Chapter 5: Recruitment and Eligibility Determination

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Chapter 5: Recruitment and Eligibility Determination

5.1 Recruitment Expectations

Each clinic site is expected to enroll at least 41 but no more than 52 participants over the projected 21-month enrollment period. This translates to an enrollment rate of approximately 2 participants per month. The requirement that participants be attending school at both the baseline and the 16-week outcome examination results in an unconventional recruitment period of only 7 months of the year (August through February). When maximum enrollment has been met for a site, the Site Coordinator and PI will be informed that they no longer need to enroll participants.

Site personnel will be able to continually monitor the recruitment of participants at each clinic site by viewing the recruitment figures accessible on the CITT-ART website. A bar chart will be used to display the total number of participants enrolled at each site (overall and during the last month). An additional line chart will be used to show the expected date of enrollment completion based on the rate of enrollment during the past 30 days and during the entire enrollment period to date. These graphical displays will foster friendly competition between sites.

Sites will be monitored to ensure that the minimal requirements of recruitment are being fulfilled. The CITT-ART Executive Committee has set a minimum recruitment of four participants every two months. At the beginning of each month the Project Coordinator at the DCC will generate a list of sites that did not meet the recruitment requirement over the previous two-month period. This list will be comprehensive (i.e., indicating the total number of consecutive months that recruitment has not been fulfilled). If a site has not met the enrollment requirement for four consecutive months, then that site will be placed on probation. That site will be required to submit to both the Study Chair and the DCC a detailed plan for boosting recruitment. If a site does not meet the requirement for six consecutive months, then that site will be eligible for closure. If closed, the site will be required to complete the treatment and follow-up of all participants previously enrolled. At the time of closing, the CITT-ART Executive Committee will determine if a new clinic site should be added or if the other CITT-ART sites can be asked to boost their enrollment to fulfill the sample size requirement.

5.2 Eligibility Criteria

Table 5-2. CITT-ART Study Eligibility Criteria

Eligibility Criteria
1. Age 9 to 14 years 2. Grades 3 through 8 3. CI Symptom Survey (CISS) score ≥ 16 4. Exophoria at near at least 4△ greater than at far 5. Receded near point of convergence (NPC) of ≥ 6 cm break 6. Insufficient positive fusional vergence (PFV) at near (i.e., failing Sheard's criterion or PFV ≤15△ base-out break) 7. Best-corrected distance and near visual acuity of 20/25 or better in each eye 8. Random dot stereopsis appreciation of 500 seconds of arc or better 9. Wearing appropriate refractive correction (spectacles or contact lenses) for at least 2 weeks prior to final determination of eligibility (Section 5.5.3) 10. Not wearing BI prism or plus add at near for 2 weeks prior to study and for duration of study 11. English is primary language spoken at home or child proficient in English as determined by the school 12. Parental permission to contact the child's teacher(s) for study purposes 13. Parent and child understand protocol and are willing to accept randomization 14. Parent does not expect child to start any new ADHD medicine or change the dose of any currently taken ADHD medicine while child is being treated in the study
Exclusion Criteria
1. Constant strabismus at distance or near 2. Esophoria of ≥ 2Δ at distance 3. Vertical heterophoria ≥ 2Δ at distance or near 4. ≥ 2 line interocular difference in best-corrected distance visual acuity 5. Monocular near point of accommodation >20 cm (accommodative amplitude <5D) as measured by push-up method 6. Manifest or latent nystagmus 7. Word Reading subtest score < 80 on the Wide Range Achievement Test (WRAT-4) 8. Kaufman Brief Intelligence Test (KBIT-2) Matrices subtest score <70 9. History of prior strabismus, intraocular, or refractive surgery 10. CI previously treated with any form of office-based vergence/accommodative therapy or home-based vergence therapy (e.g., computerized vergence therapy) 11. CI associated with head trauma or known disease of the brain 12. Diseases known to affect accommodation, vergence, or ocular motility such as multiple sclerosis, Graves orbitopathy, myasthenia gravis, diabetes mellitus, Parkinson disease 13. Inability to comprehend and/or perform any study-related test or therapy procedure 14. Speech-language disorder (e.g., stuttering) that would interfere with interpretation of digital recordings of reading tests 15. Significant hearing loss 16. Household member enrolled in present CITT-ART or treated within the past 6 months with any form of office-based vergence/accommodative therapy or home-based vergence therapy (e.g., computerized vergence therapy) 17. Household member is an eye care professional, ophthalmic technician, ophthalmology or optometry resident, or optometry student

5.3 Participant Recruitment

The primary recruitment of participants will occur from the patient care clinics of the participating clinic sites. Potential participants will be identified after routine vision examinations at these clinics. Potentially eligible children may also be identified through screenings. In addition, referrals of eligible CI participants will be sought from the surrounding optometric and ophthalmologic communities. Efforts to be implemented to enhance recruitment include a systematic plan to inform potential referral sources of the existence of the study through announcements in national and local publications and mailings to physicians and optometrists in the community along with e-mails and phone calls from investigators to potential referring sources. A pocket size laminated card (the CITT-ART Mini Eligibility Checklist) for easy reference of the study's major eligibility criteria will be available to sites to use for recruitment purposes. A CITT-ART brochure, flyer, email newsletter, and website advertisements will be developed by the CITT-ART Executive Committee. Any clinical site that wishes to use these must first obtain approval from its local IRB. In addition, announcements and study information will be included on searchable public pages on the NEI, College of Optometrists in Vision Development, and participating schools and colleges of optometry, and vision therapy-related websites. Using the methods above, there will be three ways that potentially eligible participants will be identified: 1) internal referrals, 2) external referrals, and 3) advertising.

5.3.1 Maximizing Internal Referral Rate

Based on previous studies completed by CITT personnel, we expect that regular patients at CITT-ART clinic sites will be the majority of those recruited. To maximize the recruitment from the clinical services of each site, the following techniques will be used:

- On at least a quarterly basis, all study personnel will inform other clinicians at his/her site of the study and how to identify potential candidates.
- Presentations will be made to faculty groups, residents, students and support staff educating them about the CITT-ART, eligibility criteria and mechanisms for identification, and referral of participants. A slide presentation will be provided to each CITT-ART clinic site for such presentations.
- Internal e-mails will be used on a regular basis to remind faculty, residents, students and support staff about the CITT-ART.
- Laminated Pocket cards with major CITT-ART eligibility criteria will be provided to sites. Sites can distribute these on an as-desired basis to faculty, residents and students to assist them with identification of potentially eligible participants.

5.3.2 Internal Referral Protocol

When a potentially eligible patient is identified in the clinic, study personnel (Principal Investigator, Site Coordinator, or other investigator) will be notified so that the investigator may speak to the potentially eligible child and his/her family while they are still on site if possible. The clinical trial will be briefly described as well as the intent and description of the eligibility visit. If parental consent and child assent is obtained, an eligibility visit can be scheduled at the family's earliest convenience. If the participant was prescribed a new refractive correction, the eligibility visit will be scheduled no sooner than two weeks after receiving the correction as per CITT-ART protocol**.** If it is not possible for the family to speak with an investigator at that time, the family will be given a CITT-ART brochure.

5.3.3 External Referral Protocol

All clinic sites will make a significant effort to recruit participants from local optometrists and ophthalmologists. Sample letters to eye care providers in the community will be developed by members of the CITT-ART Executive Committee and approved by the individual clinic site Institutional Review Board (IRB).

All mailings, e-mails, and advertisements distributed from the individual clinic sites will contain the Site Coordinator's name, phone number, and e-mail address for contact purposes; therefore, in most cases, the Site Coordinator will be the initial contact person when patients are referred from eye care practitioners in the community. The Site Coordinator will answer any questions that a patient or referring doctor has about the study. Using a designed set of screening questions (e.g., age 9 to 14 years, no history of strabismus surgery, CI is not due to head trauma, no prior vergence/accommodative therapy, no medical diagnosis of diabetes, Grave's disease, myasthenia gravis, etc.), the Site Coordinator can then determine if the participant is potentially eligible and, if appropriate, schedule an Eligibility & CI Baseline Testing visit. Data from our previous CITT studies were used to identify three CI Symptom Survey items most indicative of CI diagnosis and these too will be used in the screening instrument. The Site Coordinator may also mail or fax the participant the IRB-approved CITT-ART brochure and provide the participant with the CITT-ART website address.

5.4 Procedure for Informed Consent/HIPAA Authorization

Parental consent and child assent will be obtained prior to any study-specific testing. The Site Coordinator (or PI or other investigator) will educate the participant about the CITT-ART. Potentially eligible participants and their parent/guardian will be informed about the Eligibility & Baseline testing, the Reading & Attention Baseline exam and all study visits. The family will be given informed consent and assent documents and the opportunity to review these documents. HIPAA authorization will also be obtained. If a cycloplegic refraction was performed at the previous eye examination (within past 12 months) and the results are available, it does not have to be repeated. If the previous cycloplegic refraction was not completed within the prior 12 months, it must be repeated at the Eligibility & CI Baseline Examination.

5.4.1 Informed Consent

The Data and Safety Monitoring Committee may review the CITT-ART consent/ assent form templates from time to time to assure adherence to standards. Site visits performed by the Study Chair and DCC members will include verification of consent documents for each participant enrolled in the study. Each CITT-ART clinic site will meet its Institutional Review Board's requirements for informed consent procedures for minors.

The following steps should be followed when obtaining consent:

1. The parent/guardian will be given a copy of the informed consent document to review while the child will be given an assent form. Every aspect of each document will be explained to the parent and child.
2. It will be emphasized that participation is voluntary and that the family can decline to participate without it adversely affecting his/her future vision care. It will also be explained that the child can withdraw from the study at any time.

3. The investigator providing informed consent will explain that several routine eye care tests and surveys will be administered. It will be explained to the child that the risks associated with testing are the same as if the examination were performed outside the study.
4. Randomization will be explained and the consenting investigator will insure that child and parents/guardians understand that neither the child nor doctor will have a choice regarding treatment assignment. It will be explained that, based on the study design, each child has a 1 in 3 change of assignment to the placebo therapy. Each child and parent/guardian must be willing to accept and comply with whatever treatment is assigned.
5. The child and his/her parent/guardian will be informed that they will not know to which group the child was assigned until participants have completed the 1 year follow up examination.
6. The number and length of visits required will be explained. The duration of the study and the importance of commitment to the 1-year long-term follow-up will be discussed.
7. The amount of home therapy to be done will be explained. The child's availability to complete the study visits will be confirmed.
8. The travel reimbursements will be discussed. Travel reimbursements will be pro-rated based on the number of study visits completed.
9. The child and parent/guardian will be given the opportunity to ask questions.
10. Time will be given to read the informed consent and assent documents.
11. All the questions must be answered. If an answer is not known, follow-up should be promised. Clinic Site personnel may call Dr. Scheiman, CITT-ART Study Chair at 215-692-0897 to obtain the answer and then respond.
12. After obtaining signatures from both the child (assent form) and parent/guardian (informed consent form), copies will be made and provided to the parent/guardian for his/her records. The original informed assent and consent forms are then filed in the participant's CITT-ART study file at the participating clinical site.
13. To protect participant's confidentiality, the consent/assent forms are never sent to the (DCC); forms accidently sent to the DCC will result in a protocol violation.

5.4.2 Special Consent Procedures for Minors (Assent)

Because the inclusion criterion for age includes minors ages 9 to 14 years, special procedures are outlined for potentially eligible participants. Prior to eligibility testing, the minor must provide signed assent. The assent form will be written at an appropriate reading level. Great care must be taken to explain the testing and treatment procedures to both minors eligible for the study and their parent(s)/guardian(s).

5.4.3 HIPAA Authorization

The CITT-ART personnel will discuss in detail with the eligible child and his/her parent/guardian how Protected Health Information (PHI), collected during the exam, treatment visits, and masked examinations will be used, shared and protected during the research. The family will be informed that if they agree to eligibility testing, these data (and potentially reasons for not participating) will be forwarded to the DCC. However, the participant will not be identified to the DCC other than by a code. Audio recordings and results of the reading testing will be sent to the Reading Center at Western University. The participant will be identified by code to the Reading Center. HIPAA authorization will be obtained from the parent/guardian

prior to enrollment and a copy will be provided to the parent/guardian. The original HIPAA form is filed in the participant's CITT-ART file at the clinic site. To protect participant confidentiality, the HIPAA form is never sent to the DCC.

5.5 Eligibility & CI Baseline Testing Visit Procedures

When any member of the CITT-ART team, a referring doctor, or an individual responding to advertising identifies a potential participant, the Site Coordinator schedules an Eligibility & CI Baseline Testing Visit. A list of all testing to be completed at this visit can be found in MOP Chapter 4, Table 4.1. Upon arrival of a potentially eligible child, the following steps are followed:

1. After obtaining informed consent, the Unmasked Examiner administers the CISS, completes the Eligibility Exam form parts 1 and 2, Neurological Checklist form, and then administers test 2 of the CI Symptom Survey (Table 5-2).
2. While clinical testing is completed, the site coordinator should work with the parent/guardian to complete the Personal History, Prescription Medication and Contact Information forms.
3. The information collected during the clinical examination along with responses from the parent is then used to tentatively determine eligibility using the Eligibility Status Checklist form.
4. If it appears that the child is eligible, the Unmasked Examiner should administer the WRAT-4, Curriculum-based Measurements (CBM) and KBIT-2, remembering to record the testing session of the WRAT-4 and CBM for scoring at the Reading Center.
5. While the child completes the WRAT-4, CBM and KBIT-2, the Site Coordinator should also have the parents complete the parent-rated surveys (SWAN, SNAP-IV, ABS and HPC). In addition, the Site Coordinator should collect contact information for the participant's teacher(s).
6. Finally, the information from the Eligibility Status Checklist is entered into the CITT-ART web-based application to signal to both the DCC and Reading Center that a potential participant has been identified.
7. The Unmasked Examiner or Site Coordinator uploads the digital recording of the WRAT-4 Word Reading test and CBM session for scoring using RedCap. Within 48 hours of receipt, personnel at the Reading Center will score the subtest and upload the result to confirm eligibility. At this point, an email will be sent to both the DCC and clinic site to confirm whether the child is eligible.
8. Eligible children will be scheduled (either at the Eligibility & CI Baseline Testing Visit or afterwards by phone or email) for the Reading & Attention Baseline Testing visit.
9. If an eligible child elects not to participate, the Site Coordinator completes the Subject Non-Participation form and the child is referred for possible CI treatment outside of the study.
10. If during testing it is determined that the child is ineligible, the Eligibility & CI Baseline Examination can be stopped. All clinical findings collected up to that point should be recorded on the Eligibility Status Checklist form and this form along with the CISS is faxed to the DCC.
11. The Site Coordinator maintains CITT-ART files for all children tested for inclusion in the study including those determined to be ineligible for the study.

12. The Site Coordinator sends, by fax, all appropriate data forms from eligibility testing to the DCC.

Table 5-2. Eligibility & CI Baseline Testing (testing time ~ 60 minutes)

Measurement
CI Symptom Survey (CISS; test 1)
Visual acuity at distance and near
Random dot stereopsis testing
Cover testing at distance and near
Negative fusional vergence (NFV) at near
Positive fusional vergence (PFV) at near
Near point of convergence (NPC)
Monocular accommodative amplitude (OD only)
Monocular accommodative facility (OD only)
Vergence facility at near
CI Symptom Survey (CISS; test 2)
Curriculum-based measurements (R-CBM and Reading Maze)
WRAT-4 Word Reading subtest
KBIT-2 Matrices subtest
Cycloplegic refraction (if not done in prior 12 months)
Ocular health examination (if not done in prior 12 months)

KBIT = Kaufman Brief Intelligence Test; WRAT= Wide Range Achievement Test

5.5.1 Historical Information

Historical information to be elicited will include: age, date of birth, sex, ethnicity, prior CI therapy (e.g., prism, pencil push-up therapy, VT/orthoptics), pertinent medical history, medication usage and prior spectacle correction. A neurological screening comprised of neuro-ophthalmic symptoms review and general neurological symptoms review will be performed on each participant. The results will be recorded on the Eligibility Neurological Status Checklist form. Positive response on the checklist will render the participant ineligible for the CITT-ART study. The participant should then be referred to an appropriate physician for further evaluation.

5.5.2 Clinical Tests

Protocols for administering each of the clinical/vision tests that will be performed during the Eligibility & CI Baseline Testing visit are described in detail in MOP Chapter 4.

5.5.3 Guidelines for Correction of Refractive Error

The presence of uncorrected refractive error can be an obstacle to comfortable binocular vision and thus the following guidelines regarding the correction of refractive error must be adhered to:

The child must be wearing the appropriate refractive correction (spectacle or contact lenses) if refractive error is present (based on cycloplegic refraction within the last 12 months) that meets the following criteria:

- Myopia more than -0.75D spherical equivalent (SE) in either eye
- Hyperopia more than +2.00D SE in either eye
- SE anisometropia greater than 0.75D
- Astigmatism > 1.00D in either eye

Refractive correction for patients meeting the above refractive error criteria must meet the following guidelines:

- SE anisometropia must be within 0. 75D of the full anisometropic correction
- Astigmatism must be within 0.75D of full correction and axis must be within 6 degrees for astigmatism of 1.00D or greater.
- For hyperopia, the spherical component can be reduced by up to 1.50D at investigator discretion provided the reduction is symmetrical
- For myopia, the SE must be within 0.75D of the full myopic correction

This refractive correction must be worn for at least 2 weeks before eligibility testing can be administered.

5.5.3.1 Use of Contact Lenses

If a child is already wearing contact lenses and a change is required, the CITT-ART will not pay for the new contact lenses.

5.5.3.2 Use of Bifocals

If a participant is currently wearing a bifocal lens (plus add), the CITT-ART investigator must make a decision about the necessity of the bifocal. Participants who must wear bifocals to treat a significant accommodative problem are excluded from CITT-ART. However, if, the CITT-ART investigator's clinical opinion is that the bifocal lenses are not necessary, the child is eligible provided the child is willing to discontinue the use of the bifocal for the duration of the study. If glasses are required to correct for significant refractive error, a new prescription without bifocals will be prescribed without the plus add, however, CITT-ART will not cover the cost of these new glasses. The glasses must be worn at least 2 weeks, after which time the Eligibility & CI Baseline Testing will be repeated.

5.5.3.3 Use of Prism

The use of base-in prism is not permitted in the CITT-ART. A participant who has been wearing prism is excluded from the CITT-ART unless he/she agrees to eliminate the prism from his/her glasses. New glasses will be prescribed (not paid for by the study) without prism and must be worn at least 2 weeks before Eligibility & CI Baseline Testing will be repeated to determine if the child is still eligible.

If more than 1 Δ of vertical prism is required, the participant is excluded from the CITT-ART.

5.6 Determination of Eligibility

After completion of all Eligibility & CI Baseline Testing, the investigator will complete the Eligibility Status Checklist form. All inclusion and exclusion criteria are listed on this form and, therefore, it allows the investigator to quickly identify children who meet all eligibility criteria. After completing the form, the investigator (or Site Coordinator) will log onto the CITT-ART web-based application and enter the data. The software program will then determine if the child is eligible based on the testing to date. The software will also signal both the DCC and the Reading Center that a potential participant has been identified. The investigator should then

upload the recording of the WRAT-4 Word Reading subtest, R-CBM, and Reading Maze for scoring at the Reading Center. Within 48 hours of receipt, the Reading Center will update the enrollment status on the CITT-ART web-based application and eligibility status will be finalized.

Either at the completion of the eligibility examination or via phone, the Site Coordinator will schedule the participant for his/her Reading & Attention Baseline Testing visit which must occur within 21 days of the Eligibility & CI Baseline Examination.

The Eligibility & CI Baseline Examination can be stopped before completion of all testing as soon as it becomes apparent that the patient is ineligible. However, all clinical data collected thus far should be entered onto the Eligibility Status Checklist form, which together with the CISS is faxed to the DCC.

5.6.1 Assignment of Participant Identification Number

Study ID numbers will be assigned to participants and will consist of a two-digit site code, a unique identification number and the participant's first and last initials. The identification numbers are assigned starting at 1001 and numerically increased by one with each potential participant. Use of the participant's first and last initials in the study ID helps sites identify participants more quickly when queried by the DCC. For example, the first participant at The Ohio State University (Clinic Site 02; initials=LM) would be assigned participant ID "02-1001-LM".

5.7 Eligibility & CI Baseline Testing Visit Timeline

All Study sites are expected to follow the time table as shown in Table 5-3.

5.8 Repeating Eligibility & CI Baseline Testing Visit

There may be, due to unforeseen events, occasions when the initial training visit is not completed within 30 days of the Eligibility & CI Baseline Testing Visit. In these cases, clinical testing as performed during the initial eligibility visit must be repeated (CISS test 1 through CISS test 2 on Table 5-2). It is not necessary, however, to repeat the WRAT-4, R-CBM, Reading Maze or K-BIT tests. Parental surveys are also not repeated.

Table 5-3 Timeline from the Eligibility & CI Baseline Examination

Time from	To	Maximum*
Eligibility & CI Baseline Testing	WRAT-4 and KBIT recording transmitted to Reading Center	3 days
	Data forms faxed to DCC	3 days
	Data from Enrollment Checklist entered into enrollment application	3 days
	Reading & Attention Baseline Testing completed	21 days
	Randomization/Initial therapy visit	30 days
	Teacher contacted about participation	5 days
	Teacher-completed surveys received at DCC	21 days
Recording received at Reading Center	WRAT-4 scored and uploaded	48 hrs
Reading & Attention Baseline Testing	Digital files sent to Reading Center	3 days
	Initial therapy visit completed	21 days
Digital files from Reading & Attention Baseline Testing received at Reading Center	Reading test scores uploaded	7 days

*Based on calendar days
†Assuming that both Eligibility & CI Baseline testing and Reading & Attention testing have been completed

5.9 Procedure for Participants Choosing Not to Participate

Eligible participants who decline to participate in the CITT-ART will be asked to complete a CITT-ART Non-participation form. The participant will be asked to provide the reasons for non-participation on this form; however, the participant will not be identified by name on the form. The clinic site will keep a copy of all non-participation forms and periodically review them in order to determine if there are any recruitment issues that need to be addressed. Each non-participation form along with all eligibility forms will be faxed to the DCC. A protocol violation may occur if a clinic site performs eligibility testing and fails to obtain proper documentation of non-participation.

5.10 Informing Other Clinic Sites of Successful Recruitment Strategies

Site Coordinators will discuss recruitment strategies on their monthly conference calls. Successful recruitment campaigns and techniques will be included in a monthly newsletter, generated by the CITT-ART Study Chairman and the DCC. In addition, each PI will give a brief report of his/her clinic's recruitment strategies and the degree of success with those strategies at the annual CITT-ART Full Investigator Group (FIG) meeting.