from Baseline to 16 Weeks and Objective Compliance Measures in the Binocular Group at 16 Weeks according to Baseline Subgroups of Age with and without Prior Amblyopia Treatment