Treatment of Symptomatic Convergence Insufficiency in Children Enrolled in the Convergence Insufficiency Treatment Trial–Attention & Reading Trial: A Randomized Clinical Trial

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SIGNIFICANCE: These data confirm the effectiveness of office-based vergence/accommodative therapy for improving convergence in children with symptomatic convergence insufficiency. They also highlight the importance of using a primary outcome measure that is as objective as possible rather than relying solely on self-reported symptoms for studies of binocular vision in children.

PURPOSE: The purpose of this study was to report changes in clinical signs and symptoms of convergence insufficiency (secondary outcome measures) from a multicenter clinical trial (Convergence Insufficiency Treatment Trial–Attention & Reading Trial [CITT-ART]) evaluating the effectiveness of vergence/accommodative therapy for improving reading and attention in children with symptomatic convergence insufficiency.

METHODS: Three hundred eleven children aged 9 to 14 years with symptomatic convergence insufficiency were randomly assigned to 16 weeks of office-based vergence/accommodative therapy or to placebo therapy. Improvements in (1) near point of convergence (NPC), (2) positive fusional vergence (PFV), and (3) self-reported symptoms (Convergence Insufficiency Symptom Survey [CISS] score) were compared after 16 weeks of treatment.

RESULTS: Mean NPC improved 10.4 cm in the vergence/accommodative and 6.2 cm in the placebo therapy group (mean difference of –4.2 cm [95% confidence interval {CI}, –5.2 to –3.2 cm; $P < .001$]); mean PFV increased 23.2 and 8.8Δ in the vergence/accommodative and placebo therapy groups, respectively (mean difference of 14.4Δ [95% CI, 12.1 to 16.8Δ; $P < .001$]). The mean CISS score improved 11.8 and 10.4 points in the vergence/accommodative and placebo therapy groups, respectively (mean difference of 1.5 points [95% CI, –3.8 to +0.8 points; $P = .21$]).

CONCLUSIONS: Our results demonstrate that office-based vergence/accommodative therapy is effective for improving the NPC and PFV in children with symptomatic convergence insufficiency. However, given that both treatment groups had a similar reduction in self-reported symptoms, it may not be prudent to use the CISS alone as a measure of successful treatment.

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Convergence insufficiency is a binocular vision disorder in which there is a larger exodeviation at near than at far, a receded near point of convergence, and below expected positive fusional vergence measures at near.[1–6] It has an estimated prevalence of 4.2 to 17.6% in children.[1,7–10] Associated symptoms are common and can include eye-related (e.g., sore eyes, headaches, blurred vision, double vision, and words moving on page) and performance-related (e.g., loss of place, loss of concentration, reading slowly, and trouble remembering what was read) symptoms.[11,12] Clinical trials comparing office-based vergence/accommodative therapy with home-based pencil push-up and computer-based therapies have shown office-based vergence/accommodative therapy to be more effective than these two treatments for improving clinical signs and associated symptoms in children with symptomatic convergence insufficiency,[3,4,6] with recent studies showing associated changes in brain activation after treatment.[13–15]

The Convergence Insufficiency Treatment Trial–Attention & Reading Trial (CITT-ART) was a multicenter, double-masked, randomized clinical trial designed to determine if office-based vergence/accommodative therapy resulted in improvements in reading[16] and attention in 9- to 14-year-old children with symptomatic convergence insufficiency.[17] The results showed that office-based vergence/accommodative therapy was no more effective than office-based placebo therapy for improving reading performance. The trial data also provided an opportunity to report on changes in clinical measures of convergence and subject-reported symptoms. Herein, we report on these secondary outcomes of near point of convergence, positive fusional convergence, and symptoms after 16 weeks of treatment.

PATIENTS AND METHODS

The CITT-ART was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and conducted according to the tenets of the Declaration of

Helsinki at nine optometry or ophthalmology clinical sites. The institutional review boards of participating sites approved the protocol and Health Insurance Portability and Accountability Act authorization–informed consent forms. The parent or guardian (hereafter parent) of each study participant gave written informed consent, and each participant provided written assent. Study oversight was provided by an independent data and safety monitoring committee. The study is registered at www.clinicaltrials.gov (CITT-ART: NCT02207517, accessed March 3, 2019). The CITT-ART Manual of Procedures is available at https://u.osu.edu/cittart/. Relevant portions of the protocol are summarized hereinafter.

Participant Selection

The study included children 9 to 14 years of age in grades 3 to 8 who had symptomatic convergence insufficiency defined as (1) a near exodeviation at least 4Δ greater than at distance fixation (as measured with the prism and alternate cover test), (2) a receded (≥6 cm) near point of convergence, (3) insufficient positive fusional vergence (i.e., convergence amplitudes) at near defined as failing Sheard's criterion (base-out blur [break if no blur] less than twice the near phoria)[18] or minimal positive fusional vergence at near of ≤15Δ base-out break, and (4) a score of ≥16 on the Convergence Insufficiency Symptom Survey (CISS).[19,20] The full eligibility and exclusion criteria are listed in Table 1. All participants presented to a CITT-ART optometrist or ophthalmologist either for routine care or seeking treatment. Data were not collected to document the primary reason the parent and child were interested in the study (e.g., visual symptoms, poor reading, inattention, etc.).

Enrollment/Randomization

Using a standardized protocol (details described previously),[17] study-certified optometrists and ophthalmologists administered the CISS to quantify symptoms[19–22] and a sensorimotor evaluation that included the following: best-corrected visual acuity at distance and near, cover testing, near point of convergence, positive and negative fusional vergence at near (prism bar), near stereoacuity, and the other clinical tests listed in Table 3. For near point of convergence and positive fusional vergence testing, participants were instructed to "try to keep the target single for as long as possible" and "try to keep the target single and clear," respectively. These data served as the baseline measures for the children enrolled into the study. Participants were randomly allocated using a permuted block (sizes of 3, 6, and 9) design stratified by site and parent-reported attention-deficit/hyperactivity disorder status (yes/no) in a 2:1 allocation ratio to office-based vergence/accommodative therapy (hereafter vergence/accommodative therapy) or office-based placebo therapy (hereafter placebo therapy), respectively. This was accomplished using the Research Electronic Data Capture system hosted at the Ohio State University.[23]

Treatment Protocols for Both Therapy Groups

A 16-week program of weekly 60-minute in-office therapy specific to the assigned therapy (vergence/accommodative or placebo) group was administered by study-certified optometrists, with four to five therapy procedures administered in the office and 15 minutes of daily home therapy prescribed for 5 days per week. The therapy protocols, adapted from prior CITT trials,[3,4,6] were extended from 12 to 16 weeks by adding new procedures and increasing the therapy time for some procedures.

Table 2 provides an overview of the vergence/accommodative therapy program.[17,24] The placebo therapy program[17,24] comprised pre-determined sequentially administered procedures designed to appear to be genuine therapy techniques but not to stimulate vergence, accommodation, or fine saccadic eye movements beyond normal daily visual activities. Placebo procedures included standard vergence therapy techniques that were modified to be performed monocularly rather than binocularly or had zero vergence demand. Similar to real therapy, filter glasses were often worn, and participants were told that the glasses were to help the eyes work together as a team; there were protocolized objectives and goals that were conveyed to the participants; and therapists provided encouragement, feedback, and positive reinforcement for motivational purposes. The placebo therapy is described in more detail in previous articles.[25,26]

Follow-up Examinations and Test Procedures

Protocol-specified follow-up visits were conducted by study-certified optometrists and ophthalmologists masked to participants' treatment group after 4, 8, 12, and 16 weeks of therapy. The examiner administered the CISS and assessed eye alignment (by cover testing), near point of convergence, positive and negative fusional vergence at near, monocular accommodative amplitude, monocular accommodative facility, and near vergence facility.

Masking of Participants and Examiners

The masking protocols used in this trial were successfully implemented in previous CITT clinical trials.[3,4] Examiners were asked if they became unmasked to the participant's treatment group after each examination, and participants were asked upon completion of their 16-week therapy program whether they thought they had received "real" vergence/accommodative therapy or placebo therapy.

Treatment Adherence

At each therapy visit, the therapist estimated participant adherence to the prior week's prescribed home therapy (based on electronic data from the home computer program, written home therapy logs, and participant and parental feedback) using the following five-point scale: not at all, seldom, about half the time, most of the time, and always. Responses of "most of the time" and "always" were considered adherent to the prescribed treatment regimen for the prior week. The percentage of weeks (of 16) that each participant was judged to be adherent with the prescribed therapy was calculated.

Statistical Methods

The CITT-ART's pre-planned sample size of 324 participants (216 in the vergence/accommodative therapy group and 108 in the placebo group) was chosen to provide sufficient power for the trial's primary aim of determining whether treatment improved reading comprehension; these results are reported elsewhere.[16] This sample size provided >95% power with a two-sided type I error rate of 5% to detect treatment group differences in near point of convergence of ≥4 cm, CISS score of ≥10 points, positive fusional vergence of ≥10Δ, and vergence facility of ≥3 cpm.

Outcome Measures

The main analyses for this report were the between-group differences and a two-sided 95% confidence interval (CI) of the change in the near point of convergence, positive fusional vergence, and the CISS score from baseline to 16 weeks calculated using an intent-to-treat analysis that excluded participants with missing

TABLE 1. CITT-ART eligibility and exclusion criteria

Eligibility criteria
Age 9–14 y
Grades 3–8
CISS score ≥16
Exophoria at near (40 cm) at least 4Δ greater than at far (4 m)
Receded near point of convergence of ≥6-cm break
Insufficient positive fusional vergence at near (40 cm; i.e., failing Sheard's criterion or positive fusional vergence ≤15Δ BO break)
Best-corrected distance (4 m) and near visual acuity (40 cm) of 20/25 or better in each eye
Random-dot stereopsis appreciation of 500 seconds of arc or better (40 cm)
Willing to wear refractive correction for any of the following uncorrected refractive errors (based on cycloplegic refraction within prior 6 mo; correction must be worn for at least 2 weeks): Myopia >–0.75 D spherical equivalent in either eye Hyperopia >+2.00 D spherical equivalent in either eye Anisometropia >0.75 D spherical equivalent Astigmatism >1.00 D in either eye Refractive error corrections adhered to the following guidelines: full hyperopic sphere power or symmetrically reduced by no more than 1.50 D, spherical equivalent myopia and spherical equivalent anisometropia within 0.75 D of full correction, and astigmatism within 0.75 D of full correction and axis within 6° for magnitudes of ≥1.00 D.
Not wearing BI prism or plus add at near for 2 weeks before study enrollment and for duration of study
The timing of enrollment must allow a participant to be attending school at both the baseline and the 16-week outcome examination.
English is primary language spoken at home, or the child is proficient in English as determined by the school.
Parental permission to contact the child's teacher(s) for study purposes.
The parent and child understand the protocol and are willing to accept randomization.
The parent does not expect the child to start any new ADHD medicine or change the dose of any currently taken ADHD medicine while the child is being treated in the study.
Exclusion criteria
Constant strabismus at distance or near
Esophoria of ≥2Δ at distance
Vertical heterophoria ≥2Δ at distance or near
≥2-line interocular difference in best-corrected distance visual acuity
Monocular near point of accommodation >20 cm (accommodative amplitude <5 D) as measured by push-up method
Manifest or latent nystagmus
Word reading subtest score <80 on the WRAT-4
KBIT-2 matrices subtest score <70
History of strabismus, intraocular, or refractive surgery
CI previously treated with any form of office-based vergence/accommodative therapy or home-based vergence therapy (e.g., computerized vergence therapy)
CI associated with head trauma or known disease of the brain
Diseases known to affect accommodation, vergence, or ocular motility such as multiple sclerosis, Graves orbitopathy, myasthenia gravis, diabetes mellitus, Parkinson disease
Inability to comprehend and/or perform any study-related test or procedure
Speech-language disorder (e.g., stuttering) that would interfere with interpretation of digital recordings of reading tests
Significant hearing loss
Household member enrolled in the present CITT-ART or treated within the past 6 mo with any form of office-based vergence/accommodative therapy or home-based vergence therapy (e.g., computerized vergence therapy)
Household member is an eye care professional, ophthalmic technician, ophthalmology or optometry resident, or optometry student.

ADHD = attention-deficit/hyperactivity disorder; BI = base-in; BO = base-out; CI = convergence insufficiency; CISS = Convergence Insufficiency Symptom Survey; CITT-ART = Convergence Insufficiency Treatment Trial–Attention & Reading Trial; KBIT-2 = Kaufman Brief Intelligence Test-2; WRAT-4 = Wide Range Achievement Test-4.

TABLE 2. Office-based vergence/accommodative therapy procedures

CITT-ART vergence/accommodative therapy protocol	Phase 1		Phase 2		Phase 3		Phase 4	
	O	H	O	H	O	H	O	H
Gross convergence								
Brock string	✓	✓						
Barrel card	✓			✓				
Voluntary convergence				✓				
Fusional vergence								
Clown and Quoits vectograms	C		R		J		J	
Computer orthoptics (RDS)	C	C	R	R	J	J	J	J
Lifesaver cards			C	C				
Aperture rule					R		J	
Eccentric circles					C	C	J	J
Accommodative								
Monocular loose lens facility	✓		✓					
Monocular letter chart facility	✓	✓	✓					
Bull's eye rock	✓		✓					
Lens sorting	✓	✓	✓					
Stereoscope biocular facility					✓			
Prism dissociation biocular facility					✓			
Computer orthoptics accommodative rock		✓		✓	✓	✓		✓
Binocular ±2.00 D flipper facility							✓	✓

C = techniques emphasize convergence amplitudes (positive fusional vergence) only; CITT-ART = Convergence Insufficiency Treatment Trial–Attention & Reading Trial; H = home therapy; J = jump vergence procedures (some with added prism; mainly change from convergence to divergence demand, some from no vergence demand to a moderate convergence or divergence demand); O = office therapy; R = ramp/smooth positive and negative fusional vergence procedures; RDS = random-dot stereograms.

16-week data. Mixed linear models using clinical site as a random effect were fitted for change from baseline to the 16-week outcome for each of these three outcome measures. Demographics, variables with clinically relevant treatment group differences at randomization, and potential confounders were considered for inclusion in univariate models. Once identified, interactions between these baseline factors and randomization group were assessed. Variables associated at the $P < .10$ level in univariate models were included in multivariable models and retained in the final multivariable model when significantly associated ($P < .05$) with the outcome or when determined a priori to be necessary or important for inclusion (e.g., baseline value of outcome measure).

Similar to previous CITT studies,[3,4] we also evaluated four other pre-planned outcomes of success (defined herein) using chi-square tests to determine if the proportions of successful outcomes differed between the two treatment groups.

Success Criterion 1: Normal or Improved Outcome

For the near point of convergence, normal was defined as <6 cm and improved as a decrease (improvement) of ≥4 cm. For positive fusional vergence, *normal* was defined as passing Sheard's criterion[18] and having a base-out break finding >15Δ, whereas *improved* was defined as an increase of ≥10Δ. A CISS score of <16 was considered normal (asymptomatic), and a decrease of ≥10 points was considered improved.

Success Criterion 2: Normal and Improved Outcome

It is possible that when using success criterion 1, a measure that just barely met the eligibility criterion at baseline could be classified as "normal" at outcome despite improving only slightly. For example, a baseline near point of convergence of 6.5 that improved only 1 cm to a distance of 5.5 cm would meet the normal criterion at outcome, although a 1-cm improvement is not considered a clinically relevant change. To address this, success criterion 2 required that both the aforementioned criterion for normal and the pre-specified amount of clinically significant improvement be met. These definitions of success were as follows: normal near point of convergence measure of <6 cm that also improved ≥4 cm, normal positive fusional vergence (met Sheard's criterion and break value >15Δ) that also improved ≥10Δ, and a normal CISS score of <16 that also improved ≥10 points.

Success Criterion 3: Composite Convergence Outcome

A successful composite convergence outcome was defined as attainment of both a normal near point of convergence and normal positive fusional vergence.

Success Criterion 4: Composite Signs and Symptoms Outcome

The composite signs and symptoms outcome was based on changes in all three outcome measures,[3] with the criterion for

success met when all three measures met the aforementioned criteria for normal. The outcome was considered *improved* when the CISS score was normal or improved in combination with a near point of convergence or positive fusional vergence that was normal or improved.

Fragility Index Assessment

The fragility index is a recently described randomized clinical trial metric used to measure the robustness of statistically significant dichotomous outcomes.[27–31] It is defined as the minimal number of study participants whose status would need to change from a nonevent to an event (e.g., failure to success) to convert a statistically significant result to a nonsignificant result. The smaller the number, the more fragile and less robust the result.[28] Fragility indices were calculated for the near point of convergence, positive fusional vergence, the CISS score, and both composite measures.

Basic descriptive statistics were calculated using means and standard deviations for continuous variables and frequencies for categorical variables. Reported *P* values for treatment group comparisons are two-tailed and considered statistically significant at $P < .05$. Data entry and management were completed using the Research Electronic Data Capture system hosted at the Ohio State University.[23] All analyses were conducted using SAS software version 9.4 (SAS Inc., Cary, NC).

RESULTS

Enrollment and Baseline Characteristics

Between September 2014 and March 2017, 311 participants were enrolled at nine clinical sites (range of 15 to 42 participants per site; median, 37). Data from one participant found to be ineligible were excluded by institutional review board mandate, for a total of 310 participants; of these, 206 were randomly assigned to vergence/accommodative therapy and 104 to placebo therapy. The mean age was 10.8 (±1.5) years, and 171 (55%) were female. Baseline demographic and clinical characteristics were similar in both treatment groups (Table 3).

Visit Completion and Home Therapy Adherence

The 16-week primary outcome visit was completed by 199 (96.6%) of the 206 participants in the vergence/accommodative group and by 100% of the 104 participants in the placebo group (Fig. 1). Because only a few participants (n = 7) missed their 16-week outcome visit, we believe that the probability of bias is low, and thus, an imputation analysis was not conducted. Of the 4921 scheduled therapy visits, 4762 (96.8%) were completed, with no difference between the vergence/accommodative (96.8%) and the placebo (96.6%) therapy groups. There was a statistically significant difference in mean adherence with completing the prescribed home therapy most of the time or always each week between the vergence/accommodative therapy group (64.2%) and the placebo therapy group (76.3%; $P < .05$). No adverse events were reported.

Masking of Participants and Examiners

When participants were asked, at the completion of treatment, which therapy they thought they had received, 170 (87%) of 195 assigned to vergence/accommodative therapy and 75 (73%) of 103 assigned to placebo therapy indicated vergence/accommodative therapy. One masked examiner became unmasked at a study visit and then did not perform any subsequent masked examinations for that participant.

Main Clinical Signs and Symptoms Outcome Measures

The means and 95% CIs at baseline and outcome and the treatment group comparisons for the adjusted change in near point of convergence, positive fusional vergence, and CISS scores for participants who completed their 16-week outcome visit are described hereinafter and shown in Table 4.

Clinical Outcome Measure of Near Point of Convergence

A significant interaction of treatment group with baseline near point of convergence was found ($P = .004$), so although both treatment groups experienced larger changes in near point of convergence with increasing baseline values, there was a statistically significant greater rate of change in the vergence/accommodative therapy group than in the placebo therapy group. Among participants with a near point of convergence of 14.2 cm at baseline (the study average), there was a statistically significant greater mean improvement (decrease) in near point of convergence in the vergence/accommodative group (10.4 cm) compared with the placebo therapy group (6.2 cm; adjusted difference of –4.2 cm; 95% CI, –5.2 to –3.2 cm; $P < .001$). If comparisons were made using a baseline near point of convergence of 10 cm, the adjusted mean treatment group difference was –3.4 cm (95% CI, –4.6 to –2.2 cm; $P < .001$), and when made using a baseline near point of convergence of 30 cm or greater, the adjusted mean treatment group difference was –7.2 (95% CI, –9.4 to –5.0 cm; $P < .002$).

A statistically significant greater proportion of participants in the vergence/accommodative therapy group than in the placebo group met both success criterion 1 for near point of convergence (normal or improved by ≥4 cm; 95.5 vs. 67.3%; $P < .001$; Table 5) and the stricter success criterion 2 (normal and improved ≥4 cm; 74.2 vs. 30.8%; $P < .001$; Table 5).

Clinical Outcome Measure of Positive Fusional Vergence at Near

The mean improvement in positive fusional vergence was 23.2 versus 8.8Δ for participants assigned to vergence/accommodative therapy and placebo therapy, respectively, with an adjusted mean treatment group difference of 14.4Δ (95% CI, 12.1 to 16.8Δ; $P < .001$; Table 4). Univariate models showed no covariates or interactions associated with change in vergence.

A statistically significant greater percentage of participants assigned to vergence/accommodative therapy (92.4%) as compared with placebo therapy (50%) met success criterion 1 (normal or improved ≥10Δ) for change in positive fusional vergence ($P < .001$; Table 5). Likewise, there were a statistically significant greater proportion of vergence/accommodative participants (80%) who achieved the stricter success criterion 2 (normal and improved ≥10Δ) compared with the proportion of placebo therapy participants (31%; $P < .001$; Table 5).

Symptom Outcome Measure: CISS

Because univariate analyses showed that parent-reported attention-deficit/hyperactivity disorder, baseline accommodative amplitude, and baseline accommodative facility were associated with change in the CISS score, these variables and the baseline CISS score were included in the final model as covariates. Although the adjusted

TABLE 3. Baseline demographic and clinical characteristics for all enrolled participants by treatment group

	Vergence/accommodative therapy (n = 206)	Placebo therapy (n = 104)
Sex, female, n (%)	123 (60)	48 (46)
Age (y), mean (SD)	10.8 (1.5)	10.9 (1.4)
Race, n (%)		
American Indian or Alaskan Native	4 (2)	5 (5)
Asian	5 (2)	3 (3)
Black or African American	52 (25)	30 (29)
White	126 (61)	51 (49)
Other	19 (9)	15 (14)
Ethnicity, n (%)		
Hispanic or Latino	77 (37)	38 (37)
ADHD by parental report, n (%)	38 (18)	21 (20)
Spectacle wear, n (%)	42 (20)	38 (37)
Clinical findings		
CISS score, mean (SD)	29.1 (8.5)	30.4 (8.8)
Exodeviation at distance (Δ)*, mean (SD)	2.1 (2.9)	2.1 (3.5)
Exodeviation at near (Δ)*, mean (SD)	9.9 (4.1)	10.0 (4.9)
Near point of convergence break (cm), mean (SD)	13.8 (7.9)	14.9 (8.1)
Near point of convergence recovery (cm), mean (SD)	17.4 (8.7)	18.5 (8.6)
Positive fusional vergence blur (break; Δ)†, mean (SD)	11.6 (4.3)	11.3 (4.1)
Negative fusional vergence blur/break (Δ)†, mean (SD)	12.2 (4.5)	11.9 (4.9)
Near vergence facility (12Δ BI/3Δ BO; cpm), mean (SD)	8.3 (4.5)	8.5 (4.7)
Monocular accommodative amplitude (D), mean (SD)	10.6 (4.5)	10.0 (4.6)
Monocular accommodative facility (cpm) ±2.00 D, mean (SD)	7.5 (4.3)	7.7 (4.7)
Accommodative insufficiency‡, no. (%)	107 (51.9)	63 (60.6)

*Measured with the prism and alternate cover test. †Blur finding; if no blur was reported, and then the break (diplopia) finding was used. ‡Defined as monocular accommodative amplitude less than Hoffstetter's[47] minimal accommodative amplitude criteria minus 2.0 D. Δ = prism diopters; ADHD = attention-deficit/hyperactivity disorder; BI = base-in; BO = base-out; CISS = Convergence Insufficiency Symptom Survey; cpm = cycles per minute.

within-group mean improvements (decrease) in the CISS scores were statistically significant and clinically meaningful for both the vergence/accommodative (11.8) and the placebo therapy groups (10.4; $P < .001$ for the improvements in both groups), there was not a statistically significant mean treatment group difference (1.5 points; 95% CI, –3.8 to +0.8 points; $P = .21$; Table 4).

The proportion of participants meeting CISS success criterion 1 for normal (<16) or improved (≥10-point decrease) symptoms was not statistically different (61.8 vs. 58.7%) in the vergence/accommodative and the placebo therapy groups, respectively (Table 5). Similarly, there was no statistically significant difference using the stricter success criterion 2 (normal and improved ≥10 points); 38.2 and 29.8% of participants in the vergence/accommodative therapy and the placebo therapy groups, respectively, met this criterion ($P = .15$; Table 5).

Composite Outcome Measures

The proportion of participants who met success criterion 3 (composite convergence outcome criterion of both a normal near point of convergence and normal positive fusional vergence) was statistically greater in the vergence/accommodative therapy group (78%) than in the placebo therapy (29%) group ($P < .001$).

A statistically significant greater proportion of participants in the vergence/accommodative therapy group (37%) than in the placebo therapy group (14%) were classified as successful based on success criterion 4 (composite signs and symptoms outcome classification; $P < .001$). Likewise, combining participants classified as successful or improved resulted in a statistically significant greater percentage (61%) of the vergence/accommodative therapy participants than placebo therapy participants (44%) meeting this criterion ($P = .004$).

Fragility Index Assessment

For this study, statistically significant findings were robust for near point of convergence (fragility index, 58), positive fusional vergence (fragility index, 56), the convergence composite measures (fragility index, 76), and the signs and symptoms composite measures (fragility index, 27). We also used the fragility index in a reverse form to identify the required number of vergence/accommodative participants shifting from symptomatic to asymptomatic that would result in a statistically significant finding and found a fragility index of 4. Five participants assigned to vergence/accommodative therapy had a CISS score of 16 at the outcome examination (none in the placebo therapy group

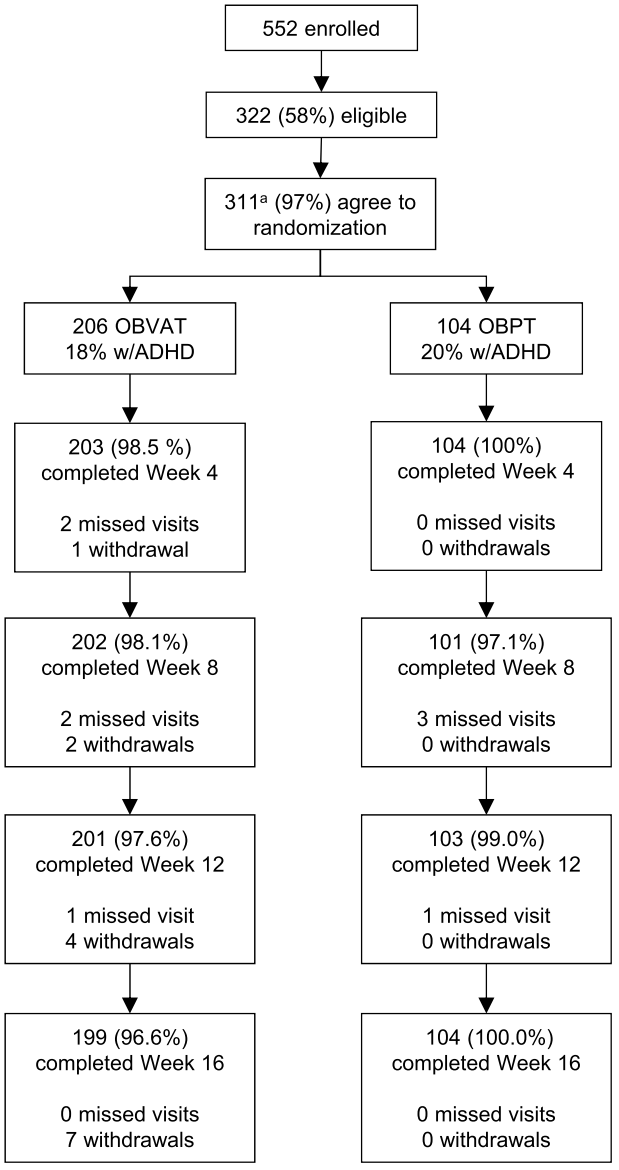

FIGURE 1. Flowchart of CITT-ART randomized clinical trial study visits. CITT-ART = Convergence Insufficiency Treatment Trial–Attention & Reading Trial. [a]One participant was determined to be ineligible after randomization; site's IRB stated no data collected beyond baseline could be used.

scored 16). If four of those five had instead scored 15.5 (or less), the resulting chi-square analysis would have indicated a statistically significant difference between the vergence/accommodative and placebo therapy groups ($P = .04$). This half-point reduction in the CISS score equates to reporting 1 point lower in frequency on 1 of the 15 symptoms.

Adverse Events

No adverse events were reported.

DISCUSSION

This article reports the results for the clinical outcomes (secondary outcomes) from the CITT-ART randomized trial that compared the effectiveness of office-based vergence/accommodative therapy with office-based placebo therapy in improving reading and attention.[16] After 16 weeks of treatment, office-based vergence/accommodative therapy was found to be significantly more effective than office-based placebo therapy in improving the clinical measures of near point of convergence and positive fusional vergence in 9- to 14-year-old children with symptomatic convergence insufficiency. In contrast, the improvements found in symptoms, as measured by the CISS, were not significantly different between the two treatment groups.

The mean improvements in near point of convergence in this study were similar to those found in our previous two trials for both treatment groups (Table 6),[3,4] with only the vergence/accommodative group reaching a normal value (<6 cm; Table 6). The percentages of participants in the present study who met the success criterion that required both an improvement of ≥4 cm and a normal near point of convergence were 74 and 31% for the vergence/accommodative and placebo therapy groups, respectively, similar to the 78 and 20% success rates found in our last trial.[3]

Similarly, the resultant changes in positive fusional vergence in this study were comparable with those found in our previous CITT studies with mean improvements in the vergence/accommodative therapy groups ranging from 19.3 to 22.2Δ across studies (Table 6). In contrast, the mean improvements in the placebo therapy groups ranged from 6.9 to 8.5Δ (Table 6) and were less than the 10Δ threshold that likely represents real change based on the coefficient of repeatability for positive fusional vergence.[32]

The composite convergence measure that considers the change in both the near point of convergence and positive fusional vergence may represent a more robust indication of successful treatment for convergence insufficiency. Paralleling the aforementioned results for the clinical measures alone, the proportions of participants in the vergence/accommodative and placebo therapy groups meeting this criterion in the present study were 78 and 29%, respectively, compared with the 73 and 35% found in our last trial.[3]

Despite consistent treatment outcomes across the CITT studies for near point of convergence and positive fusional vergence, the outcome for the CISS score in the present study was incongruent with our prior two trials. Although the mean CISS reduction of 11.8 points in the vergence/accommodative therapy group was statistically significant and clinically meaningful, it was less than the 22.6- and 14.8-point improvements found in the previous two CITT studies[3,4] (Table 6).

Given that there were statistically significant differences in improvements in both clinical measures of convergence between the vergence/accommodative and placebo therapy groups in the present study and also that there was a statistically significantly greater improvement in symptoms found in the vergence/accommodative therapy group in both of our prior trials (Table 6), the lack of statistical difference between the two treatment groups in the present study is unexpected. Whether this finding is simply due to chance or whether there is another explanation is not certain. Using the CISS, a subjective survey, as a visually-related outcome measure for children has been met with skepticism by some.[33–35] It has been proposed that children's responses in regard to symptom occurrence "when reading or doing close work" may depend on the type of near activity the child is envisioning when queried[33] (e.g., doing homework, playing videogames, or interacting with smart devices) or whether reading is for pleasure or required for school.[33] It is also possible that the increased use of electronic devices may have impacted the validity of the CISS since its development approximately 20 years ago. Finally, comorbid ocular (e.g.,

TABLE 4. Change in outcomes measures at 16 weeks by treatment group

Outcome measure	Vergence/accommodative therapy, mean (95% confidence interval)	Placebo therapy, mean (95% confidence interval)
Near point of convergence break (cm)		
Baseline*	14.0 (12.9 to 15.1)	14.9 (13.3 to 16.5)
Week 16, unadjusted	3.9 (3.5 to 4.4)	8.3 (7.2 to 9.5)
Change from baseline to 16-week outcome, adjusted†	–10.4 (–11.3 to –9.6)	–6.2 (–7.2 to –5.2)
Positive fusional vergence blur or break (Δ) at near‡		
Baseline*	11.5 (10.9 to 12.1)	11.3 (10.5 to 12.1)
Week 16, unadjusted	34.5 (33 to 36)	20.0 (18.3 to 21.8)
Change from baseline to 16-week outcome, adjusted§	23.2 (20.8 to 25.6)	8.8 (6.1 to 11.5)
CISS score		
Baseline*	28.9 (27.7 to 30.1)	30.4 (28.7 to 32.1)
Week 16, unadjusted	17.8 (16.3 to 19.3)	20.0 (17.8 to 22.3)
Change from baseline to 16-week outcome, adjusted¶	–11.8 (–13.4 to –10.3)	–10.4 (–12.4 to –8.4)

*Baseline values for participants who completed 16-week outcome. †Adjusted for baseline near point of convergence and the interaction of baseline near point of convergence with treatment group. ‡The blur finding was used, but if blur was not reported, the break finding was used. §Adjusted for baseline positive fusional vergence. ¶Adjusted for parent-reported attention-deficit/hyperactivity disorder, baseline accommodative amplitude, baseline accommodative facility, and baseline CISS score. CISS = Convergence Insufficiency Symptom Survey.

dry eye and allergies) or even nonocular conditions may result in positive responses on the CISS,[34,35] which could account for the lack of a relationship between the severity of clinical signs and intensity of symptoms as reported by our group and others.[36,37] It may be necessary to revise the CISS for use as an outcome measure in future studies of convergence insufficiency.

Although the improvements in clinical signs were significantly less in the placebo group, it could be speculated that the placebo therapy in the present study was not purely a sham treatment. Although the placebo activities did not involve saccades that imitated reading eye movements or stimulation of accommodation or vergence beyond viewing at ≥40 cm, some procedures involved directed eye movements, and keeping the target clear and single was emphasized in an attempt to mimic vergence/accommodative therapy. Thus, it is possible that both the vergence/accommodative and placebo therapies shared elements responsible for some symptom improvement in both groups.

Improved symptoms could be related to response bias, a placebo effect, or both. Response bias, a well-known phenomenon where study participants want to please the researcher by providing what they think the researcher wants them to report,[38,39] can account for all or part of a subjective treatment response. In addition, it is

TABLE 5. Percentage of participants in each treatment group classified as normal or improved for each outcome measure at the 16-week outcome visit

Outcome	Therapy group	n	Condition			
			% (n)			
Near point of convergence break (cm)			Receded NPC but improved ≥4 cm	Normal NPC but improved <4 cm	Normal NPC and improved ≥4 cm	Normal NPC and/or improved ≥4 cm*
	Vergence/accommodative	198†	9.6 (19)	11.6 (23)	74.2 (147)	95.5 (189)
	Placebo	104	22.1 (23)	14.4 (15)	30.8 (32)	67.3 (70)
Positive fusional vergence blur or break (Δ)			Insufficient PFV but improved ≥10Δ	Normal PFV but improved <10Δ	Normal PFV and improved ≥10Δ	Normal PFV and/or improved ≥10Δ*
	Vergence/accommodative	198†	6.6 (13)	6.1 (12)	79.8 (158)	92.4 (183)
	Placebo	104	3.8 (4)	15.4 (16)	30.8 (32)	50.0 (52)
CISS score			CISS still ≥16 but improved by ≥10 points	CISS <16 but improved <10 points	CISS <16 and improved ≥10 points	CISS <16 and/or improved ≥10 points*
	Vergence/accommodative	199	15.1 (30)	8.5 (17)	38.2 (76)	61.8 (123)
	Placebo	104	22.1 (23)	6.7 (7)	29.8 (31)	58.7 (61)

*Total of three preceding columns. †Missing data for one participant. Δ = prism diopters; CISS = Convergence Insufficiency Symptom Survey; NPC = near point of convergence; PFV = positive fusional vergence.

TABLE 6. CITT-ART outcome results compared with previous CITT studies

	Near point of convergence (cm)		Positive fusional vergence (Δ)		CISS score (points)	
Study	Vergence/accommodative therapy	Placebo therapy	Vergence/accommodative therapy	Placebo therapy	Vergence/accommodative therapy	Placebo therapy
Change from baseline to outcome examination*						
CITT pilot (n = 47)	9.2	6.2	19.3	7.7	22.6	6.5
CITT (n = 218)	10.4	3.9	19.7	6.9	14.8	7.8
CITT-ART (n = 303)	10.0	6.6	22.2	8.5	11.1	10.3
Mean at outcome examination*						
CITT pilot (n = 47)	4.5	9.3	31.8	19.8	9.5	24.2
CITT (n = 218)	4.0	10.3	30.5	17.8	15.0	21.9
CITT-ART (n = 303)	4.0	8.3	33.5	19.6	17.0	20.1

*Twelve weeks of therapy for CITT pilot and CITT; 16 weeks of therapy for CITT-ART. CISS = Convergence Insufficiency Symptom Survey; CITT-ART = Convergence Insufficiency Treatment Trial–Attention & Reading Trial; NPC = near point of convergence; PFV = positive fusional vergence.

not uncommon for participants to become attached to research team members and not want to disappoint their provider who seems invested in the outcome of the trial.[40] Alternatively, there could be a genuine placebo response of symptom amelioration, which is more commonly found when outcomes are based on subjective self-reports[39] and when the participant-provider relationship is supportive and has potentially placebogenic components such as compassion, reassurance, therapeutic optimism, enthusiasm, and collaborative trust.[40–42] The placebo effect has also been reported to be greater when sham treatment involves a more elaborate treatment ritual such as the use of a device or more involved procedures than simply taking a pill.[39,43–45] Furthermore, study participant awareness of a greater likelihood of receiving active treatment in a clinical trial, as was the case in this study, is associated with a smaller separation between treatment groups at outcome.[42,46] Thus, it is possible that a greater improvement in symptoms might be found in children receiving a higher dosage (16 weeks) of one-on-one therapy including computerized and noncomputerized equipment administered by the same caring and supportive doctor. However, without having had a no-treatment group, symptom response cannot be distinguished from the natural course of the disease, regression to the mean, or the effects of other factors such as the aforementioned response bias.[38,39]

The fragility index, a metric that assesses the robustness of statistically significant dichotomous outcomes in randomized clinical trials,[27–31] suggested that our findings were robust for near point of convergence, positive fusional vergence, the composite convergence outcome, and the composite signs and symptoms outcome. However, it suggested that the lack of difference between treatment groups in the CISS score was not robust, in that only four symptomatic participants in the vergence/accommodative group would have needed to convert to asymptomatic (e.g., change in score from 16 to 15) for the difference in the mean CISS scores between the two groups to have reached statistical significance.

Like all studies, our clinical trial had some limitations. A no-treatment group would have helped to clarify the role of natural history of the disease, regression to the mean, response bias, and various placebo effects. However, because of randomization, there is no reason to assume that any of these phenomena would have occurred unequally in our treatment groups and affected the group differences reported. Nonetheless, our placebo group had the advantage of being less susceptible to bias than an unmasked "no-treatment" control group where the participant and investigator would both know that an active treatment was not being received, which can affect self-reported outcomes and the likelihood of participants receiving treatment outside the study.

It is worthwhile to interpret our study in light of the participants enrolled into the study and the therapy regimen prescribed. Although the results apply only to 9- to 14-year-old children with symptomatic convergence insufficiency, the eligibility criteria were broad, allowing the enrollment of children with numerous comorbidities including learning disabilities, attention-deficit/hyperactivity disorder, and mild to moderate reading disorders and those taking various systemic medications.

CONCLUSIONS

Consistent with previous randomized clinical trials, office-based vergence/accommodative therapy was found to result in statistically significant and clinically relevant improvements in clinical measures of convergence ability in children with symptomatic convergence insufficiency. However, in contrast to the prior clinical trials, self-reported symptom severity as measured by the CISS did not correspond with the improvements in convergence function. Thus, the CISS, in its present form, may no longer adequately quantify the change in symptoms attributable to the change in visual function in children with convergence insufficiency.

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