Supplementary Online Content

Gao TY, Guo CX, Babu RJ, et al; the BRAVO Study Team. Effectiveness of a binocular video game vs placebo video game for improving visual functions in older children, teenagers, and adults with amblyopia: a randomized clinical trial. *JAMA Ophthalmol*. Published online January 4, 2018. doi:10.1001/jamaophthalmol.2017.6090

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

eMethods 1. Calculation of binocular function score

Randot Preschool Test result (seconds of arc)	Worth 4-Dot test result at the same visit	Binocular Function Score (log(seconds of arc))
40	Not used	1.60
60	Not used	1.78
100	Not used	2.00
200	Not used	2.30
400	Not used	2.60
800	Not used	2.90
Nil	4 or 5 dots	4.00
Nil	2 or 3 dots	5.00

The Worth 4-Dot test was performed using the Lichtenstein Fixation Box (Good-Light Co.), viewed at 6 meters through red-green anaglyphic glasses with the red lens over the right eye.

eMethods 2. Sensitivity analyses for stereoacuity outcomes

The Binocular Function Score (described above) was the main outcome analysis for stereoacuity. Sensitivity analyses for Randot Preschool Test results were conducted using fixed values of 3.00 (1000 seconds), 3.20 (1600 seconds) or 4.00 (10000 seconds) to replace nil stereopsis instead of the Worth 4-Dot test result.

Fly Stereo Acuity Test results were analyzed using a log-transformation with a value of 4.00 (equivalent 10000 seconds) for nil stereopsis.

eAppendix. List of protocol violations

Participants with major protocol violations (listed in Figure 1) were excluded from the Per Protocol primary outcome analyses in Table 2 and eTable 4. Protocol violations were reviewed and confirmed by the study Management Committee after data collection was complete but prior to unmasking of treatment allocation. Some participants had more than one protocol violation, thus the total number excluded from analysis is less than the sum of all categories.

Total number of participants excluded from Per Protocol analyses:

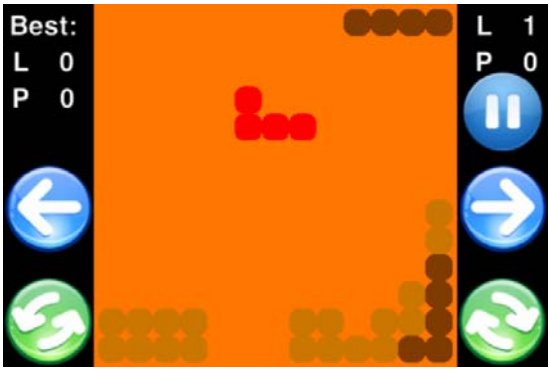
Active group n=26

Placebo group n=17

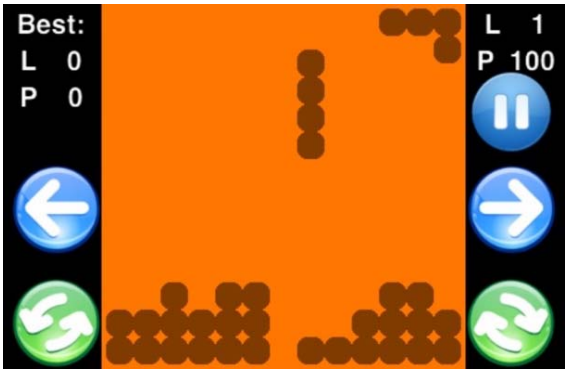
- **Poor compliance with videogame (Active group n=12, Placebo group n=8)**: defined as playing ≤25% of the total prescribed gameplay time (≤10.5 cumulative hours at 6 weeks).
- **Received placebo game with contrast change (Placebo group n=6)**: An early version of the placebo videogame contained a software bug. Both eyes saw all game elements at low contrast, and contrast increased symmetrically in the both eyes as participants played the game. Both eyes saw the same game elements at all times, thus we do not anticipate any dichoptic treatment effect from this version of the placebo game.
- **Randomized without meeting all eligibility criteria (Active group n=6, Placebo group n=2)**:
  - Participant had primary microtropia and did not meet the protocol criteria for anisometropia or strabismus (n=1)
  - Corrective lenses did not meet study refractive criteria (n=3)
  - Randomized more than 3 days after baseline vision measurements (n=1)
  - Randomized before VA met the stability criteria of ≤0.10 logMAR (1 line or 5 letters) change across at least 4 weeks during the optical treatment phase (n=2)
  - Amblyopic eye VA at baseline better than 0.30 logMAR (n=4)
    These last two protocol violations were caused by an early misinterpretation of outputs from the Electronic Visual Acuity testing system, which displayed a score out of 100 and rounded test results to the nearest Snellen Equivalent line. Results of 0.26 and 0.28 logMAR were rounded to 20/40. The conversion of the score to logMAR was later clarified in the clinical trial procedures.
- **Missing 6-week primary outcome (Active group n=6, Placebo group n=2)**: refers to participants who withdrew before the 6-week follow-up visit.
- **6-week visit out of time window (Active group n=2, Placebo group n=2):** The analysis time window for the 6-week visit was ±7 days. While clinicians always endeavored to assess participants within 6 to 7 weeks post-randomization (to avoid shortening the videogame training period), this was not always possible.
- **Poor compliance with refractive correction (Active group n=2, Placebo group n=2)**: refers to full-time wear during the six-week videogame training period, including while playing the videogames and other times. Non-compliance with full-time refractive correction after the six-week videogame training period was counted as a minor protocol violation and did not warrant exclusion from analysis.

eFigure 1. Video games used in the BRAVO clinical trial

A: Active videogame



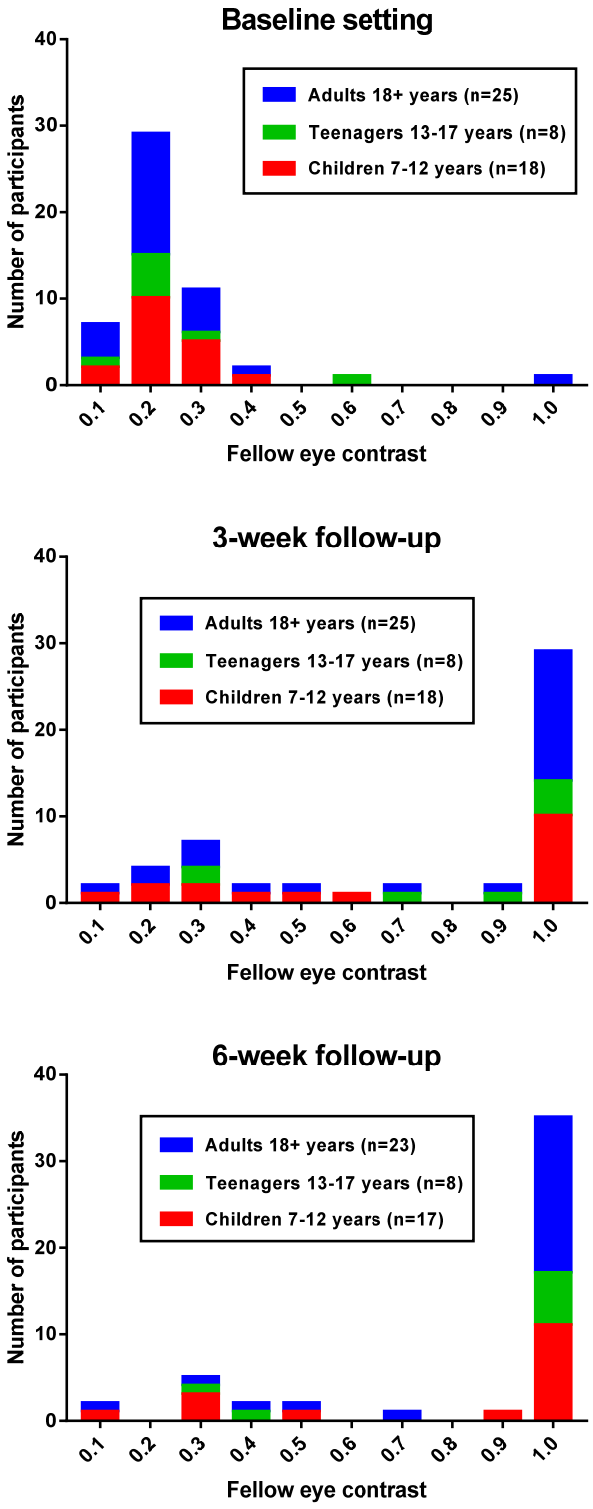
B: Placebo videogame



C: Nonius cross alignment

Participants in both the active and placebo groups were instructed to wear red-green anaglyphic glasses over appropriate refractive correction, with the green lens worn over the amblyopic eye. The active game (A) is shown at 20% fellow eye contrast. The nonius cross alignment task was displayed with an interocular contrast offset at the beginning of each gameplay session for both the active and placebo videogames, but the alignment setting and contrast offset were only used in the active game.

eFigure 2. Video game fellow eye contrast for active group participants

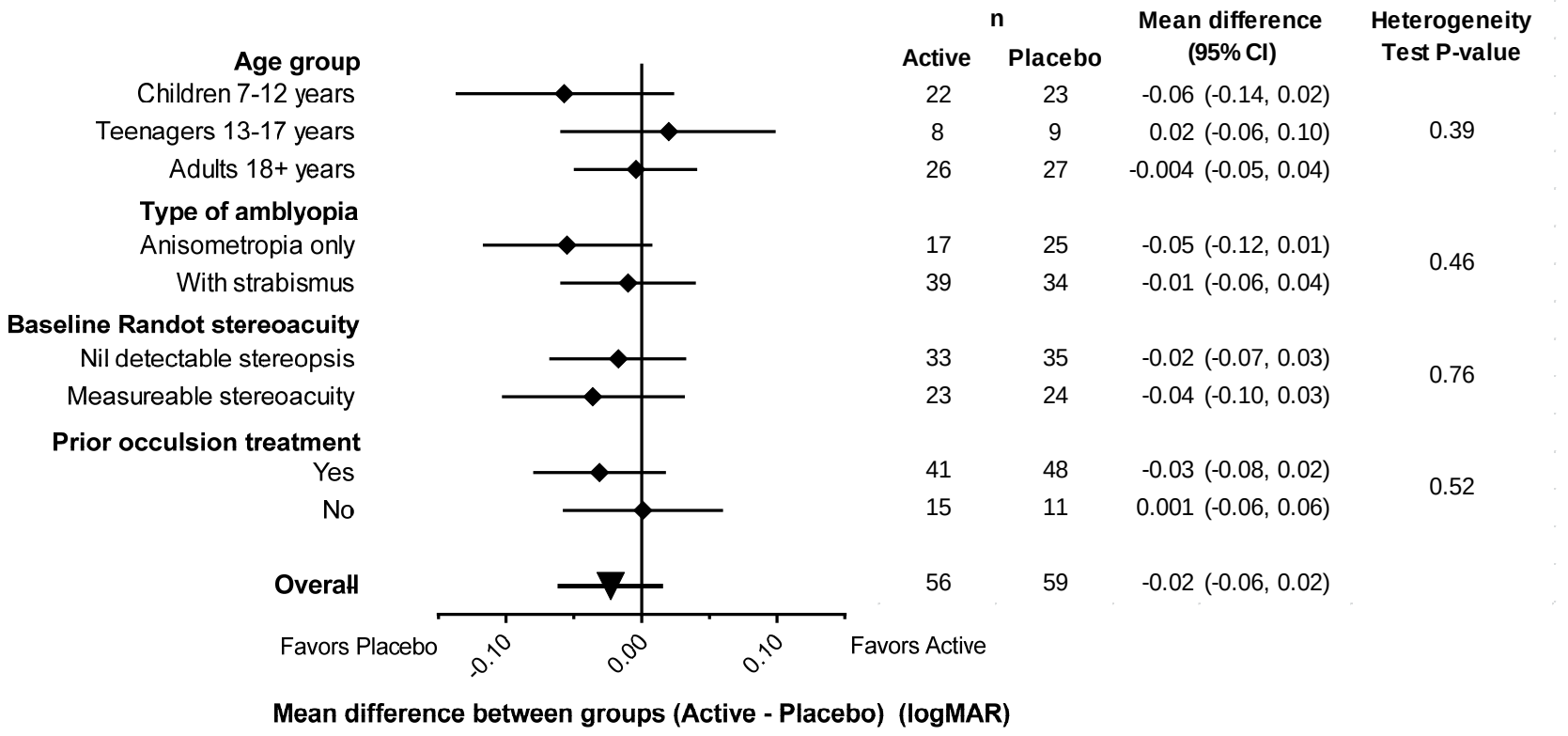


Histograms showing fellow eye contrast in the active videogame at baseline (treatment allocation), 3-week follow-up, and 6-week follow-up visits. Contrast values were binned to the nearest 0.1 (for example, 0.34 would be counted as 0.3, and 0.36 would be counted as 0.4).

The baseline fellow eye contrast in the active videogame was set according to interocular suppression measured at the visit immediately prior to randomization. Amblyopic eyes always viewed active game elements at full (1.0) contrast. Fellow eye contrast increased with successful daily gameplay. The aim was to reach >0.9 contrast in the fellow eye so that the participant can tolerate similar contrast in the two eyes during videogame play. At 3 weeks, 31 participants reached a fellow eye contrast of >0.9. At 6 weeks, 36 participants reached a fellow eye contrast of >0.9.

One adult participant had an interocular suppression result of 100% contrast at baseline (no suppression) and was able to perceive all game elements in the active game while viewing full contrast to each eye. Thus a fellow eye contrast of 1.0 was used as their initial setting. This adult played >48 hours of the active game over six weeks, so the contrast did not hinder their ability to play.

eFigure 3. Forest plot showing prespecified subgroup analyses of the primary outcome



The primary outcome was the between-group difference in amblyopic eye VA change from baseline at 6 weeks.

Anisometropia was defined as a difference in spherical equivalent of ≥0.50D, or a difference in astigmatism of ≥1.50D in any meridian, based on cycloplegic refraction results. Strabismus was classified as heterotropia at distance and/or near fixation, history of strabismus surgery, or resolution of strabismus following spectacle correction. Participants with mixed mechanism amblyopia (combined anisometropia and strabismus) were categorized in the "with strabismus" group. Baseline Randot stereoacuity was determined by results of the Randot Preschool Test at the visit immediately prior to randomization. Prior occlusion treatment included both patching and atropine therapies.

The pre-specified analysis based on amblyopia severity could not be conducted as only 17 participants (7 in the active group and 10 in the placebo group) had severe amblyopia, defined as amblyopic eye visual acuity worse than 0.70 logMAR (20/100).

eTable 1. Reasons for participant ineligibility at the study entry clinical assessment

	Children 7-12 years	Teenagers 13-17 years	Adults 18+ years	Overall
Total number assessed	119	39	188	346
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**
Eligible	47 (39)	15 (38)	53 (28)	115 (33)
Ineligible	72 (61)	24 (62)	135 (71)	231 (67)
Reasons for ineligibility[a]				
Did not meet inclusion criteria:				
Unilateral strabismic, anisometropic or mixed mechanism amblyopia present	13 (18)	6 (25)	24 (18)	43 (19)
Amblyopic eye VA between 0.30-1.00 logMAR	46 (64)	13 (54)	94 (70)	153 (66)
Fellow eye VA of 0.10 logMAR or better, combined with an interocular VA difference of 0.20 logMAR or more	17 (24)	8 (33)	29 (21)	54 (23)
Refractive status[b]	26 (36)	14 (58)	72 (53)	112 (48)
Able to pass nonius cross test on the iPod[c]	27 (38)	6 (25)	42 (31)	75 (32)
Participant able to comply with the protocol (understanding the videogame and attending visits)	10 (14)	1 (4)	1 (1)	12 (5)
Met exclusion criteria:				
Myopia exceeding 6.00 DS spherical equivalent in either eye	0 (0)	1 (4)	11 (8)	12 (5)
Alternating strabismus under normal binocular viewing conditions at either distant or near	5 (7)	0 (0)	9 (7)	14 (6)
Presence of amblyopia not due to strabismus and/or anisometropia	2 (3)	0 (0)	9 (7)	11 (5)
Participant has amblyopia that is caused by anisometropia only, and their current anisometropia is <0.50 DS	0 (0)	0 (0)	5 (4)	5 (2)
Ocular pathology other than amblyopia	2 (3)	1 (4)	23 (17)	26 (11)
Diagnosed neurological condition[d]	2 (3)	0 (0)	3 (2)	5 (2)

No. = number of participants, % = percentage of total, VA = visual acuity, logMAR = logarithm of the minimum angle of resolution, DS = Diopters sphere

[a] Percentages below this used the number of ineligible participants as denominator. Most ineligible participants had more than one reason for exclusion, thus percentages will add to more than 100% within columns.

[b] Refractive status criterion was met if participant wore appropriate refractive correction full-time for at least 4 months prior to study entry, or if the participant demonstrated stable VA during pre-randomization optical treatment.

[c] A nonius cross alignment task was shown at the beginning of each gameplay session in both the active and placebo games, and was used to offset the positions of game elements in the active game to compensate for ocular deviations. To pass this screening test at study entry, participants needed to see both cross elements (with appropriate contrast offset for baseline interocular suppression) and align them within tolerances of <0.5cm on the iPod screen, so that sufficient screen space remained to play the falling-blocks game. This excluded participants with large angles of strabismus who would not be able to play if allocated to the active group.

[d] Neurological conditions that qualified for exclusion were: migraine, epilepsy, and previous severe head trauma. Other conditions were assessed by the Steering Committee on a case-by-case basis. Autism and Attention Deficit Hyperactivity Disorder were not causes for exclusion as long as participants were willing and able to comply with study procedures and treatments.

eTable 2. Baseline characteristics of randomized participants summarized by age group

		Children 7-12 years		Teenagers 13-17 years		Adults 18+ years	
		Active	Placebo	Active	Placebo	Active	Placebo
Characteristic		**n=22**	**n=23**	**n=8**	**n=9**	**n=26**	**n=27**
Gender							
Female	No. (%)	8 (36)	8 (35)	3 (38)	5 (56)	11 (42)	15 (56)
Ethnicity[a]							
Caucasian/White	No. (%)	20 (91)	20 (87)	7 (88)	5 (56)	15 (58)	16 (59)
Asian	No. (%)	2 (9)	3 (13)	0 (0)	3 (33)	9 (35)	11 (41)
Other	No. (%)	3 (14)	4 (17)	2 (25)	1 (11)	5 (19)	6 (22)
Age at randomization (years)							
Mean age (years)	Mean (SD)	9.4 (1.7)	9.6 (1.6)	14.8 (1.3)	14.0 (1.4)	35.0 (9.5)	33.0 (10.9)
Age range (years)	Min - Max	7 - 12	7 - 12	13 - 17	13 - 17	19 - 52	19 - 55
Prior amblyopia treatment							
Optical[b]	No. (%)	19 (86)	22 (96)	7 (88)	8 (89)	23 (89)	25 (93)
Patching	No. (%)	19 (86)	23 (100)	7 (88)	8 (89)	15 (58)	17 (63)
Atropine[c]	No. (%)	12 (55)	7 (30)	0 (0)	2 (22)	2 (8)	1 (4)
Type of amblyopia							
Anisometropia only	No. (%)	5 (23)	8 (35)	5 (63)	6 (67)	7 (27)	11 (41)
Mixed mechanism	No. (%)	12 (55)	14 (61)	2 (25)	3 (33)	16 (62)	14 (52)
Strabismus only	No. (%)	5 (23)	1 (4)	1 (13)	0 (0)	3 (12)	2 (7)
Spherical equivalent of cycloplegic refraction							
Amblyopic eye (Diopters)	Mean (SD)	4.14 (3.38)	4.18 (2.66)	4.09 (2.16)	4.63 (1.40)	2.75 (2.36)	3.03 (2.41)
Fellow eye (Diopters)	Mean (SD)	2.36 (2.28)	1.49 (1.91)	0.30 (0.97)	0.99 (1.05)	0.40 (2.05)	0.25 (1.60)

		Children 7-12 years		Teenagers 13-17 years		Adults 18+ years	
		Active	**Placebo**	**Active**	**Placebo**	**Active**	**Placebo**
Distance visual acuity (e-ETDRS test at 3 meters)							
Amblyopic eye (logMAR)	Mean (SD)	0.54 (0.17)	0.54 (0.19)	0.62 (0.10)	0.56 (0.18)	0.50 (0.15)	0.47 (0.17)
Snellen equivalent of mean		20/63-2	20/63-2	20/80-1	20/63-2	20/63	20/63+1
Range (logMAR) [d]	Min - Max	0.28 - 0.94	0.30 - 0.94	0.44 - 0.72	0.38 - 0.92	0.28 - 0.88	0.24 - 0.98
Fellow eye (logMAR)	Mean (SD)	-0.08 (0.09)	-0.09 (0.07)	-0.17 (0.06)	-0.10 (0.08)	-0.12 (0.09)	-0.13 (0.08)
Snellen equivalent of mean		20/16-1	20/16-1	20/12-2	20/16	20/16+1	20/16+1
Range (logMAR)	Min - Max	-0.24 - 0.10	-0.22 - 0.04	-0.24 - 0.08	-0.18 - 0.08	-0.26 - 0.06	-0.24 - 0.04
Visual acuity at 40cm (Sloan letter near card)							
Amblyopic eye (logMAR)	Mean (SD)	0.64 (0.17)	0.60 (0.21)	0.68 (0.13)	0.53 (0.20)	0.61 (0.20)	0.54 (0.19)
Snellen equivalent of mean		20/80-2	20/80	20/100+1	20/63-2	20/80-1	20/63-2
Range (logMAR)	Min - Max	0.34 - 1.00	0.21 - 0.34	0.46 - 0.84	0.28 - 0.92	0.34 - 0.98	0.22 - 1.02
Fellow eye (logMAR)	Mean (SD)	0.02 (0.13)	-0.03 (0.10)	-0.06 (0.04)	-0.02 (0.10)	-0.04 (0.10)	-0.04 (0.08)
Snellen equivalent of mean		20/20-1	20/20+1	20/16-2	20/20+1	20/20+2	20/20+2
Range (logMAR)	Min - Max	-0.24 - 0.38	-0.20 - 0.18	-0.12 - 0.00	-0.10 - 0.22	-0.20 - 0.20	-0.18 - 0.10
Baseline Stereoacuity (Randot Preschool Test)							
Binocular Function Score (log arcsec)	Mean (SD)	3.88 (1.07)	3.74 (0.97)	3.73 (1.03)	3.80 (1.16)	3.67 (1.12)	3.58 (1.19)
Median Binocular Function Score (log arcsec)	Median (IQR)	4.00 (2.90)	4.00 (2.90)	4.00 (2.80)	4.00 (2.90)	4.00 (2.60)	4.00 (2.60)
Nil stereoacuity	No. (%)	13 (59)	14 (61)	5 (63)	6 (67)	15 (58)	15 (56)
Interocular suppression - Dichoptic Global Motion Test							
Able to complete test	No. (%)	12 (55)	17 (74)	8 (100)	8 (89)	26 (100)	27 (100)
Dichoptic contrast ratio (Amblyopic eye/Fellow eye)	Mean (SD)	0.30 (0.32)	0.30 (0.30)	0.64 (0.32)	0.52 (0.35)	0.48 (0.31)	0.53 (0.31)
Initial contrast for fellow eye in treatment videogame [e]							
Game data available	No. (%)	18 (82)	23 (100)	8 (100)	9 (100)	25 (96)	27 (100)
Initial contrast	Mean (SD)	0.22 (0.06)	0.26 (0.18)	0.25 (0.15)	0.26 (0.13)	0.23 (0.17)	0.32 (0.15)

		Children 7-12 years		Teenagers 13-17 years		Adults 18+ years	
		Active	Placebo	Active	Placebo	Active	Placebo
Worth 4-Dot test at near							
Suppression (2 or 3 dots)	No. (%)	4 (18)	3 (13)	0 (0)	2 (22)	1 (4)	2 (7)
Fusion (4 dots)	No. (%)	18 (82)	19 (83)	7 (88)	6 (67)	20 (77)	19 (70)
Diplopia (5 dots)	No. (%)	0 (0)	1 (4)	1 (13)	1 (11)	5 (19)	6 (22)
Worth 4-Dot test at distance							
Suppression (2 or 3 dots)	No. (%)	14 (64)	10 (43)	4 (50)	3 (33)	11 (42)	12 (44)
Fusion (4 dots)	No. (%)	8 (36)	9 (39)	4 (50)	5 (56)	14 (54)	10 (37)
Diplopia (5 dots)	No. (%)	0 (0)	3 (13)	0 (0)	1 (11)	1 (4)	5 (19)
Unable to perform	No. (%)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)
Maximum angle of strabismus at near[f]							
Orthotropic	No. (%)	8 (36)	12 (52)	6 (75)	7 (78)	11 (42)	19 (70)
1-9Δ	No. (%)	12 (55)	9 (39)	1 (13)	1 (11)	13 (50)	5 (19)
≥10Δ	No. (%)	2 (9)	2 (9)	1 (13)	1 (11)	2 (8)	3 (11)
Maximum angle of strabismus at distance[f]							
Orthotropic	No. (%)	9 (41)	10 (43)	6 (75)	7 (78)	11 (42)	16 (59)
1-9Δ	No. (%)	12 (55)	9 (39)	2 (25)	1 (11)	14 (54)	7 (26)
≥10Δ	No. (%)	1 (5)	4 (17)	0 (0)	1 (11)	1 (4)	4 (15)

No. = number of participants, % = percentage, SD = standard deviation, IQR = inter-quartile range, e-ETDRS = electronic Early Treatment of Diabetic Retinopathy Study, logMAR = logarithm of the minimum angle of resolution, Δ = prism diopters.

Baseline vision-related measurements were taken at the study entry visit for participants who did not require optical treatment, and at the last optical treatment follow-up before randomization for participants who underwent the optical treatment phase.

[a] Percentages in this subsection may add to more than 100% as some participants identified with more than one ethnicity.

[b] Refers to optical treatment before enrolling in this clinical trial. Six additional participants (3 in active group and 3 in placebo group) underwent optical treatment for the first time prior to randomization in this trial.

[c] All participants in this trial who had atropine therapy also had patching prior to or concurrently with atropine eye drops. None had atropine as the sole first-line treatment.

[d] Four early participants had amblyopic eye distance VA of 0.24-0.28 logMAR, better than the inclusion range of 0.30-1.00 logMAR, and were randomized as the Electronic Visual Acuity Tester rounded this to a Snellen Equivalent of 20/40. The logMAR score conversion was later clarified in the clinical trial procedures.

[e] Both active and placebo videogames had an initial contrast setting based on each participant's baseline interocular suppression. For the active game, this was used to offset contrast of game elements displayed to each eye. For the placebo game, the contrast offset was only applied to a nonius cross task at the start of each game session, and not to the game elements.

[f] Measured using prism alternate cover test through optimal refractive correction.

eTable 3. Video game treatment compliance at 3-week and 6-week follow-up

	Children 7-12 years		Teenagers 13-17 years		Adults 18+ years		Overall	
	Active game Total n=22	Placebo game Total n=23	Active game Total n=8	Placebo game Total n=9	Active game Total n=26	Placebo game Total n=27	Active game Total n=56	Placebo game Total n=59
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Weeks 1-3								
Played >75% of prescribed	5 (23)	9 (39)	3 (38)	5 (56)	14 (54)	15 (56)	22 (39)	29 (49)
Played 50%-75% of prescribed	4 (18)	6 (26)	2 (25)	3 (33)	2 (8)	5 (19)	8 (14)	14 (24)
Played 25%-50% of prescribed	5 (23)	2 (9)	1 (13)	1 (11)	4 (15)	4 (15)	10 (18)	7 (12)
Played ≤25% of prescribed	3 (14)	5 (22)	2 (25)	0 (0)	2 (8)	3 (11)	7 (13)	8 (14)
Withdrew/Refused to play	4 (18)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	6 (11)	0 (0)
High score <1000 points[a]	1 (5)	1 (4)	0 (0)	0 (0)	2 (8)	0 (0)	3 (5)	1 (2)
Weeks 4-6								
Played >75% of prescribed	6 (27)	6 (26)	3 (38)	4 (44)	10 (38)	12 (44)	19 (34)	22 (37)
Played 50%-75% of prescribed	2 (9)	3 (13)	0 (0)	1 (11)	4 (15)	5 (19)	6 (11)	9 (15)
Played 25%-50% of prescribed	2 (9)	8 (35)	0 (0)	2 (22)	3 (12)	3 (11)	5 (9)	13 (22)
Played ≤25% of prescribed	6 (27)	6 (26)	5 (63)	2 (22)	4 (15)	5 (19)	15 (27)	13 (22)
Withdrew/Refused to play	5 (23)	0 (0)	0 (0)	0 (0)	3 (12)	2 (7)	8 (14)	2 (3)
High score <1000 points[a]	1 (5)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	3 (5)	0 (0)
Overall compliance for 6 weeks								
Played >75% of prescribed	5 (23)	7 (30)	3 (38)	5 (56)	11 (42)	15 (56)	19 (34)	27 (46)
Played 50%-75% of prescribed	4 (18)	7 (30)	0 (0)	0 (0)	5 (19)	3 (11)	9 (16)	10 (17)
Played 25%-50% of prescribed	3 (14)	3 (13)	3 (38)	4 (44)	2 (8)	5 (19)	8 (14)	12 (20)
Played ≤25% of prescribed	4 (18)	6 (26)	2 (25)	0 (0)	3 (12)	2 (7)	9 (16)	8 (14)
Withdrew/Refused to play	5 (23)	0 (0)	0 (0)	0 (0)	3 (12)	2 (7)	8 (14)	2 (3)
High score <1000 points[a]	1 (5)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	3 (5)	0 (0)

No. = number of participants, % = percentage of column total

Prescribed treatment was at least 1 hour per day, totaling to a minimum of 21 hours per 3 week period, and 42 hours in total at 6 weeks follow-up. Percentage of prescribed gameplay was calculated based on these minimum hours.

Due to technical software issues, 2 active group and 2 placebo group participants had gaps in logfile data ranging from 2-18 days. These gaps were filled using information from their written recording diary.

[a] All of the participants who did not reach at least 1000 points during training also did not reach 25% of the prescribed dose. For active group participants, this meant that their fellow eye contrast in the game did not increase.

eTable 4. Primary outcomes for each age group

Primary outcome analyses for children 7-12 years age group.

Analysis method	Active group N	Active group Adjusted Mean[a]	Active group SE	Placebo group N	Placebo group Adjusted Mean[a]	Placebo group SE	Adjusted treatment group difference (Active - Placebo, logMAR) Mean difference[b]	95% CI	P-value
Intention-to-treat with Last Value Carried Forward.[c]	22	0.05	0.03	23	0.11	0.03	-0.06	(-0.14, 0.02)	0.16
Intention-to-treat with multiple imputations.	22			23			-0.03	(-0.12, 0.06)	0.47
Complete case analysis: Excluded missing 6-week visits.	18	0.08	0.03	23	0.11	0.03	-0.03	(-0.12, 0.05)	0.46
Per Protocol analysis: Excluded protocol violations or missing 6-week visits.	12	0.09	0.04	14	0.11	0.04	-0.03	(-0.15, 0.09)	0.65

Primary outcome for the teenager 13-17 years age group[d]

	Active group N	Active group Mean	Active group SD	Placebo group N	Placebo group Mean	Placebo group SD
Change in amblyopic eye visual acuity from baseline	8	0.06	0.07	9	0.05	0.08

Primary outcome analyses for adults 18+ years age group.

Analysis method	Active group N	Active group Adjusted Mean[a]	Active group SE	Placebo group N	Placebo group Adjusted Mean[a]	Placebo group SE	Adjusted treatment group difference (Active - Placebo, logMAR)[b] Mean difference[b]	95% CI	P-value
Intention-to-treat with Last Value Carried Forward.[c]	26	0.05	0.02	27	0.06	0.02	-0.004	(-0.05, 0.04)	0.85
Intention-to-treat with multiple imputations.	26			27			-0.03	(-0.09, 0.03)	0.28
Complete case analysis: Excluded missing 6-week visits.	24	0.05	0.02	25	0.06	0.02	-0.01	(-0.06, 0.04)	0.76
Per Protocol analysis: Excluded protocol violations or missing 6-week visits.	15	0.05	0.02	19	0.08	0.02	-0.01	(-0.09, 0.03)	0.28

N = number of participants analyzed, SE = standard error of the mean.

[a] Means were adjusted for baseline amblyopic eye VA and age groups.

[b] Positive treatment group differences indicate the active group improved more than the placebo group.

[c] Missing 6-week data was imputed using Last Value Carried Forward, which assumed participants with missing data showed no change in amblyopic eye VA.

[d] The teenager 13-17 years age group did not reach a sufficient sample size for regression analyses (n<10 in both groups).

eTable 5. Sensitivity analyses for stereoacuity outcomes

Change from baseline[a]	Active group (total n=56) N	Adjusted Mean[b]	SE	Placebo group (total n=59) N	Adjusted Mean[b]	SE	Treatment group difference (Active - Placebo) Mean difference[c]	95% CI	P-value
Randot Preschool Test:									
Main analysis: Binocular Function Score (log(seconds of arc))	52	0.16	0.09	58	0.15	0.08	0.01	(-0.21, 0.23)	0.92
Nil Stereo replaced with 3.00 (equivalent 1000 seconds of arc)	52	0.04	0.03	58	0.06	0.03	-0.02	(-0.10, 0.05)	0.54
Nil Stereo replaced with 3.20 (equivalent 1600 seconds of arc)	52	0.03	0.04	58	0.06	0.03	-0.03	(-0.12, 0.06)	0.49
Nil Stereo replaced with 4.00 (equivalent 10000 seconds of arc)	52	0.02	0.07	58	0.08	0.06	-0.07	(-0.23, 0.10)	0.45
Fly Stereo Acuity Test									
Nil Stereo replaced with 4.00 log(equivalent 10000 seconds of arc)	52	0.17	0.05	58	0.20	0.05	-0.02	(-0.15, 0.10)	0.69

N = number of participants analysed, SE = standard error of the mean.

All means and standard errors are reported in log(seconds of arc) units. 0.30 log(seconds of arc) = 1-octave or 2-fold change in threshold.

[a] Change is calculated as (Baseline - Follow-up). Positive values indicate improvement in stereoacuity.

[b] All models are adjusted for baseline value and age groups. Missing data were excluded from analysis.

[c] Positive treatment group differences indicate the the active group improved more than the placebo group.

eTable 6. Treatment acceptability questionnaire

Parent questionnaire for participants 7-17 years of age at baseline

	3-weeks follow-up						6-weeks follow-up					
	Active Group (total n=30)			Placebo Group (total n=32)			Active Group (total n=30)			Placebo Group (total n=32)		
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Adverse effects domain	26	4.21	0.51	30	4.16	0.46	25	4.28	0.45	31	4.23	0.36
Adverse effects domain, excluding ambiguous questions[a]	26	4.15	0.49	30	4.11	0.52	25	4.25	0.47	31	4.22	0.38
Treatment compliance domain	26	3.80	0.80	30	3.82	0.81	25	3.78	0.79	31	3.72	0.84
Social stigma domain	26	4.21	0.58	30	4.24	0.49	25	4.15	0.66	31	4.35	0.50

Adult questionnaire for participants 18+ years at baseline

	3-weeks follow-up						6-weeks follow-up					
	Active Group (total n=26)			Placebo Group (total n=27)			Active Group (total n=26)			Placebo Group (total n=27)		
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Adverse effects domain	23	4.13	0.49	25	3.94	0.54	23	4.00	0.46	25	3.97	0.63
Adverse effects domain, excluding ambiguous questions[a]	23	3.98	0.56	25	3.83	0.52	23	3.84	0.55	25	3.94	0.63
Treatment compliance domain	23	3.98	0.54	25	3.82	0.48	23	3.87	0.55	25	3.69	0.55
Social stigma domain	23	4.17	0.61	25	4.20	0.58	23	4.25	0.52	25	3.95	0.57

N = number of participant questionnaires completed, SD = standard deviation

Each domain score is the mean of Likert-type items with 5 response choices ranging from "strongly agree" to "strongly disagree". Higher numerical values indicate more adverse impact.

[a] This treatment acceptability questionnaire was adapted from the Amblyopia Treatment Index questionnaire, which was designed to assess adverse impacts of patching and atropine treatments. Three questions in the adverse events domain relating to "outdoor activities", "near vision activities" and "playing with toys/daily activities such as cooking, driving or typing" (for the parent and adult versions respectively) were ambiguous, as it was not possible

to perform these activities concurrently with playing a videogame. Thus we also present the adverse effects domain score after excluding these three questions.

eTable 7. Quality of life for adult participants 18 years and older at baseline

Quality of Life was assessed using the World Health Organisation Quality of Life - BREF questionnaire at baseline and the 24-weeks visits.

	Active group (Adults n =26)						Placebo group (Adults n=27)						Treatment group difference for change in quality of life
	Baseline			Change at 24-week visit			Baseline			Change at 24-week visit			
	n	Mean	SD	n	Adjusted Mean[a]	SE	n	Mean	SD	n	Adjusted Mean[a]	SE	P-value
Physical health domain	25	86.9	9.7	22	2.9	1.9	27	77.6	11.6	19	-0.7	2.1	0.24
Psychological domain	25	77.3	12.4	22	1.5	1.4	27	73.0	12.1	19	1.7	1.5	0.90
Social relationships domain	25	77.3	16.2	22	2.3	2.6	27	69.7	14.9	19	-1.5	2.8	0.33
Environment domain	25	78.0	10.2	22	1.3	2.0	27	77.0	14.3	19	-0.7	2.2	0.50

n = number of questionnaires completed, SD = standard deviation, SE = standard error of the mean

[a] Analyses of change for each domain were conducted using linear regression with adjustment for baseline value. Positive change values indicate improvement in the Quality of Life questionnaire score.

eTable 8. Adverse events summary

	Active group total n=56	**Placebo group** total n= 59
Related to the treatment videogames		
Asthenopia and mild headache during videogame play and other screen work[a]	2	1
Device-related events		
Videogame software issues	7	6
Damage to iPod charger	1	1
Misplaced iPod	1	0
Unknown password set on the iPod	0	1
Not related to treatment videogames		
Occurred during the 6 weeks videogame training period		
Gastrointestinal infection	1	0
Common cold/flu/other upper respiratory tract infections	1	4
Diagnosed mental health issue (depression, anxiety)	1	1
Knee surgery	1	0
Shoulder injury	0	1
New diagnosis of migraine[b]	0	1
Mild dry eye	1	0
New onset of floaters	0	1
Occurred during post-treatment follow-up		
Common cold/flu/other upper respiratory tract infections	2	1
Minor injuries and/or broken spectacles	0	4
New diagnosis of migraine[b]	1	0

Additionally, there were 3 adverse events (flu, muscle cramps, chicken pox) during the pre-randomisation optical treatment phase. In all cases, the participants were allowed to recover before re-checking eligibility and performing randomization.

[a] In all three cases, asthenopia and headache symptoms either resolved spontaneously after the videogame treatment period or were resolved by dividing daily treatment into shorter sessions of 15-20 minutes duration.

[b] Diagnosed migraine was an exclusion criteria for this clinical trial. Two participants were newly diagnosed with migraine during trial participation. In both cases their symptoms and diagnoses were unrelated to the videogame treatment.