

Chapter 5: Recruitment and Eligibility	2
5.1 Recruitment Expectations	2
5.2 Eligibility Criteria.....	2
5.2.1 Inclusion Criteria	2
5.2.2 Exclusion Criteria	3
5.3 Subject Recruitment.....	4
5.3.1 Internal Referrals	5
5.3.1.1 Internal Referral Protocol	5
5.3.2 External Referrals	6
5.3.2.1 External Referral Protocol	6
5.3.3 Advertising Referrals.....	6
5.3.3.1 Advertising Referrals Protocol	6
5.4 Procedure for Informed Consent/HIPAA Authorization for Eligibility Examination.....	7
5.4.1 Informed Consent.....	7
5.4.2 Special Consent Procedures for Minors (Assent)	8
5.4.3 HIPAA Authorization	8
5.5 Eligibility Examination Procedures	8
5.5.1 Historical Information.....	9
5.5.2 Tests Administered at the Eligibility Examination.....	10
5.5.3 Guidelines for Correction of Refractive Error	10
5.5.3.1 Use of Contact Lenses	11
5.5.3.2 Use of Bifocals.....	11
5.5.3.3 Use of Prism.....	11
5.6 Determination of Eligibility for Randomized Clinical Trial.....	11
5.7 Assignment of Subject Identification Numbers.....	12
5.8 Procedure for Subjects Choosing Not to Participate.....	12
5.9 Informing Other Clinic Sites of Successful Recruitment Strategies.....	13
Chapter 5 Appendix	14
Sample Letter to Optometrists Requesting Help with Recruitment.....	15
Sample Letter to Ophthalmologists Requesting Help with Recruitment.....	16
Sample CITT Flyer	18
Sample Internal CITT Clinic Site Advertisement.....	19
Sample School Newspaper Recruitment Ad.....	20
Sample Website Advertisement.....	21
Parent/Guardian Informed Consent Form – Eligibility Examination	22
Child Assent Form – Eligibility Examination	25

Chapter 5: Recruitment and Eligibility

5.1 Recruitment Expectations

Each clinic site is expected to enroll at least 25 but no more than 41 subjects over 18 months. This translates to an enrollment rate of a little more than 1 subject per month. The CITT Executive Committee has set the expected enrollment rate of 3 subjects during any two consecutive months. When maximum enrollment has been met for a site, the Site Coordinator and PI will be informed that they no longer need to enroll subjects.

Site personnel will be able to continually monitor the recruitment of subjects at each clinic site by viewing the recruitment figures accessible on the CITT website. A bar chart will be used to display the total number of subjects 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. The Executive Committee hopes that these graphical displays will foster friendly competition between sites.

It is important to monitor sites to be sure that the minimal requirements of recruitment are being fulfilled. The CITT Executive Committee has set a minimum recruitment of three subjects every two months. At the beginning of each month the Project Coordinator at the Data Coordinating Center 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 4 consecutive months, then that site is on probation. That site will be required to submit to both the Study Chair and the Data Coordinating Center a detailed plan for boosting recruitment. If a site does not meet the requirement for 6 consecutive months, then that site will be closed. This site will be required to complete the treatment and follow-up of all subjects previously enrolled.

5.2 Eligibility Criteria

5.2.1 Inclusion Criteria

If the following conditions are satisfied, the subject may be enrolled in the study:

- a. Age: 9 to <18 years. *We eliminated children below the age of 9 years because of their limited ability to respond reliably to subjective testing and treatment procedures. In our preliminary study of the CI Symptom Survey, we found that children age 9 years and older were able to respond reliably. We excluded subjects 18 years of age or older from this trial because children are most commonly treated for CI and the results of our pilot study showed a greater treatment effect in subjects aged 9 to <18 years.*
- b. Sex: *either*
- c. Race: *any*; Ethnicity: *any*
- d. Best corrected visual acuity of $\geq 20/25$ in each eye at distance and near. *Binocular vision can be affected by reduced visual acuity.*
- e. Willingness to wear eyeglasses or contact lenses to correct refractive error, if necessary. *The first step in the treatment of CI is correction of any significant refractive error.*

Because refusal to wear glasses or contact lenses would lead to decreased vision and possibly an adverse effect on binocular vision, we will require all subjects to wear the appropriate refractive correction.

- f. Exophoria at near at least 4Δ greater than at far. *Exophoria at near greater than at distance is part of our definition of CI.*
- g. Insufficient positive fusional convergence (i.e., failing Sheard's criterion or positive fusional vergence (PFV) $\leq 15\Delta$ base-out blur or break) Base-out to blur should be used if present otherwise use base-out to break. *Insufficient PFV is part of our definition of CI.*
- h. Receded near point of convergence (NPC) of ≥ 6 cm break. *A receded NPC is part of our definition of CI.*
- i. Appreciation of random dot stereopsis using a 500 seconds of arc target. *The presence of random dot stereopsis is necessary to perform some of the home therapy procedures associated with VT/Orthoptics.*
- j. CI Symptom Survey score ≥ 16 . *Because the main reason CI subjects seek eye care is symptoms associated with close work, this is an important eligibility criterion. Although asymptomatic CI subjects exist, they are rarely motivated to initiate treatment. Including such subjects would create retention problems.*
- k. Informed consent and willingness to participate in the study and be randomized.
- l. Willing to discontinue wearing a plus-add at near or base-in prism.
- m. If new glasses or a change in prescription is necessary, the subject must be willing to wear the new glasses for two weeks and return for eligibility testing.
- n. Must have had a cycloplegic refraction within the last 2 months.

5.2.2 Exclusion Criteria

- a. CI previously treated with pencil push-up therapy (more than two weeks of treatment). *There are two reasons to exclude these subjects: 1) They may have been unsuccessful because of poor compliance and motivation, and 2) If they were previously unsuccessful it might affect their outcome.*
- b. CI previously treated with home- or office-based VT/orthoptics. *These subjects are excluded because they could possibly become unmasked because they would have knowledge about VT/orthoptics.*
- c. Amblyopia (≥ 2 line difference in best corrected visual acuity between the two eyes). *Amblyopia is known to have a negative effect on binocular vision. Treatment of CI associated with amblyopia may require additional treatments such as occlusion therapy.*
- d. Constant strabismus. *Constant exotropia is an unusual presentation for CI and suggests an etiology different from the typical CI subjects we are studying.*
- e. History of strabismus surgery. *Unstable binocular vision and CI can occur after strabismus surgery for intermittent exotropia. A CI subject with this history suggests an etiology different from the typical CI subjects we are studying.*
- f. High Refractive Error based on cycloplegic refraction: Myopia $\geq 6.00D$ sphere, Hyperopia $\geq 5.00D$ sphere, Astigmatism $\geq 4.00D$. *High degrees of refractive error may be associated with binocular vision problems.*
- g. Anisometropia $\geq 2.0D$ spherical equivalent. *Anisometropia is known to have a negative effect on binocular vision and may complicate the treatment of CI.*
- h. Prior refractive surgery. *The subject's symptoms could be related to complications associated with refractive surgery.*

- i. Vertical heterophoria greater than 1Δ . *A significant degree of vertical heterophoria would be expected to have a negative effect on binocular vision and could be a causative factor of the CI.*
- j. Systemic diseases known to affect accommodation, vergence and ocular motility such as: multiple sclerosis, Graves thyroid disease, myasthenia gravis, diabetes, Parkinson's disease.
- k. Accommodative amplitude <5 D in either eye as measured by the Donder's push-up method. *We want to exclude CI that is associated with a primary accommodative insufficiency (pseudo-CI). The etiology in such cases is different from the typical CI subject we are studying.*
- l. Manifest or latent nystagmus. *Visual acuity will generally be reduced in these cases and the presence of nystagmus would complicate the treatment of CI.*
- m. Developmental disability, mental retardation, attention deficit hyperactivity disorder (ADHD), or learning disability diagnosis in children that in the investigator's discretion would interfere with treatment. *Children with these conditions may be difficult to treat with all treatment modalities. Compliance problems are common and these children may be unable to concentrate and attend for long enough periods of time to be successful with any of the treatment approaches.*
- n. Family or household member or sibling already enrolled in the CITT. *We are concerned that if two household members are randomized, they could share information on their specific treatment options and thus become unmasked.*
- o. Family or household member of an eye care professional, ophthalmic technician, ophthalmology or optometry resident or optometry student. *These individuals may have access to literature or in the course of exposure and conversing lead to unmasking.*
- p. CI secondary to acquired brain injury or any other neurological disorder. *CI has been reported to be a common problem associated with brain injury and indicates an etiology different from the typical CI subjects we are studying.*

5.3 Subject Recruitment

Each clinic site is expected to recruit at least 25 but no more than 41 subjects over 18 months. The primary recruitment of subjects will occur from the patient care clinics at one of the participating clinic sites. Potential subjects will be identified after routine vision examinations at these clinics. In addition, referrals of eligible CI subjects 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, mailings to physicians and optometrists in the community, and phone calls from investigators to potential referring sources. A pocket size laminated card (the CITT Mini Eligibility Checklist) will be distributed for easy reference of the study's major eligibility criteria. In addition, announcements and study information will be included on searchable public pages on the NEI, College of Optometrists in Vision Development, American Academy of Optometry, American Optometric Association, participating schools and colleges of optometry, and vision therapy-related websites.

The three ways that potentially eligible subjects will be identified are: 1) internal referrals, 2) external referrals, and 3) advertising.

5.3.1 Internal Referrals

Based on the CITT Pilot Study we expect that regular patients at CITT clinic sites will form the bulk of those recruited for CITT. To maximize the recruitment from the clinical services of CITT clinic sites, the following techniques will be used at all CITT clinic sites:

1. All study personnel from each CITT clinic site will inform other clinicians at his/her site of the study and how to identify potential candidates on a monthly/quarterly basis.
2. Presentations will be made to faculty groups, residents, students and support staff educating them about the CITT, eligibility criteria and mechanisms for identification, and referral of subjects. A slide presentation will be provided to each CITT clinic site for such presentations.
3. Internal e-mails will be used on a regular basis to remind faculty, residents, students and support staff about the CITT.
4. Laminated Pocket cards with major CITT eligibility criteria will be provided to all faculty, residents and students to assist them with identification of potentially eligible subjects.

5.3.1.1 Internal Referral Protocol

When a patient in the appropriate age range is identified in the clinic as having CI, CITT personnel (Principal Investigator or Site Coordinator) will be notified so that the CITT investigator may speak to the potentially eligible subject while he/she is still on site. The clinical trial will be briefly described as well as the intent and description of the eligibility examination. If the subject consents, an eligibility examination can be performed while the subject is still on site in the clinic. If a CITT examiner is unavailable, the subject has already received eye drops during the eye examination, the subject does not have adequate time to stay for further testing, or the subject was prescribed a new or significant change of refractive correction, the subject will be scheduled for an eligibility examination at the subject's earliest convenience. In cases where a new refractive correction was prescribed, the eligibility examination will be scheduled no sooner than two weeks after receiving the correction as per CITT protocol.

If it is not possible for the subject to speak with CITT Principal Investigator or Site Coordinator, the subject will be given a CITT brochure, and the site coordinator will follow up with the subject by phone to explain the study and schedule the eligibility testing. During the eligibility examination, a CITT examiner will determine eligibility and obtain baseline measurements. If the subject is eligible and interested in the CITT randomized trial, a second informed consent for the trial will be obtained. The baseline data will be entered onto the CITT new subject module of the CITT database. Subjects will be assigned a unique identification number and those willing to participate will be randomized into one of the four treatment groups. Regardless of participation status, the eligibility forms for all subjects who consent to testing will be sent to the DCC.

5.3.2 External Referrals

All clinic sites will make a significant effort to recruit subjects from local optometrists and ophthalmologists. Sample letters to community eye care providers are contained within the appendix of this chapter.

5.3.2.1 External Referral Protocol

All mailings 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 subjects are referred from community eye care practitioners. The site coordinator will answer any questions that a subject or referring doctor has about the study and then confirm if the subject is potentially eligible by verifying the eligibility/exclusion criteria that can be determined verbally (e.g., age 9 to <18 years, no history of strabismus surgery or closed head trauma, no medical diagnosis of diabetes, Grave's disease, myasthenia gravis, etc.). Data from our pilot study were used to identify 3 CI Symptom Survey items most indicative of CI diagnosis. These survey items will also be used to identify potential subjects. If the site coordinator determines that the subject is potentially eligible, she/he will schedule the subject with a CITT examiner for an eligibility examination. In the meantime, the site coordinator will mail or fax the subject the CITT brochure and provide the subject with the CITT website address. As with all subjects, informed consent will be obtained prior to performing the eligibility examination.

5.3.3 Advertising Referrals

The CITT brochure, flyer, newspaper and website advertisements are in the appendix within this chapter. Any clinical site who wishes to use these must first obtain approval from its local IRB. In most cases, people who respond to these advertisements will be contacting the site coordinator and thus the protocol described in section 5.3.1 will be followed.

5.3.3.1 Advertising Referrals Protocol

Any of the following advertising strategies to recruit potential subjects through publicity/advertising can be used:

- Announcements at local, state, and national research and continuing education meetings. A slide presentation will be provided to each Principal Investigator for use in such presentations.
- Website advertisements. Examples are included in the appendix of this chapter.
- Local school system newspapers. Many local school systems have weekly, bi-weekly or monthly newspapers that are distributed to all families. We will place advertisements in these newspapers to allow us to target children.

Copies of these templates can be found in the Appendix of this chapter.

5.4 Procedure for Informed Consent/HIPAA Authorization for Eligibility Examination

After a potentially eligible subject is identified through a vision examination by either an internal or external referral source, the Site Coordinator (or PI) will educate the subject about the CITT. Potentially eligible subjects and their parent/guardian will be informed about the eligibility testing, given an informed consent/assent document and given the opportunity to review the consent/assent document and ask questions. HIPAA authorization will also be obtained. Subjects who provide assent and whose parent/guardian provides consent will be scheduled for an eligibility examination. If a cycloplegic examination was performed at the previous eye examination (within past 2 months) it does not have to be repeated. If the previous cycloplegic refraction was not within the prior 2 months, it must be repeated at the eligibility examination. Consecutive, presenting subjects who satisfy the inclusion and exclusion criteria will be asked to participate in this study.

5.4.1 Informed Consent

The CITT requires that a written informed consent be obtained from each subject's parent / guardian and assent be obtained from the subject prior to eligibility examination as outlined in the proceeding sections. Completion of the eligibility/enrollment examination should take place within 2 months of the patient's last comprehensive examination. If it has been more than 2 months, all clinical testing (including cycloplegic examination) must be repeated to ensure eligibility, appropriateness of refractive correction, and the presence of good ocular health. After completion of the eligibility testing, eligible subjects proceed to enrollment (Chapter 6). The signed consent/assent forms will be kept in the subject's file at the participating CITT clinic site.

To insure high standards for the administration of the study, the Data and Safety Monitoring Committee may review the CITT 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 subject enrolled in the study.

The following steps should be followed when obtaining consent for eligibility testing:

1. The parent/guardian will be given a copy of the informed consent document (See Appendix). Subjects will be given the child 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 subject can decline to participate without it adversely affecting his/her future vision care. It will also be explained that the subject can withdraw from the study at any time.
3. Convergence insufficiency is explained to the subject and parent/guardian, if necessary.
4. The subject and parent /guardian must be informed that we are only determining eligibility for a study on the treatment of CI. An overview of the study will be provided.
5. The clinician should explain that several routine eye care tests along with a questionnaire will be administered. It will also be explained that in order to obtain the most accurate test results, the questionnaire will be repeated and two of the vision tests will be performed three times.
6. It will be explained to the subject that the risks associated with testing are the same as if the examination were performed outside the study.

7. The subject and parent/guardian will be given the opportunity to ask questions.
8. Time will be given to read the informed consent and assent documents.
9. An opportunity to ask questions will be provided.
10. All the questions must be answered. If an answer is not known, and the Clinic Site PI is unable to answer the question, the clinician should admit frankly that it is not known and follow-up should be promised. The Clinic Site calls Dr. Scheiman, CITT Study Chair at 215-276-6057, to obtain the answer and then responds to the subject and parent/guardian.
11. After the subject signs the assent form and the parent/guardian signs the informed consent form, the forms are copied, and the subject and parent/guardian receive a copy of each. The original informed assent and consent forms are then filed in the subject's file at the participating Clinic.
12. To protect subject confidentiality, the consent/assent forms are never sent to the Data Coordinating Center. If signed forms are accidentally sent to the Data Coordinating Center, they are returned and a protocol violation will be issued to the clinic site.

5.4.2 Special Consent Procedures for Minors (Assent)

Because the inclusion criterion for age includes minors ages 9 to <18 years, special procedures are outlined for potentially eligible subjects who are minors. Prior to eligibility testing a signed informed consent must be obtained from the minors' legally authorized guardian. In addition, the minor must provide signed assent. The assent form will be written at an appropriate reading level. All procedures to be performed in the eligibility examination are within the realm of ordinary eye care. 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).

Each CITT clinic site will meet its Institutional Review Board's requirements on informed consent procedures for minors. A sample assent form can be found in the appendix of this chapter.

5.4.3 HIPAA Authorization

The CITT personnel discuss in detail with the subject and his/her parent/guardian how Protected Health Information (PHI), collected during the exam, treatment visits, phone calls, and masked examinations will be used, shared and protected during the research. The subject and parent/guardian will be informed that if the subject agrees to eligibility testing, his/her data (and potentially his reasons for not participating) will be forwarded to a Data Coordinating Center. However, the subject will not be identified to the DCC other than by a code. HIPAA authorization will be obtained from the parent/guardian prior to enrollment/randomization. After the parent/guardian signs the HIPAA form, the form is copied, and the subject receives the copy. The original HIPAA form is filed in the subject's file at the participating clinic. To protect subject confidentiality, the HIPAA form is never sent to the Data Coordinating Center.

5.5 Eligibility Examination Procedures

When any member of the CITT team, a referring doctor, or an individual responding to advertising identifies a potential CI subject, the Site Coordinator schedules an eligibility examination and the following steps are followed:

1. Site Coordinator selects packet of relevant forms and contacts unmasked examiner.
2. PI, Site Coordinator or unmasked examiner explains eligibility testing to the potential subject and obtains informed consent/assent.
3. Along with the parent/guardian, the potential subject is asked to complete the Personal History form, Contact Information form, Consent for Use of Information and Persona form and the Academic Performance form.
4. After obtaining informed consent for eligibility testing, the unmasked examiner completes the Eligibility Exam form parts 1 and 2, administers the CI Symptom Survey, and Eligibility Exam form part 1 and 2, Neurological Checklist form, Eligibility Medication form, and CI Symptom Survey Test 1 and 2 and determines eligibility using the Eligibility Status Checklist form.
5. If during testing it is determined that the patient is ineligible, the examination can be stopped. All available information is entered on the Eligibility Status Checklist form and only this form is faxed to the DCC.
6. Regardless of eligibility status, the Site Coordinator uses the new subject module of the CITT database to enter the information from the Eligibility Checklist form and obtain the subject's identification number. If testing was stopped when it became apparent that the subject was ineligible, the user should enter "unknown" in the Yes/No fields and "999" in the numeric fields for data not obtained.
7. If the subject is eligible and gives informed consent/assent for enrollment in the CITT, the database also provides a group assignment for the subject.
8. The Site Coordinator then uses the scheduling module of the database to receive a full, 12-week appointment schedule. If the subject is in either of the office-based group, the schedule includes all treatment sessions and masked examinations. If the subject is in either of the home-based groups, the initial treatment session, all weekly phone appointments and masked examinations are included in the schedule.
9. The Site Coordinator can work with the subject to ensure that all scheduled study visits are feasible. If necessary, the Site Coordinator can change the date of study visits to better suit the subject's schedule. The changes can only be if they maintain the study visit window specifications.
10. If an eligible subject decides not to participate, the Site Coordinator completes the Subject Non-Participation form and the subject is referred to a licensed eye care professional who is not participating in the CITT for further care.
11. The Site Coordinator maintains files for all subjects including those determined to be ineligible for the study.
12. The Site Coordinator sends all appropriate data forms from eligibility testing to the DCC. Subjects' names must be covered with an ID label prior to sending the forms to the DCC.

5.5.1 Historical Information

Historical information to be elicited will include: age, gender, ethnicity, prior convergence insufficiency therapy (e.g., prism, glasses, 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 subject. The results will be recorded on the Eligibility Neurological Status Checklist form. Positive response on the checklist will render the subject ineligible for the CITT study. The subject must then be referred to a primary care physician for further evaluation.

5.5.2 Tests Administered at the Eligibility Examination

1. CI Symptom Survey (first test performed and repeated after all other tests performed)
2. Cover testing at distance and near
3. Near point of convergence (tested 3 times)
4. Positive fusional vergence at near (tested 3 times)
5. Negative fusional vergence at near (tested 1 times)
6. Accommodative amplitude
7. Accommodative facility
8. A cycloplegic examination is required at the eligibility examination if it has not been performed within 2 months.

Protocols for administering each of these tests are described in detail in Chapter 4.

5.5.3 Guidelines for Correction of Refractive Error

The presence of uncorrected refractive error can be an obstacle to binocular vision and may exacerbate a pre-existing convergence insufficiency or in some cases be an etiological factor. In addition, the CITT inclusion and exclusion criteria make several references to visual acuity and refractive error. It is, therefore, important to specify clear guidelines regarding the correction of refractive error.

The CITT will not pay for new eyeglasses except in the case of patients who have originally been prescribed bifocals or prism glasses as a treatment for their CI. These patients must agree to discontinue wearing the bifocal or prism glasses during the study. Guidelines follow in section 5.5.3.2 and 5.5.3.3.

Each center should establish relationships with opticians to provide the eyeglasses to CITT subjects who need to be refit. This agreement is documented by using the CITT Optician Agreement form. The optician must agree to accept a maximum of \$150.00 towards payment of the eyeglasses (frames and lenses). The optician can be part of the optical center at the clinical site or a cooperating optician outside the institution.

A refractive correction must be prescribed for subjects when the degree of uncorrected refractive error or change in refractive error (based on a cycloplegic refraction performed within 2 months) in either eye:

- A. Differs from the current prescription by greater than or equal to 0.50 D in spherical equivalent for myopia. The full amount of myopia should be prescribed.
- B. Differs from the current prescription by greater than or equal to 0.75 D of astigmatic correction. The full amount of astigmatism should be prescribed.
- C. Differs from the current prescription by greater than or equal to 1.50D in spherical equivalent for hyperopia. To minimize problems with blur due to latent hyperopia and an increase in exophoria, investigators may reduce the prescription up to 1.25 D. If a subject is hyperopic and the investigator plans to reduce the correction, the identical amount of

plus should be reduced symmetrically in both eyes to ensure that the full amount of anisometropia is corrected.

- D. When the degree of anisometropia is greater than or equal to 0.75 D in spherical equivalent or greater than or equal to 1.50 D of meridional difference. The full amount of anisometropia should be prescribed. If a subject is hyperopic and the investigator plans to reduce the correction, the identical amount of plus should be reduced symmetrically in both eyes to ensure that the full amount of anisometropia is corrected.

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 subject is already wearing contact lenses and a change is required, the CITT will not pay for the new contact lenses.

5.5.3.2 Use of Bifocals

If a subject is currently wearing a bifocal lens, the CITT investigator must make a decision about the necessity of the bifocal. Subjects who must wear bifocals to treat a significant accommodative problem are excluded from CITT. However, if, in the CITT investigator's opinion, the bifocal is not necessary, the subject will be eligible for CITT. The subject must then agree to change his/her glasses and eliminate the bifocal. In such cases, new glasses will be prescribed without the bifocal and these glasses will be covered by the CITT. The glasses must be worn at least two weeks after which time all eligibility testing will be repeated. If the subject still meets eligibility criteria, randomization will occur and treatment will begin.

5.5.3.3 Use of Prism

The use of base-in prism is not permitted in the CITT. A subject who has been wearing base-in prism to treat a CI is excluded from the CITT unless he/she agrees to eliminate the prism from his/her glasses. New glasses will be prescribed (paid for by the study) without prism and must be worn at least 2 weeks before eligibility testing can be repeated to determine if the subject still meets eligibility criteria.

Less than or equal to 1 Δ of vertical prism is permitted. However, if more than 1 Δ of vertical prism is required, the subject is excluded from the CITT.

5.6 Determination of Eligibility for Randomized Clinical Trial

After the eligibility examination, the CITT investigator will complete the Eligibility Status Checklist form. All inclusion and exclusion criteria are listed on this form and, therefore, it allows the clinician to quickly identify subjects who meet all eligibility criteria.

If sometime during the eligibility examination it is determined that the patient is ineligible testing can be stopped. All available data is entered onto the Eligibility Status Checklist form. After

accessing the new subject module and obtaining a CITT ID number, only the Eligibility Status Checklist form is faxed to the DCC.

CITT Clinic Site personnel are informed at the beginning of the study and at annual CITT group meetings that randomization of an ineligible subject is a serious protocol violation. As an additional safeguard, the CITT new subject module is designed to notify the Site Coordinator whether or not the subject is eligible for CITT according to the data entered and only eligible subjects are randomized. The DCC Principal Investigator or CITT study chair may be contacted when there are questions regarding eligibility.

5.7 Assignment of Subject Identification Numbers

After eligibility testing is completed, the Site Coordinator logs onto the CITT new subject module and enters the subject data. To access the CITT database, the Site Coordinator must key in his or her unique identifier and password. It is then necessary to enter the subject's first and last initials (used to create a unique subject identifier) and respond to questions that are shown on the CITT Eligibility Checklist. The software will then determine if the subject is eligible to participate. If so, the coordinator will be queried as to the subject's willingness to be randomized. If the subject is willing, the treatment group assignment will be displayed on the screen along with the subject's unique identification number. The first treatment session will then be scheduled. This first treatment session must occur within 30 days of the eligibility examination although every effort will be made to schedule it within 7 days. For those subjects ineligible for the study or those who choose not to be randomized, the new subject module will display the subject's unique identification number only. Subjects who choose not to participate in the study will be asked to complete the non-participation form. This information will be used to track reasons for nonparticipation in the study and could be used to enhance the information used to educate subjects about the study.

Study ID numbers will be assigned to subjects and will consist of a two-digit site code, a unique subject number and the subject's first and last initials. The subject numbers are assigned starting at 1001 for those subjects who agree to be randomized and 1501 for all other subjects. With each additional subject, the subject number is incremented by one. Use of the subject's first and last initials in the study ID helps sites identify subjects more quickly when queried by the Data Coordinating Center. For example, the first eligible subject at The Ohio State University (Clinic Site 02) who agrees to randomization (initials=LM) would be assigned subject ID "02-1001-LM". In contrast, if this same person was ineligible or did not wish to be randomized the subject ID would be assigned as "02-1501-LM".

5.8 Procedure for Subjects Choosing Not to Participate

Eligible subjects who decline to participate in the CITT will be asked to complete a CITT Non-participation form. The subject will be asked to provide the reasons for non-participation on this form; however, the subject 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 Data Coordinating Center. A protocol violation may occur if a clinic site performs eligibility testing and fails to obtain proper documentation.

5.9 Informing Other Clinic Sites of Successful Recruitment Strategies

Principal investigators will discuss recruitment strategies at monthly conference calls chaired by the CITT Study Chair. Successful recruitment campaigns and techniques will be included in a monthly newsletter, generated by the CITT Study Chairman and the Data Coordinating Center. In addition, each CITT Principal Investigator will give a brief report of his/her clinic's recruitment strategies and the degree of success with those strategies at the annual CITT FIG meeting.

Chapter 5 Appendix

Sample Letter to Optometrists Requesting Help with Recruitment

Dear Dr.

We are pleased to announce our involvement in the Convergence Insufficiency Treatment Trial (CITT) - a randomized, masked, placebo controlled, clinical trial funded by the National Eye Institute, a division of the National Institutes of Health. Despite the high prevalence and symptoms associated with convergence insufficiency, the best treatment for this disorder is unknown. The CITT is a national multi-centered, collaborative research project designed: 1) to determine the best treatment for convergence insufficiency, 2) to develop more precise estimates of the success rates of convergence insufficiency treatment; and 3) to identify factors that may be associated with successful treatment of convergence insufficiency. Participating clinical study centers include:

- Bascom Palmer Eye Clinic, Miami, FL
- Mayo Clinic Department of Ophthalmology, Rochester, MN
- NOVA School of Optometry, Ft. Lauderdale, FL
- The Ohio State University, College of Optometry, Columbus, OH
- Pennsylvania College of Optometry, Philadelphia, PA
- Ratner Children’s Eye Center – University of California, San Diego, CA
- Southern California College of Optometry, Fullerton, CA
- State University of New York, College of Optometry, New York, NY
- University of Alabama, College of Optometry, Birmingham, AL

We are recruiting eligible patients with symptomatic convergence insufficiency between the ages of 9 to < 18 years to participate in this study. Approximately 208 subjects will be entered into the study and cared for by participating study centers. There will be 12 weeks of active treatment for each subject and an additional 12 months of follow-up. Subjects who remain symptomatic at the end of the active treatment phase will receive an alternative treatment at no cost. There will be no fee for any of the treatment visits. Participants will be partially compensated for time/travel cost incurred.

We are trying to establish a select number of local doctors who will refer patients for this study. I invite you to consider referring potential candidates to us. This would be of great value in helping us recruit subjects for this study. It would also be a valuable service to your patients because they would be eligible to receive treatment for convergence insufficiency at no cost.

Thank you for your consideration. If you have any questions, would like further information, or are interested in referring patients for the CITT Study, please give me a call at XXX-XXX-XXXX.

Sincerely,
XXXXXXXXXXXXXXXXXX, OD
Principal Investigator
CITT Clinical Center

Sample Letter to Ophthalmologists Requesting Help with Recruitment

Dear Dr.

I am pleased to announce our involvement in the Convergence Insufficiency Treatment Trial (CITT) - a randomized, masked, placebo controlled, clinical trial funded by the National Eye Institute, a division of the National Institutes of Health. Despite the high prevalence and symptoms associated with convergence insufficiency, the best treatment for this disorder is unknown. The CITT is a national multi-centered, collaborative research project developed by a group of both pediatric ophthalmologists and optometrists. Participating clinical study centers include:

Bascom Palmer Eye Clinic, Miami, FL
Mayo Clinic Department of Ophthalmology, Rochester, MN
NOVA School of Optometry, Ft. Lauderdale, FL
The Ohio State University, College of Optometry, Columbus, OH
Pennsylvania College of Optometry, Philadelphia, PA
Ratner Children's Eye Center – University of California, San Diego, CA
Southern California College of Optometry, Fullerton, CA
State University of New York, College of Optometry, New York, NY
University of Alabama, College of Optometry, Birmingham, AL

The objectives of the CITT are: 1) to determine the best treatment for convergence insufficiency, 2) to develop more precise estimates of the success rates of convergence insufficiency treatment; and 3) to identify factors that may be associated with successful treatment of convergence insufficiency.

We are recruiting eligible patients with symptomatic convergence insufficiency between the ages of 9 to < 18 years to participate in this study. Approximately 208 subjects will be entered into the study and cared for by participating study centers. There will be 12 weeks of active treatment for each subject with an additional 12 months of follow-up. Subjects who remain symptomatic at the end of the active treatment phase will receive an alternative treatment at no cost. There will be no fee for any of the treatment visits. Participants will be partially compensated for their time/travel costs incurred.

As you may know, there is no consensus regarding the most effective treatment for CI. The two most common treatments are “pencil push-ups” and vision therapy/orthoptics. Significant differences exist between the two procedures in cost and number of visits required, with pencil push-ups the less expensive alternative.

The quality of the currently available vision therapy research literature has been widely criticized. We have developed a rigorous study design that takes these criticisms into consideration. Our hope is that this clinical trial will provide quality data about the treatment of convergence insufficiency.

We are trying to establish a select number of local doctors who will be willing to refer potential patients for this study.

I invite you to consider referring potential candidates to us. This would be of great value in helping us recruit subjects for this study. It would also be a valuable service to your patients because they would be eligible to receive treatment for convergence insufficiency at no cost.

Thank you for your consideration. If you have any questions, would like further information, or are interested in referring patients for the CITT Study, please contact me at XXX-XXX-XXXX. Sincerely,

XXXXXXXXXXXXXXXXXXXX

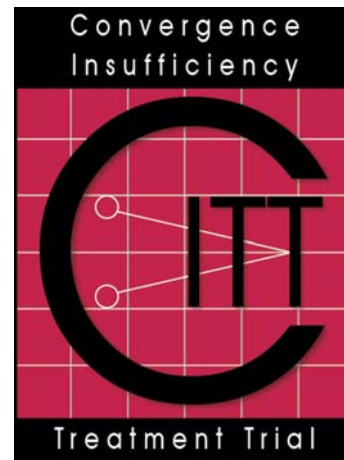
Principal Investigator

CITT Clinical Center

Sample CITT Flyer

When You Read.....Do You Have?

- Eyestrain
- Headaches
- Tired eyes
- Blur
- Words moving, jumping, or appearing to float on the page
- Poor concentration
- Frequent loss of place



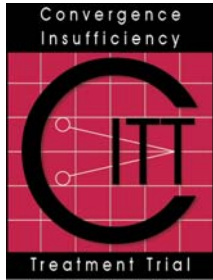
If so, you may qualify for a research study comparing treatments for an eye-teaming problem called convergence insufficiency. Qualified persons (9 to < 18 years of age) will receive free treatment. The treatment program is 12 weeks in length with a 6 and a 12-month follow-up examination (15 months total). Subjects will be paid at most a total of \$410 after the completion of all treatment/follow-up exams, to partially compensate for time/travel costs incurred.

For further information or to schedule a vision screening to see if you qualify, please contact:

Name
Institution
Phone
E-mail

Supported by the National Eye Institute, National Institutes of Health, Department of Health and Human Services

Sample Internal CITT Clinic Site Advertisement



Convergence Insufficiency Treatment Trial

Recruitment is underway for a NIH-sponsored study...

The Convergence Insufficiency Treatment Trial (CITT) was developed to investigate the best treatment for convergence insufficiency.

The study is conducted at several institutions across the United States and is supported by a grant from the National Eye Institute, National Institutes of Health, and the Department of Health and Human Services. Approximately 208 subjects will be entered into the study and cared for by participating eye doctors.

Study Specifics

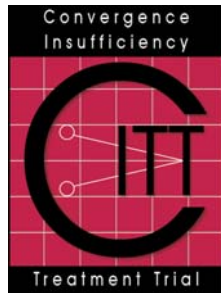
- Subjects between the ages of 9 to <18 years with symptomatic convergence insufficiency
- Random assignment to either Home-based Pencil Push-ups, Home-based Pencil Push-ups with Computer VT/Orthoptics, Office-based Vision Therapy/Orthoptics, or a control group
- Active treatment phase of 12 weeks
- Follow-up period of 12 months after completion of active treatment phase
- Exclusion criteria include: strabismus, amblyopia, nystagmus, or any convergence insufficiency subject previously treated with pencil push-ups or vision therapy.
- Eligible subjects who enroll will receive all treatment visits and therapy equipment at no cost and up to a maximum of \$410 to partially defray travel costs incurred.

How Can I Help?

- Your assistance is needed in referring symptomatic convergence insufficiency subjects between the ages of 9 to <18 years.
- Referrals can be sent to the investigators listed below or for more information, please contact:

Principal Investigator
CITT Clinical Center
Address
Phone

Sample School Newspaper Recruitment Ad



Supported by grants from the National Eye Institute, National Institutes of Health, Department of Health and Human Services

When You Read...Do You Have?

- Eyestrain
- Double vision
- Headaches
- Tired eyes
- Blur
- Words moving, jumping, or appearing to float on the page
- Poor concentration
- Frequent loss of place

If so, you may qualify for a research study comparing treatments for an eye-teaming problem called **convergence insufficiency**. Qualified persons (9 to < 18 years of age) will receive free treatment plus up to a maximum of \$410 to defray travel costs. The treatment program is 12 weeks in length with 12 months of follow-up.

For further information or to schedule a free vision screening to see if you qualify, please contact:

Principal Investigator

CITT Clinical Center

Address

Phone

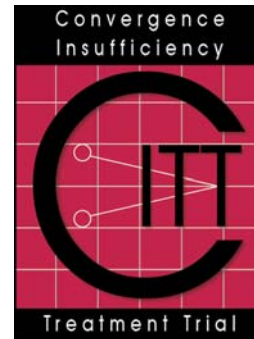
www.optometry.ohio-state.edu/citt

Sample Website Advertisement

RESEARCH SUBJECTS NEEDED FOR VISION THERAPY STUDY

When You Read.....Do You Have?

- Eyestrain
- Headaches
- Tired eyes
- Blur
- Words moving, jumping, or appearing to float on the page
- Poor concentration
- Frequent loss of place



If so, you may qualify for the CONVERGENCE INSUFFICIENCY TREATMENT TRIAL (CITT). The study is supported by a grant from the National Eye Institute, National Institutes of Health, Department of Health and Human Services. This study is comparing treatments for an eye-teaming problem called convergence insufficiency in order to compare commonly used treatments. Qualified persons (9 to <18 years of age) will receive **FREE treatment** (treatment program is 12 weeks in length with 12 months of follow-up after completion of treatment). Subjects are also incrementally compensated a total of \$410 to partially compensate for time/travel costs incurred.

Study sites are located in Alabama, California, Florida, Minnesota, New York, Pennsylvania and Ohio

For further information please contact:

Principal Investigator

CITT Clinical Center

Address

Phone

or

Go directly to the CITT Website for information

www.optometry.ohio-state.edu/citt/

NOTE: Grade 8.0 level

Parent/Guardian Informed Consent Form – Eligibility Examination
(Name of Institution)
Convergence Insufficiency Treatment Trial

DESCRIPTION OF STUDY

1. Introduction

You have been asked to let your child take part in a national multi-center research study. The study is funded by the National Eye Institute (NEI). The NEI is a part of the National Institutes of Health, which is the branch of the federal government that funds medical research. The NEI has reviewed this study to make sure that the science is good. In addition, it is providing the funding for the study.

First, we want you to know that having your child take part in this study is up to you. You may choose not to let your child to take part. In addition, you may remove your child from the study at any time without penalty or loss of eye care.

What follows is a description of the research study. Before you decide whether to have your child take part, please take as much time as you need to ask any questions of the doctor and staff. In addition, you may talk about this study with family, friends, or your family doctor.

2. Information about the Study

The eye exam that your child had recently, showed that your child may have convergence insufficiency (CI). CI is an eye-teaming problem in which the eyes would like to turn out when a person is reading or doing close work. If the eyes actually turn out, the person has double vision. To stop double vision from happening one must make extra effort to make the eyes turn back in. This added effort can cause symptoms that can affect reading and working at near. These symptoms include eye strain, blurred vision, mild to moderate headaches, double vision, difficulty concentrating, and loss of place when reading or doing tasks at near.

The purpose of this visit is only to see if your child might qualify for a study designed to figure out the best treatment for CI.

Each clinic site will enroll about 25 children to participate in this research study.

3. Study Procedures

Your child's eye doctor feels that your child might qualify for a study designed to look for the best treatment for CI. To figure this out, we need to do some more eye tests. The tests will measure how well your child's eyes can focus and work together as a team. We will test your child's eyes using eye charts, lenses, and using other standard eye tests. In addition, we may need to check your child's prescription after putting eye drops in his/her eyes. All of these tests are routine eye tests and take about one hour to complete. Your child will also have to answer a short survey about his/her eyes. You will be asked a few questions about your child's school performance.

Parent/Guardian Informed Consent Form – Eligibility Examination

Your child may need glasses for the first time or may need a change in glasses. If this is the case, then we will ask your child to wear the new eyeglasses for two weeks. After this time, we will repeat the testing just described.

4. Risks

The risks from this eye exam are the same whether your child had the eye exam as part of this study or not. For each of the eye tests to be done, the risks include mild headaches, eyestrain, and blurred vision during and right after the testing. If your child receives eye drops, he/she may have blurry vision for about 4-8 hours. Sometimes people feel uncomfortable for 10-15 minutes after the testing is finished. There are no known serious or long-lasting risks associated with this study.

Although we have tried to list all possible risks and discomforts, there may be others that we do not know about at this time. However, these unknown risks would be the same whether your child was part of this study or not.

5. Benefits

Your child may not directly benefit from taking part in this phase of the study. However, the results of this study may directly affect the eye care of children who develop CI in the future.

6. Confidentiality

All data from the study will be kept confidential in a separate record. A copy of the data will be kept and evaluated at a central Data Coordinating Center at the Ohio State University. The Data Coordinating Center will not know your child's name, since all information kept there will be by patient ID number only. However, 100% confidentiality cannot be promised, as research records can be requested by court order.

Results of the study may be reported in vision journals and may be presented at meetings. However, at no time will any patient in the study be named.

Our Site Coordinator will have the contact information that you give us in case he/she needs to contact you.

7. Costs and Compensation

There is no charge to you for this visit. You will be given a \$20 American Express check at the end of the visit. This is to help cover time and travel costs.

8. Research-Related Injuries

It is unlikely that your child would be physically injured by being in this study. However, if this happened, medical treatment is available, but you or your insurance company would have to pay for the treatment. There are no payments for lost wages and/or direct or indirect losses. The (Name of Institution) will not pay for medical costs or for research-related injuries. Further information about research-related injuries is available from the (Name of IRB Chair) (Office of the Institutional Review Board) at (IRB Chair Telephone).

Parent/Guardian Informed Consent Form – Eligibility Examination

9. Right to Refuse or Withdraw

You understand that if you do not let your child take part in this study your child can still get eye care at the (Name of Institution). You know that you are free to

change your mind; you can stop your child's participation in this study at any time and no one will hold it against you.

10. Questions

(Name of PI) is in charge of this study at (Name of Institution). In your child has discomfort or other symptoms, or you have any other questions about the study, (Name of PI) can be reached at (PI Telephone) *or* the Study Coordinator (*name*) *at* (*phone number*). If (Name of PI) or (Study Coordinator) cannot be reached or if there is an emergency, the (Name of Institution) can be reached at the following emergency number: (*Emergency telephone*).

You have been given the chance to ask any questions. All your questions have been answered to your liking. You have also had the chance to talk with any person outside of (Name of Institution) and to ask his/her opinion and recommendations.

If you have questions about your child's rights as a research subject, you should call the person in charge of the Institutional Review Board (Name of IRB Chair) (IRB Chair Telephone).

11. Your Obligation to the Study

As said before, your child's taking part in this study is voluntary. If you decide for your child to take part, you can quit the study at any time and ask that we no longer contact you. If you have any doubts about this or any questions about the study now or in the future, you should speak with (Name of PI) (PI Telephone)

Please keep a copy of these papers in case you want to read it again. You will be given a signed and dated copy of this form to keep.

Your signature, below, will mean that you have decided for your child to take part in this research study. It also means that you have read and understand the information above.

Patient's Name Printed _____

Parent/Guardian Name Printed _____

Parent/Guardian Signature

Date

Investigator's Signature

Date

Reading Level 7.1

Child Assent Form – Eligibility Examination
(Name of Institution)
Convergence Insufficiency Treatment Trial

Purpose of the Study: The last doctor you saw thinks you might have an eye problem called convergence insufficiency or CI. CI is an eye-teaming problem where the eyes would like to turn out when reading or doing close work. If the eyes really turn out, double vision happens. To stop double vision from happening one must try hard to make the eyes turn back in.

We are doing a study called CITT to figure out the best treatment for CI. The study will include about 208 children across the United States. In order to see if you are the right person for this study, we need to do some vision testing. If you turn out to have CI, you may be able to get 12 weeks of free treatment.

Study Procedures: If the doctors think that you might be able to be in the CITT study, and you want to be in the CITT study, you will sign this form. Then the doctors will do a few eye tests. The eye tests will be done at (Name of Institution). The doctor will test your eyes with an eye chart, special lights, and lenses to find out if your eyes are focusing and working well together as a team. For example, while you look at small letters the eye doctor will ask you if the letters become blurred or double. Also, we may need to check your prescription after putting eye drops in your eyes. All of these tests are routine eye tests. You will also have to answer a short survey about your eyes.

If the doctor finds that you need glasses for the first time, or if your glasses need to be changed, you will have to wear these glasses for two weeks and come back. When you come back, the doctor will repeat the eye tests.

Benefits: After the doctor does the eye exam, the doctor will let you and your parents know if you have CI. If you have CI, you may be able to get free treatment. Signing up for this brief study does not guarantee that your eyes will get better. The results from the study may help other kids who get CI in the future.

Risks: You have been told that the eye tests are just like regular eye tests that you would receive even if you were not in the study. There is a very small chance that your eyes may feel tired or strained during testing. Also, if you receive eye drops your eyes will be blurry for about 4-8 hours. However, you understand that the testing will not do anything that can hurt you in any way.

Confidentiality: The doctors will not tell anyone the results of the eye tests except for your parents. Also, we will use a code number so the people who work where all the results are sent will never know your name.

You know that you do not have to be in this study if you do not want to. In fact, you can refuse any of the eye testing at any time. If you enroll in the study, you can also change your mind later if you want to stop.

Questions: If you or your parents have any questions, you can call the doctor in charge (Name of PI) at (PI Telephone). You may also call (Name of IRB Chair) who watches over the research projects at (Name of Institution) at (Phone).

You have been given a chance to ask all the questions you have, and all of your questions have been answered. Again, the research project is voluntary and if you do not want to be in it, you do not have to. Your signature below means that you have decided to volunteer for this research study and that you have read and understood the information written above.

Patient's Name Printed _____

Patient Signature

Date

Investigator's Signature

Date