Non-surgical interventions for convergence insufficiency (Review)

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[Intervention Review]

Non-surgical interventions for convergence insufficiency

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ABSTRACT

Background

Convergence insufficiency is a common eye muscle co-ordination problem in which the eyes have a strong tendency to drift outward (exophoria) when reading or doing close work. Symptoms may include eye strain, headaches, double vision, print moving on the page, frequent loss of place when reading, inability to concentrate, and short attention span.

Objectives

To systematically assess and synthesize evidence from randomized controlled trials (RCTs) on the effectiveness of non-surgical interventions for convergence insufficiency.

Search strategy

We searched *The Cochrane Library*, MEDLINE, EMBASE, Science Citation Index, the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com) and ClinicalTrials.gov (www.clinicaltrials.gov) on 7 October 2010. We manually searched reference lists and optometric journals.

Selection criteria

We included RCTs examining any form of non-surgical intervention against placebo, no treatment, sham treatment, or each other.

Data collection and analysis

Two authors independently assessed eligibility, risk of bias, and extracted data. We performed meta-analyses when appropriate.

Main results

We included six trials (three in children, three in adults) with a total of 475 participants. We graded four trials at low risk of bias.

Evidence from one trial (graded at low risk of bias) suggests that base-in prism reading glasses was no more effective than placebo reading glasses in improving clinical signs or symptoms in children.

Evidence from one trial (graded at high risk of bias) suggests that base-in prism glasses using a progressive addition lens design was more effective than progressive addition lens alone in decreasing symptoms in adults. At three weeks of therapy, the mean difference in Convergence Insufficiency Symptoms Survey (CISS) score was -10.24 points (95% confidence interval (CI) -15.45 to -5.03).

Evidence from two trials (graded at low risk of bias) suggests that outpatient (or office-based as used in the US) vision therapy/orthoptics was more effective than home-based convergence exercises (or pencil push-ups as used in the US) in children. At 12 weeks of therapy, the mean difference in change in near point of convergence, positive fusional vergence, and CISS score from baseline was 3.99 cm (95% CI 2.11 to 5.86), 13.13 diopters (95% CI 9.91 to 16.35), and 9.86 points (95% CI 6.70 to 13.02), respectively.

In a young adult population, evidence from one trial (graded at low risk of bias) suggests outpatient vision therapy/orthoptics was more effective than home-based convergence exercises in improving positive fusional vergence at near (7.7 diopters, 95% CI 0.82 to 14.58), but not the other outcomes.

Evidence from one trial (graded at low risk of bias) comparing four interventions, also suggests that outpatient vision therapy/orthoptics was more effective than home-based computer vision therapy/orthoptics in children. At 12 weeks, the mean difference in change in near point of convergence, positive fusional vergence, and CISS score from baseline was 2.90 cm (95% CI 0.96 to 4.84), 7.70 diopters (95% CI 3.94 to 11.46), and 8.80 points (95% CI 5.26 to 12.34), respectively. Evidence was less consistent for other pair-wise comparisons.

Authors' conclusions

Current research suggests that outpatient vision therapy/orthoptics is more effective than home-based convergence exercises or homebased computer vision therapy/orthoptics for children. In adult population, evidence of the effectiveness of various non-surgical interventions is less consistent.

PLAIN LANGUAGE SUMMARY

Non-surgical treatments for eyes with convergence insufficiency

Convergence insufficiency is a common eye muscle co-ordination problem in which the eyes have a strong tendency to drift outward (exophoria) when reading or doing close work. This systematic review aimed to search for, assess, and synthesize evidence from randomized controlled trials (RCTs) on the effectiveness of non-surgical interventions for convergence insufficiency.

We included six RCTs conducted in the United States with a total of 475 participants. We assessed four trials at low risk of bias. Evidence suggests that:

1. Base-in prism reading glasses was no more effective than placebo reading glasses in improving clinical signs or symptoms in children;

2. Outpatient vision therapy/orthoptics is more effective than home-based convergence exercises or home-based computer vision therapy/orthoptics in improving clinical signs and symptoms in children; and

3. The effectiveness of various non-surgical interventions in adult population is less consistent.

BACKGROUND

Description of the condition

Convergence insufficiency is a common binocular vision disorder (eye muscle co-ordination problem) in which the eyes have a strong tendency to drift outward (exophoria) when reading or doing close work. As a result the eyes do not converge adequately and this condition may lead to symptoms including eye strain, headaches, double vision, print moving on the page, frequent loss of place when reading, inability to concentrate, and short attention span. Convergence insufficiency is diagnosed when exophoria is greater at near than at distance and the patient has one or both of the following: a remote near point of convergence or decreased positive fusional vergence.

There is considerable variability in the reported prevalence of convergence insufficiency. The estimates of prevalence based on population studies range from 2.25% to 8.3% (Letourneau 1979; Letourneau 1988; Porcar 1997; Rouse 1999). There is a paucity of data regarding whether the prevalence of convergence insufficiency varies by ethnicity, race, age, sex, geographic location, or socioeconomic status.

Description of the intervention

Various non-surgical treatments are prescribed for treating convergence insufficiency including base-in prism reading glasses, homebased convergence exercises (or pencil push-ups as used in the US), home-based vision therapy/orthoptics, and outpatient (or officebased as used in the US) vision therapy/orthoptics (Chin 1995; Gallaway 2002; Griffin 2002; Grisham 1998; Hugonnier 1969; Pratt-Johnson 2001; Press 1997; Scheiman 2002a; Scheiman 2002b; von Noorden 1994; von Noorden 1996). Although surgery is a potential treatment option for convergence insufficiency, it is rarely used because of the comparative invasive nature of surgery with its potential complications.

Base-in prism reading glasses

There are various methods for determining the amount of prism to prescribe (Scheiman 2008). In a Convergence Insufficiency Treatment Trial (CITT) trial of children nine to 17 years of age (CITT 2005a), the investigators prescribed prism based on Sheard's Criterion (Sheard 1930). This criterion states that the magnitude of the prism should be sufficient to insure that the compensatory fusional vergence is equal to twice the magnitude of the phoria. The adult base-in prism study (Teitelbaum 2009) based the prescription of prism on the associated phoria measurement.

Home-based convergence exercises

The home-based convergence exercises are described by Duke-Elder (Duke-Elder 1973). "Exercises to improve the near point of convergence are carried out simply by the subject holding a target at arm's length and then gradually bringing it towards the eye, all the time maintaining bifoveal fixation. These exercises should be carried out several times each day for a few minutes." Use of a target providing physiological diplopia is often recommended (Hugonnier 1969; Press 1997; Scheiman 2002a; Scheiman 2002b; von Noorden 2001). Recent studies surveying the ophthalmic community suggest that home-based convergence exercises is the most commonly prescribed treatment by both ophthalmologists and optometrists (Chin 1995; Scheiman 2002a; Scheiman 2005). In two CITT trials (CITT 2005c; CITT 2008), the home-based convergence exercises procedures (referred to as pencil push-ups in the trials) used a pencil with 20/60 size letters and a white index card placed in the background to provide a suppression check by using physiological diplopia awareness. The goal of the procedure was to move the pencil to within 2 cm to 3 cm of the brow, just above the nose on each push up while trying to keep the target single and clear. Patients were instructed to perform the pencil push-ups procedure 15 minutes per day, five days per week.

Home-based computer vergence/accommodative therapy

Some clinicians recommend home-based therapy that is more intensive than pencil push-ups (Scheiman 2002a; Scheiman 2002b). Additional home-based techniques include the use of prism, stereoscopes, and computer software programs designed for vision therapy/orthoptics (Scheiman 2002a; Scheiman 2005).

In the large-scale CITT trial (CITT 2008) patients in this group were taught to perform the aforementioned pencil push-up procedure as well as procedures on the Home Therapy System (HTS/ CVS; www.visiontherapysolutions.com) computer software. Using this program, the patients performed fusional vergence and accommodative therapy procedures. These procedures were designed to improve convergence and divergence amplitudes and accommodative ability. Patients were instructed to do pencil pushups five minutes per day and the HTS software program for 15 minutes per day.

Outpatient vision therapy/orthoptics

Outpatient vision therapy/orthoptics involves a sequence of activities prescribed and monitored by an eye care professional to develop efficient visual skills. It incorporates purposeful, controlled manipulation of target blur, disparity, and proximity, with the aim of normalizing the accommodative and vergence systems and their mutual interactions (Ciuffreda 2002).

In two CITT trials (CITT 2005b; CITT 2008), patients in the outpatient (referred to as office-based in the trials) vergence/accommodative therapy group received weekly 60-minute in-office therapy with additional prescribed procedures to be performed at home for 15 minutes a day, five days per week. At each office-based therapy session, the patient performed four to five procedures with constant supervision and guidance from the therapist. The therapist followed a detailed and specific protocol from the CITT Manual of Procedures (accessed at www.optometry.osu.edu/research/CITT/4363.cfm); this document describes each procedure, amount of time used, expected performance, and criteria for ending the procedure and advancing to a more difficult level.

Outpatient placebo therapy

In two CITT trials (CITT 2005b; CITT 2008) patients in the outpatient (referred to as office-based in the trials) placebo therapy group received placebo therapy during a weekly 60-minute office visit and were prescribed procedures to be performed at home for 15 minutes per day, five days per week. The placebo therapy program consisted of 16 in-office therapy procedures and four home therapy procedures, which were designed to look like real vergence/accommodative therapy procedures yet not stimulate vergence, accommodation or fine saccadic eye movement skills beyond normal daily visual activities. The therapist followed a detailed protocol from the CITT Manual of Procedures (accessed at www.optometry.osu.edu/research/CITT/4363.cfm).

Non-surgical interventions for convergence insufficiency (Review)

How the intervention might work

The two main categories of intervention for convergence insufficiency are base-in reading glasses and vision therapy/orthoptics. Vision therapy/orthoptics can be subdivided into convergence exercises (i.e., pencil push-ups), more intensive home-base vision therapy/orthoptics, and outpatient vision therapy/orthoptics, as described above.

Patients with convergence insufficiency are often symptomatic because they need to use excessive convergence to compensate for high exophoria at near. Base-in prism reading glasses are believed to work by relieving the need to use this excessive convergence, thereby relieving discomfort. While the exact mechanism is not known for how vision therapy works, the hypothesis is that vision therapy increases positive fusional vergence and convergence ability, thereby relieving the symptoms associated with convergence insufficiency.

The three vision therapy/orthoptics treatment approaches (homebased convergence exercises, home-based computer vergence/accommodative therapy, and outpatient vision therapy/orthoptics) differ in: 1) ability to control/manipulate stimulus parameters; 2) dosage; 3) mode of administration; 4) use of motor learning theory and patient feedback; and 5) cost.

Controlling/manipulating stimulus parameters

To increase fusional vergence amplitudes a therapy procedure must either maintain accommodation at the plane of regard and change the vergence stimulus, or maintain vergence at the plane of regard and change the stimulus to accommodation (Scheiman 2002b). Instrumentations using a variety of stimuli are available that allow manipulation of these variables to create a vergence demand that is appropriate for an individual patient.

The three vision therapy/orthoptics treatment approaches described above vary significantly in their ability to allow the manipulation of stimulus parameters. With home-based convergence exercises, the stimulus is a small letter on a pencil that is moved closer to the patient. To maintain single vision, a combination of proximal, accommodative, and fusional vergence is used with accommodation and convergence synchronized. In contrast, outpatient vision therapy/orthoptics uses a wide variety of instrumentation that is designed to improve the dynamics of the fusional vergence and accommodative systems, typically using stimuli that require an accommodative demand different from the vergence demand. Hence, fusional vergence must be used while proximal and accommodative vergence is minimized. Home-based convergence exercises plus computer-based vergence/accommodative therapy provides an intermediate level of manipulation of the vergence/ accommodative relationship, but lacks the variety of stimuli available with outpatient vergence/accommodative therapy.

Dosage

More time is generally spent in outpatient vision therapy/orthoptics than either home-based option. In all three therapy approaches the patient must practice procedures at home. In the outpatient treatment there is an additional 60 minutes per week of therapy in the doctor's office. Total therapy time prescribed tends to be least with home-based convergence exercises and most with outpatient vision therapy/orthoptics.

Mode of administration

In outpatient vision therapy/orthoptics a trained therapist administers the treatment, providing the patient with motivation and feedback regarding performance and varying procedures based on the patient's progress. In the two home-based vision therapy/orthoptics approaches, close supervision from a trained therapist is not available, although parents are expected to supervise children prescribed this therapy.

Motor learning principles and patient feedback

Learning is a set of internal processes associated with practice or experience that results in a relatively permanent change in responding (Schmidt 1988). These processes are believed to be central nervous system phenomena in which sensory and motor information is organized and integrated (Aikon 1988; Arbib 1981; Lisberger 1988) with an ultimate goal of transferring the motor learning outside of the therapy setting.

For motor learning, numerous variables are considered important determinants. These include use of feedback, modeling and demonstration, transfer of training, part to whole task practice, variability in practice, and positive reinforcement. Of the three therapy approaches, outpatient vision therapy/orthoptics uses these principles of motor learning and patient feedback most frequently and consistently (Birnbaum 1977; Scheiman 2002b).

Why it is important to do this review

Although various treatments are prescribed for patients with convergence insufficiency there is a lack of consensus regarding the most effective treatment. Significant differences exist in the time commitment for the patient, number of office visits, cost, and complexity of the treatment. A systematic review of clinical trials will help summarize the available evidence on the effectiveness of interventions for patients with convergence insufficiency and will help clinicians select the most appropriate treatments for patients with this condition.

Non-surgical interventions for convergence insufficiency (Review)

OBJECTIVES

The objective of this review was to systematically assess and synthesize evidence from randomized controlled trials (RCTs) on the effectiveness of non-surgical treatment options for convergence insufficiency.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized and quasi-randomized clinical trials in this review.

Types of participants

We included trials in which participants had been treated for convergence insufficiency using non-surgical treatment. The definition of convergence insufficiency varies considerably from study to study. For this review convergence insufficiency is defined as a condition characterized by higher exophoria at near than at far distance, and one or both of the following objective clinical signs:

1. A receded near-point of convergence (6 cm or greater) (Hayes 1998; Scheiman 2003);

2. Insufficient positive fusional vergence at near (i.e., less than twice the near phoria (Sheard's criterion) or positive fusional vergence less than 15 prism diopters) which is one standard deviation below the mean (Sheard 1930; Scheiman 2002b).

Types of interventions

We included RCTs examining any form of non-surgical intervention against placebo, no treatment, sham treatment, or each other for patients with convergence insufficiency.

Types of outcome measures

Primary outcomes

The primary outcomes for this review were near point of convergence and positive fusional vergence at near at 12 weeks of intervention. We analyzed the primary outcomes as continuous variables whenever data were available. We planned to analyze the primary outcomes as dichotomous variables if continuous data were not reported in the included trials.

We used currently accepted normative data to determine whether patients had achieved normal levels for these clinical findings. A near point of convergence that was < 6 cm after completion of treatment was considered a normal finding (Yes/No); positive fusional vergence at near that was either twice the magnitude of the exophoria at near or > 15 prism diopters after completion of treatment was considered normal (Yes/No).

We analyzed primary outcomes at other follow-up times when long-term follow-up data were available.

Secondary outcomes

The secondary outcome for this review was patient symptoms at different follow-up times as reported in the included studies. We assessed patient symptoms whenever trials had used some formal instrument for examining symptoms (Borsting 2003; Maples 2002; Rouse 2004). One instrument that has been developed and validated for assessing convergence insufficiency symptoms before and after treatment is the Convergence Insufficiency Symptom Survey (CISS) Version -15, a 15-item questionnaire that measures symptoms experienced when reading or doing other close work (Borsting 2003). The higher the CISS score, the more symptoms. CISS has demonstrated a sensitivity of 96% and a specificity of 88%, when using a score of \geq 16 for children and \geq 21 for adults differentiating individuals with symptomatic convergence insufficiency from those with normal binocular vision (Borsting 2003). We reported compliance to treatment as an ad hoc secondary outcome because the success of treatment depends on compliance. Three trials included in our review reported compliance data.

Adverse outcomes

Adverse effects of interest included:

- 1. Worsening of diplopia (double vision);
- 2. Worsening of headaches;
- 3. Convergence spasm.

We summarized the reported adverse effects related to each intervention.

Quality of life data

We planned to describe data on quality of life when available from included trials.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2010, Issue 10, part of *The Cochrane Library*. www.thecochranelibrary.com (accessed 7 October 2010), MED-LINE (January 1950 to October 2010), EMBASE (January 1980 to October 2010), the *meta*Register of Controlled Trials

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(*m*RCT) (www.controlled-trials.com) (October 2010) and ClinicalTrials.gov (www.clinicaltrials.gov) (October 2010). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 7 October 2010.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), *m*RCT (Appendix 4) and ClinicalTrials.gov (Appendix 5).

Searching other resources

We searched the reference lists of identified trial reports to find additional trials. We used the Science Citation Index (SCI) to find studies that had cited the reports of included trials. We contacted the primary investigators of identified trials for details of additional trials.

We also conducted manual searches of the following optometric journals:

Optometry, Journal of Behavioral Optometry (1990 to 2009);

Optometry Vision Development (1969 to 2009);

American Orthoptic Journal (1951 to 2009);

Australian Orthoptic Journal (1973 to 2009); and

British and Irish Orthoptic Journal (formerly the *British Orthoptic Journal*) (1954 to 2009).

Data collection and analysis

Selection of studies

At least two authors independently reviewed the titles and abstracts resulting from the electronic and manual searches according to the inclusion criteria stated above. We classified abstracts as 'definitely exclude', 'unsure' or 'definitely include'. We obtained the full text for articles in the 'unsure' and 'definitely include' categories and re-assessed them for final eligibility. After examining the full text, studies labeled as 'excluded' by both authors were excluded from the review and the reasons for exclusion documented. Included studies were further assessed for their methodological quality. We resolved discrepancies through discussion and consensus.

Data extraction and management

At least two review authors independently extracted the data onto paper data collection forms. We resolved discrepancies through discussion. One review author (TL) entered all data into Review Manager (RevMan 2008). Data entered were verified by a second author (MS). We extracted the following details from the studies: methods, participants, interventions, outcomes, adverse events, quality of life issues, economic data and important information on captured otherwise.

Assessment of risk of bias in included studies

At least two review authors assessed the sources of potential systematic bias in trials according to the methods described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). The following parameters were considered: a) randomization sequence generation; b) allocation concealment; c) masking (blinding) of the primary and secondary outcome assessors; d) completeness of outcome data for the primary and secondary outcomes; e) selective outcome reporting; and f) intention-to-treat analysis. Each of the parameters was graded as: 'Yes', at low risk of bias, 'No', at high risk of bias, and 'Unclear', at unclear risk of bias. Because of the nature of the intervention, masking of participants and care providers was not possible in all trials, and consequently was not used as a quality parameter in this review.

Measures of treatment effect

We followed the guidelines in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008) for data analyses. We calculated a summary risk ratio for dichotomous outcomes and mean difference between intervention arms for continuous outcomes. We reported estimate of effect and associated confidence intervals (CI).

Unit of analysis issues

We conducted a person-based analysis because convergence insufficiency is a binocular vision disorder. None of the trials included in this review used cluster or cross-over design. If cluster-randomized trials and cross-over trials are to be included in future updates of this review, we will extract data from an analysis that properly accounts for the non-independence of the cluster and cross-over design. If the primary studies fail to report appropriate analyses, we will perform the analyses following section 9.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008).

Dealing with missing data

We contacted the lead investigator of the trial in an attempt to obtain additional information. We pre-specified that whenever the authors did not respond within four weeks, we would continue the review based on the available information.

Assessment of heterogeneity

We assessed clinical and methodological heterogeneity qualitatively by examining the characteristics of each included trial. We assessed statistical heterogeneity quantitatively using the Chi^2 test and the I² values. We pre-specified that a P-value of less than 0.1 from the Chi^2 test and I² statistic of greater than 50% indicated substantial statistical heterogeneity.

Assessment of reporting biases

We planned to use a funnel plot to assess publication bias when a sufficient number of trials were identified.

Data synthesis

We pre-specified that we would combine the results in a metaanalysis using both the fixed-effect and random-effects models if little clinical, methodological, and statistical heterogeneity were present. Whenever substantial variation were detected between trials, we would not combine study results but would present them with estimates of effect and associated confidence intervals.

Subgroup analysis and investigation of heterogeneity

We examined potential sources of heterogeneity qualitatively. Variables that could be related to heterogeneity and were candidates for stratified analysis included patient age, types of test and comparison intervention, and study design parameters.

Sensitivity analysis

We pre-specified that we would conduct sensitivity analyses to determine the impact of exclusion of studies at higher risk of bias, unpublished studies, and industry-funded studies.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The electronic searches identified 529 titles and abstracts of which 27 appeared to be relevant on initial review. After reading the full text reports of these 27 titles and abstracts, 18 were excluded; 13 were not RCTs, and the other five studies were not conducted in the study population of interest.

The remaining nine articles reporting six trials were relevant to this systematic review (Birnbaum 1999; CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008, Teitelbaum 2009).

We did not find any additional trials by searching the reference lists of the included studies, the WHO ICTRP, the SCI website, or by manually searching the above mentioned optometry journals.

Included studies

We have presented the clinical characteristics for each included study in the 'Characteristics of included studies' table.

Types of participants

We included six trials with a total of 475 participants with convergence insufficiency. All six trials were conducted in the United States. The trials varied in size with the smallest enrolling 29 participants (Teitelbaum 2009) and the largest enrolling 221 participants (CITT 2008). Four of the six trials were conducted by the Convergence Insufficiency Treatment Trial (CITT) Study Group (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008). These four CITT trials randomized 81.3% (386/475) of all participants included in this systematic review. Symptomatic convergence insufficiency was defined consistently across the four CITT trials and the eligibility criteria were comparable. Of the remaining trials, Birnbaum 1999 enrolled 60 adult male participants from a Veterans Medical Center, and Teitelbaum 2009 enrolled 29 patients affected by presbyopia (a condition in which the lens of the eye loses its ability to focus, making it difficult to see objects up close) from a private practice.

We found clinical heterogeneity in several aspects, mainly in the age distribution of trial participants. Three trials were conducted in children nine to 17 or 18 years old (CITT 2005a; CITT 2005b; CITT 2008); one trial was conducted in adults 19 to 30 years old (CITT 2005c); the remaining two trials were conducted in adults aged 40 years or older (Birnbaum 1999, Teitelbaum 2009). Birnbaum 1999 did not report explicitly the baseline characteristics of included participants.

CITT 2005b included participants with higher accommodative amplitude (a measurement of the eye's ability to focus clearly on objects at near distances) and less exophoria at distance than the other three trials. The lower accommodation is due to the age difference since accommodation is indirectly related to age. The baseline refractive error also varied across trials.

Because of potential differences in accommodation and accommodative vergence with aging, it is important to analyze findings for children separately from young adults and presbyopes.

Types of test interventions and comparison interventions

The included trials evaluated a variety of interventions, including passive treatment with base-in prism reading glasses, and active treatments such as a specific outpatient vision therapy/orthoptics called office-based vergence/accommodative therapy, home-based convergence exercises, home-based computer vergence/accommodative therapy plus convergence exercises, and placebo or sham procedures. The interventions and comparison interventions are described in detail in the 'Characteristics of included studies' table and Table 1. We kept the same terms that were used in the trials to refer to each intervention (e.g., instead of convergence exercises, we used pencil push-ups to describe the intervention tested in the CITT trials).

Non-surgical interventions for convergence insufficiency (Review)

Table 1. Types of comparisons in the included trials

Study ID	Office- based vi- sion ther- apy/ orthoptics	Home- based pen- cil push- ups	Home- based com- puter ver- gence/ accom- modative therapy and pencil push-ups	Other therapy	Prism reading glasses	Placebo reading glasses	Pro- gressive ad- dition lens	Population
Birnbaum 1999								Male adult ≥ 40 years old
CITT 2005a								Children aged 9 to 18 years
Teitel- baum 2009								
СІТТ 2005Ь								Children aged 9 to 18 years
CITT 2005c								Young adults aged 19 to 30 years
CITT 2008								Children aged 9 to 17 years

CITT 2005a randomly assigned 72 children nine to18 years of age with symptomatic convergence insufficiency to wear either base-in prism reading glasses or placebo reading glasses. Patients assigned to base-in prism reading glasses received glasses that corrected for the patient's refractive error, when necessary, and base-in prism. Patients in the placebo reading glasses group received glasses that corrected their refractive error, or plano lenses for those who did not require refractive correction. Patients were asked to wear these glasses for all reading and near tasks requiring more than five minutes for six weeks.

Teitelbaum 2009 randomly assigned 29 presbyopic patients aged 45 to 68 years with symptomatic convergence insufficiency to ei-

ther base-prism in a progressive addition lens or progressive addition lenses with no prism. Participants wore each pair of glasses for three weeks and completed the CISS at the end of three weeks. CITT 2005b was considered as a pilot study by the CITT Study Group. In this study, 47 children were randomly assigned to receive a 12-week program of home-based pencil push-ups, office-based vision therapy/orthoptics, or office-based placebo therapy. The same treatment modalities were further tested in 46 adults in CITT 2005c.

CITT 2008 randomly assigned 221 children to receive a 12week program of home-based pencil push-ups, home-based com-

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puter vergence/accommodative therapy plus pencil push-ups, office-based vergence/accommodative therapy with home reinforcement, or office-based placebo therapy. The home-based computer vergence/accommodative therapy plus pencil push-ups group was considered a more intensive regimen than pencil push-ups alone, sometimes used by both ophthalmologists and optometrists. The other three treatment modalities were essentially the same as those in the aforementioned CITT trials.

Birnbaum 1999 randomly assigned 60 male adult patients to receive office-based vision therapy/orthoptics with supplemental home therapy, home vision therapy, or no treatment. The exact treatment modalities differed from those used in the CITT trials.

Types of outcomes

The four CITT Study Group trials and Teitelbaum 2009 used a consistent method to measure outcomes.

The primary outcome measure for four CITT trials was the Convergence Insufficiency Symptom Survey (CISS) V-15 (Borsting 2003). CITT 2005a measured the primary outcome after six weeks of therapy, and the other three CITT trials (CITT 2005b; CITT 2005c; CITT 2008) measured the primary outcome after 12 weeks of therapy. Secondary outcome measures in these four trials were

near point of convergence and positive fusional vergence at near. Teitelbaum 2009 measured symptoms with CISS V-15 after three weeks of therapy.

Birnbaum 1999 did not specify the primary or secondary outcome, although the author reported "success" and "failure" for each individual participant on the basis of improvement shown with respect to the asthenopia (eye strain) and functional criteria. No harms were reported from any of the six trials.

Excluded studies

We excluded 18 studies that initially appeared to be relevant; 13 were not RCTs or CCTs, and the other five did not address the study population of interest. We have listed reasons for excluding each study in the 'Characteristics of excluded studies' table.

Risk of bias in included studies

We evaluated the risk of bias in each of the six included trials using eight pre-specified criteria. Two trials (Birnbaum 1999; Teitelbaum 2009) were judged to have high potential for bias, and the other four trials (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008) were judged to have low potential for bias (see Figure 1: Methodological quality summary).

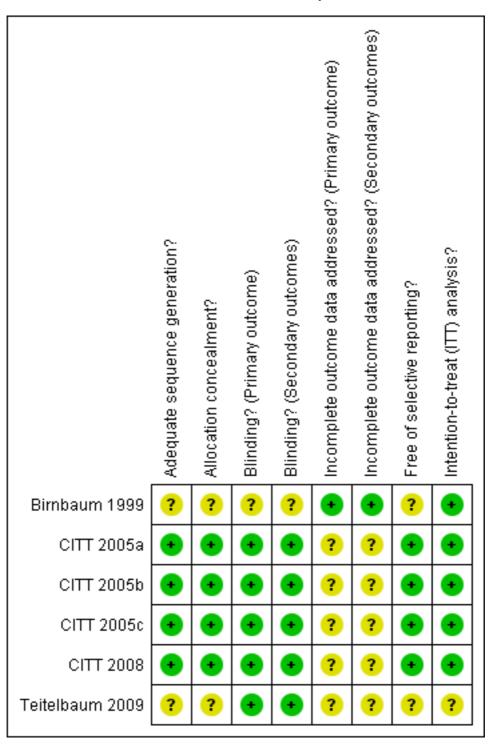


Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

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Allocation

Birnbaum 1999 and Teitelbaum 2009 did not report the procedure used to generate random sequences and whether the intervention allocation was concealed until assigned. When patient assignment involves a non-random approach, confounding and selection bias may be introduced. The other four RCTs (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008), designed and conducted by the CITT Study Group, used a central study website to randomize study participants and the treatment assignment was concealed to researchers enrolling and allocating participants until that time.

Blinding

Birnbaum 1999 did not report whether the primary or the secondary outcomes were measured by masked personnel. Inadequate masking may introduce information bias. The other five trials (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008; Teitelbaum 2009) reported that masking was used for measuring the primary and secondary outcomes.

Incomplete outcome data

No participants were lost to follow-up in Birnbaum 1999 or Teitelbaum 2009. The remaining four trials had missing data. Personal contact with the CITT trial statistician revealed that missing data were not imputed in the four CITT trials (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008), and therefore, only available outcome data were used in the analyses. One participant in CITT 2008 was excluded from the analysis because of early withdrawal. Three participants from CITT 2005a and five participants from CITT 2005b were excluded from analyses because only baseline data were available. Birnbaum 1999, CITT 2005a, CITT 2005b, CITT 2005c and CITT 2008 reported that participants were analyzed by the treatment group to which they were assigned.

Selective reporting

We had insufficient information to assess the risk of selective reporting bias in Birnbaum 1999 and Teitelbaum 2009. All the outcomes described in the study protocol of the four CITT trials (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008) were reported.

Other potential sources of bias

The primary outcome was not defined in Birnbaum 1999. Further, although the authors reported data for each individual participant in this trial, no between treatment group comparison was made in the analyses except one outcome.

Effects of interventions

Two of the six trials included in the review reported data for the comparison between base-in prism reading glasses and other reading glasses; the remaining four trials reported data for the comparisons between various types of vision therapy (office- and home-based vision therapy/orthoptics). We present outcomes by interventions compared in the trials, and report outcomes in children and adult populations separately.

We reported difference in change scores between two arms whenever possible except for Analysis 2, where only follow-up values were available to us. Patients with more severe signs and symptoms would have higher baseline values for the CISS score and near-point of convergence, and a lower value for positive fusional vergence at near. If an intervention is effective, one would expect CISS score and near-point of convergence go from a higher value to a lower value, while positive fusional vergence at near goes from a lower to a higher value. To facilitate interpretation of the treatment effect based on a difference in change scores between two arms, change in near-point of convergence and CISS score was defined as baseline value minus follow-up value, and change in positive fusional vergence at near was defined as follow-up value minus baseline value. Using this definition, if the test intervention is more effective than the comparison intervention, all three estimates would be greater than 0.

• EFFECTIVENESS OF BASE-IN PRISM READING GLASSES

Analysis I. Base-in prism reading glasses versus placebo reading glasses in children

One trial examined this comparison in 72 children up to age 18 (CITT 2005a). At six weeks of therapy, there was no statistically significant effect of base-in prism reading glasses compared with placebo reading glasses in children in terms of change in near point of convergence, change in positive fusional vergence, or decrease in convergence insufficiency symptoms measured by CISS. At six weeks of therapy:

the mean difference in change in near point of convergence between the prism reading glasses and the placebo reading glasses was 2.81 cm (95% CI -1.67 to 7.29) (Analysis 1.1);

the mean difference in change in positive fusional vergence was - 0.69 diopters (95% CI -3.96 to 2.58) (Analysis 1.2);

the mean difference in decrease in CISS score was -4.26 (95% CI -10.42 to 1.90) (Analysis 1.3).

Few participants in either group achieved a normal near point of convergence or positive fusional vergence at near.

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Analysis 2. Base-in prism reading glasses using a progressive addition lens design versus progressive addition lens alone in adults

One trial examined this comparison (Teitelbaum 2009) in adults. This trial did not report near point of convergence or positive fusional vergence after the treatment. At three weeks of therapy, base-in prism glasses using a progressive addition lens design was found to be more effective than progressive addition lens alone in decreasing convergence insufficiency symptoms measured by CISS in adults. At three weeks of therapy:

the difference in CISS score between the base-in prism glasses using a progressive addition lens design and progressive addition lens alone was -10.24 (95% CI -15.45 to -5.03) (Analysis 2.1). We were not able to calculate a change in CISS score from baseline between the two treatment arms because the standard deviation for the change was not reported.

• EFFECTIVENESS OF VISION THERAPY

Analysis 3. Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults

Two trials examined this comparison in children (CITT 2005b; CITT 2008). At 12 weeks of therapy, based on a meta-analysis of the two trials (CITT 2005b; CITT 2008), office-based vision therapy/orthoptics was found to be more effective than home-based pencil push-ups in terms of change in near point of convergence, positive fusional vergence at near, and convergence insufficiency symptoms measured by CISS in children. At 12 weeks of therapy: the mean difference in change in near point of convergence between office-based vision therapy/orthoptics and home-based pencil push-ups was 3.99 cm (95% CI 2.11 to 5.86) (Analysis 3.1); the mean difference in change in positive fusional vergence at near was 13.13 diopters (95% CI 9.91 to 16.35) (Analysis 3.2);

the mean difference in change in CISS score was 9.86 (95% CI 6.70 to 13.02) (Analysis 3.3).

One trial examined this comparison in young adults between 19 to 30 years old (CITT 2005c). At 12 weeks of therapy, officebased vision therapy/orthoptics was found to be more effective than home-based pencil push-ups in terms of change in positive fusional vergence at near, but not more effective than home-based pencil push-ups in change in near point of convergence or patient symptoms measured by CISS in a young adult population. At 12 weeks of therapy:

the mean difference in change in near point of convergence between office-based vision therapy/orthoptics and home-based pencil push-ups was 2.8 cm (95% CI -2.41 to 8.01) (Analysis 3.1); the mean difference in change in positive fusional vergence at near

was 7.7 diopters (95% CI 0.82 to 14.58) (Analysis 3.2);

the mean difference in change in CISS score between the two arms was 4.7 (95% CI -1.45 to 10.85) (Analysis 3.3).

Analysis 4. Office-based vision therapy/orthoptics versus home-based computer assisted vision therapy/orthoptics in children

One trial examined this comparison (CITT 2008) in children. At 12 weeks of therapy, office-based vision therapy/orthoptics was found to be more effective than home-based computer assisted vision therapy/orthoptics in terms of change in near point of convergence, positive fusional vergence, and convergence insufficiency symptoms measured by CISS in children. At 12 weeks:

the mean difference in change in near point of convergence between office-based vision therapy and home-based vision therapy was 2.90 cm (95% CI 0.96 to 4.84) (Analysis 4.1);

the mean difference in change in positive fusional vergence at near was 7.70 diopters (95% CI 3.94 to 11.46) (Analysis 4.2);

the mean difference in change in CISS score was 8.80 (95% 5.26 to 12.34) (Analysis 4.3).

Analysis 5. Home-based pencil push-ups versus homebased computer assisted vision therapy/orthoptics in children

One trial examined this comparison (CITT 2008) in children. At 12 weeks of therapy, there was no statistically significant effect of home-based pencil push-ups compared with home-based computer assisted vision therapy/orthoptics in terms of change in near point of convergence or patient symptoms in children. At 12 weeks:

the mean difference in change in near point of convergence between home-based pencil push-ups and home-based vision therapy was -1.10 cm (95% CI -3.07 to 0.87) (Analysis 5.1);

the mean difference in change in CISS score was 1.10 (95% CI - 2.55 to 4.75) (Analysis 5.3).

Based on the same trial (CITT 2008), home-based computer vision therapy/orthoptics was found to be more effective than homebased pencil push-ups alone in change in positive fusional vergence. At 12 weeks:

the mean difference in change in positive fusional vergence between home-based pencil push-ups and home-based computer vision therapy/orthoptics was -4.10 diopters (95% CI -7.93 to -0.27) (Analysis 5.2) in favor of home-based computer vision therapy/orthoptics plus pencil push-ups.

Analysis 6. Home-based pencil push-ups versus officebased placebo in children

One trial examined this comparison (CITT 2008) in children. At 12 weeks of therapy, home-based pencil push-ups was found to be more effective than office-based placebo in change in near point of convergence. There was no statistically significant effect of home-based pencil push-ups compared with office-based placebo in terms of change in positive fusional vergence or patient symptoms measured by CISS. At 12 weeks:

the mean difference in change in near point of convergence between home-based pencil push-ups and office-based placebo was 2.50 cm (95% CI 0.53 to 4.47) (Analysis 6.1);

the mean difference in change in positive fusional vergence was 1.00 diopters (95% CI -2.77 to 4.77) (Analysis 6.2);

the mean difference in change in CISS score was -0.70; (95% CI -4.32 to 2.92) (Analysis 6.3).

Analysis 7. Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children

One trial examined this comparison (CITT 2008) in children. At 12 weeks of therapy, home-based computer assisted vision therapy/ orthoptics was found to be more effective than office-based placebo in change in near point of convergence and positive fusional vergence. There was no statistically significant effect of home-based computer vision therapy/orthoptics compared with office-based placebo in change in patient symptoms measured by CISS. At 12 weeks:

the mean difference in change in near point of convergence between home-based computer vision therapy/orthoptics and officebased placebo was 3.60 cm (95% CI 1.64 to 5.56) (Analysis 7.1); the mean difference in change in positive fusional vergence was 5.10 diopters (95% CI 1.31 to 8.89) (Analysis 7.2);

the mean difference in change in CISS score was -1.80; (95% CI -5.46 to 1.84) (Analysis 7.3).

Analysis 8. Office-based vision therapy/orthoptics versus office-based placebo in children

One trial examined this comparison (CITT 2008) in children. At 12 weeks of therapy, office-based vision therapy/orthoptics was found to be more effective than office-based placebo in change in near point of convergence, positive fusional vergence, and patient symptoms measured by CISS. At 12 weeks:

the mean difference in change in near point of convergence between home-based computer vision therapy/orthoptics plus pencil push-ups and office-based placebo was 6.50 cm (95% CI 4.56 to 8.44) (Analysis 8.1);

the mean difference in change in positive fusional vergence was 12.80 diopters (95% CI 9.09 to 16.51) (Analysis 8.2);

the mean difference in change in CISS score was 7.00; (95% CI 3.49 to 10.51) (Analysis 8.3).

Compliance with treatment

Compliance to treatment was reported in all four of the CITT trials but in neither of the other two trials. In the base-in prism study (CITT 2005a) compliance was assessed by asking the patient "What percentage of the time did you wear the glasses we gave you while you were reading or doing near work (0%, 25%, 50%, 75%, or 100%)?" The child was also asked "How sure are you

about this answer (very sure, pretty sure, somewhat sure, a little sure, not sure at all)?" Parents were asked the same questions about their child's wearing of the reading glasses. In the base-in prism group, 90% of patients reported wearing their glasses at least 75% of the prescribed time and 81% of parents said their child wore his or her glasses at least 75% of the prescribed time. There was agreement between child and parent on percentage of time worn for 55% of the responses. In the placebo group, 79% of patients reported wearing their glasses at least 75% of the prescribed time and 79% of parents said their child wore his or her glasses at least 75% of the prescribed time. Reported the placebo glasses were worn 42% of the time. Reported wearing time was not statistically different between the two reading glasses groups using the patients' (P = 0.18) or parents' responses (P = 0.24).

In the three studies in which office- and home-based vision therapy/orthoptics were evaluated, the therapist asked the patient questions about the home-based treatment component and then answered the following question on the CITT follow-up form "What percent of the time do you feel the patient adhered to the treatment protocol?" The choices were: 0%, 1% to 24%, 25% to 49%, 50% to 74%, 75% to 99% or 100%.

In the CITT pilot study (CITT 2005b), there were no differences in the therapist's assessment of patient compliance between the three treatment groups at any visit. After 12 weeks of treatment, the therapists estimated that 73% of patients in the office-based vision therapy/orthoptics group, 92% of patients in the placebo officebased vision therapy/orthoptics group, and 73% of the patients in the pencil push-ups group were performing their home therapy at least 75% of the time (Kruskal-Wallis P = 0.3454).

In the larger CITT study (CITT 2008), at 12 weeks the percentage of CITT patients rated by therapists as compliant with the home therapy protocol at least 75% of the time was 67.3% in the home-based computer therapy group, 84.9% in the pencil pushups group, 87% in the office-based placebo group, and 91.4% in the office-based vision therapy group. Accounting for the observed differences in estimated adherence did not affect the results of the treatment group comparisons for symptom score, near point of convergence, and positive fusional vergence.

Economic data

The cost of materials and equipment is lowest for home-based pencil push-ups and estimated to be equivalent for base-in prism reading glasses, home-based computer vision therapy/orthoptics, and office-based vision therapy/orthoptics. If office visits are considered, costs are expected to be highest for office-based vision therapy/orthoptics, followed by home-based vision therapy/orthoptics and least expensive for base-in reading glasses. Although cost analysis data were not reported from any of the studies, it is possible to estimate the cost of office-based vision therapy/orthoptics, the most effective treatment option based on findings from

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this systematic review. The office visit fee varies from \$75 to \$100 per session across regions in the United States. Twelve sessions would, therefore, cost about \$900 to \$1200 per patient. Officebased vision therapy/orthoptics is a covered service by most insurance companies in the United States. The direct patient cost would be reduced significantly depending on insurance coverage.

Harms

No adverse effects related to study treatments were reported for any of the included studies.

DISCUSSION

Summary of main results

This systematic review aimed to identify and synthesize available RCT evidence on the effectiveness of various non-surgical treatments for symptomatic convergence insufficiency in children and adults.

Summary of main results in children

The CITT Study Group, a group of almost 100 investigators (optometrists, pediatric ophthalmologists, and orthoptists), completed four randomized clinical trials (all assessed as having low potential for bias) in recent years investigating the effectiveness of non-surgical treatments for convergence insufficiency in children. Treatments evaluated included both passive therapy (base-in prism reading glasses) and active therapy (office or home-based vision therapy/orthoptics).

In this systematic review, evidence from the CITT clinical trials suggests that office-based vision therapy/orthoptics with home reinforcement is more effective than home-based pencil push-ups and home-based computer vision therapy/orthoptics for improving both the clinical signs and symptoms of children with symptomatic convergence insufficiency. Base-in prism was found to be no more effective than placebo reading glasses for improving either clinical signs or symptoms.

The evidence also shows that home-based computer vision therapy/orthoptics was more effective than home-based pencil pushups for improving near point of convergence and positive fusional vergence. However, home-based computer vision therapy/orthoptics was no more effective than home-based pencil push-ups for improving symptoms. In fact, neither home-based treatment option was more effective than placebo treatment for improving symptoms.

Summary of main results in adults

Data from three clinical trials were available for the adult population. However, only one of these studies (CITT 2005c) was graded at low risk of bias. The other two (Birnbaum 1999; Teitelbaum 2009) were graded at high risk of bias. In Teitelbaum 2009, base-in prism progressive addition lenses were more effective than placebo glasses for improving symptoms in presbyopic adults. Because the authors used a lens design that is not commercially available the ability to generalize their data is limited.

The two clinical trials of adults studied heterogeneous populations. The CITT study of adults (CITT 2005c) included young adults (19 to 30 years of age, mean age 24.4), while the Birnbaum 1999 included older adults only (40 and older, mean age 63.9 years). Evidence from CITT 2005c suggests that office-based vision therapy/orthoptics with home reinforcement is more effective than home-based pencil push-ups, and office-based placebo therapy/ orthoptics for improving both the clinical signs of young adults with symptomatic convergence insufficiency. There was no difference among treatment groups for reducing symptoms in these patients. The trial investigators speculated (CITT 2005c) that perhaps young adults in college or in the work force spend more time reading or on computers; and/or experience more non-visually related symptoms that mimic symptoms tested on the CISS. Evidence for this speculation exists in the higher mean scores for patients 19 to 30 years compared to those patients nine to18 years and in the higher cut-point for an asymptomatic score on the CISS V-15.

Placebo effect

Could the improvement in the office-based vision therapy/orthoptics group be due to patient-provider interaction or the patient's belief in the effectiveness of the treatment in the absence of full masking? The placebo effect is viewed as a change in a patient's condition or symptoms attributable to the symbolic aspect of a treatment and not to any specific pharmacologic or physiologic properties (Brody 1985). Placebo response rates for a variety of medical conditions have been reported to range from 15% to 58% with an average placebo effectiveness of 35% (Beecher 1955). While this rate is similar to the effectiveness rates found in the CITT officebased placebo therapy and placebo glasses groups, it is unknown how much of the effect in these groups was from the placebo effect versus regression to the mean and/or natural history of the disease because a no-treatment control group was not included. The effect sizes for all three outcome measures were large between the officebased vision therapy/orthoptics and placebo groups. Therefore, the presence of the office-based placebo group provide strong evidence for a real treatment effect with office-based vision therapy/ orthoptics.

Overall completeness and applicability of evidence

The four CITT clinical trials, graded at low risk of bias, used a consistent definition of convergence insufficiency, and consistent outcome measures. The most commonly prescribed clinical treatments were evaluated in these trials leading to high quality evidence that can be applied in clinical practice, particularly for children with symptomatic convergence insufficiency. Only one of the four CITT trials enrolled adult participants. This small trial was limited to participants aged between 19 and 30 years old (CITT 2005c). Thus, the completeness and applicability of the evidence is limited for the adult population. In addition, the length of the treatment was purposely limited to 12 weeks in the four CITT trials because of the ethical and logistical challenges of successfully following a group of symptomatic patients in a placebo group. Thus, findings from these trials do not reveal the maximum treatment effect that could be achieved with the various treatments. Finally, none of the included trials reported changes in reading, attention, quality of life, or the cost utility of the various treatments for convergence insufficiency.

Quality of the evidence

Four trials (CITT 2005a; CITT 2005b; CITT 2005c; CITT 2008), including 81.3% of participants of this review were graded at low risk of bias. Teitelbaum 2009 and Birnbaum 1999 were graded at high risk of bias because of inadequate random sequence generation and inadequate allocation concealment. In addition, Birnbaum 1999 did not define the primary and secondary outcomes.

Clinical heterogeneity was reflected in differences in the age distribution of study participants and variation in treatment methods across trials. Such clinical heterogeneity and methodological limitations made it difficult to pool the effect estimates in a metaanalysis for the adult population.

Potential biases in the review process

We took several measures to prevent potential bias in the systematic review process, including having pre-specified eligibility criteria, performing an extensive literature search, and having two review authors working independently to evaluate eligibility, assess risk of bias, and abstract data. We also contacted trial investigators for additional information.

There is a potential conflict of interest as the lead author of this review (Dr. Mitchell Scheiman) is also the Principal Investigator for the four CITT trials. Another limitation is that compliance to treatment was reported incompletely, as an *ad hoc* secondary outcome, and not assessed by any validated method.

Agreements and disagreements with other studies or reviews

Findings from our systematic review are consistent with findings from recent narrative reviews on the same topic (Cacho 2009; Scheiman 2009). There of the six trials included in our systematic review were also included in a non-Cochrane systematic review addressing a related topic (Lavrich 2010).

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review provides an up-to-date summary of the best available evidence for doctors, patients, and other decision makers about the effectiveness of various non-surgical interventions for symptomatic convergence insufficiency in children and adults. Current research suggests that office-based vision therapy/orthoptics is more effective than home-based pencil push-ups or homebased computer vision therapy/orthoptics for children. Evidence is less consistent for the adult population.

Evidence from the included trials suggests that:

• Office-based vision therapy/orthoptics is more effective than either home-based pencil push-ups or home-based computer vergence/accommodative therapy in children and young adults.

• Home-based computer vergence/accommodative therapy may provide greater improvement in positive fusional vergence than home-based pencil push-ups.

• Base-in prism reading glasses are no more effective than placebo glasses in children.

• Base-in reading glasses may be an effective treatment for symptomatic convergence insufficiency in presbyopic patients.

Implications for research

This systematic review identified key gaps in research including:

- Would a longer duration of office- and home-based therapies have been effective in a higher percentage of children?
- Are certain office-based vergence/accommodative therapy procedures more effective than others in treating convergence insufficiency? Is there an office-based therapy program that would be equally as effective or perhaps even more effective but could be administered for a shorter duration?

• Would a protocol that more closely monitors and encourages adherence affect the outcome for home-based computer vergence/accommodative therapy groups?

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• Are there different home-based therapy combinations (e.g., computer therapy combined with therapy procedures such as loose prism or free-space fusion cards rather than pencil push-ups) and/or a modified computer therapy program that might be more effective than the combined computerized therapy and pencil push-up approach that has been prescribed?

• Is there a better method of prescribing prism, such as based on fixation disparity testing, that might be more effective in reducing symptoms of convergence insufficiency?

• What effect does successful treatment of symptomatic convergence insufficiency have on various aspects of reading performance?

• What effect does the successful treatment of convergence

insufficiency have on behavior rating scales in children with convergence insufficiency and Attention-Deficit Hyperactivity Disorder whose behaviors are still an issue despite medical management for the latter?

• What exactly is the cost utility of each of the various treatments for convergence insufficiency?

A C K N O W L E D G E M E N T S

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* Indicates the major publication for the study

Non-surgical interventions for convergence insufficiency (Review)

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Birnbaum 1999

Methods	 Study design: RCT Number randomized: 60 (21 assigned to office-based therapy with supplemental home therapy; 20 assigned to home therapy group; and 19 assigned to control group) Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 60 (100%) Number of centers: 1 Date of first enrolment: not reported Length of follow-up: planned: 26 weeks after initiation of treatment; actual: varied Sample size estimation: not reported
Participants	 Country of recruitment: United States Mean age: 63.9 years in the office-based therapy group, 61.1 in home therapy group, and 62.9 in control group Sex: 100% male Key inclusion criteria: male adults aged 40 years with symptomatic convergence insufficiency; demonstrated asthenopic symptoms; and failed at least two of the four criteria for convergence insufficiency. Key exclusion criteria: patients with systemic neurologic disease; use of psychotropic medications that might influence vergence or accommodation; constant or noncomitant strabismus; visual acuity poorer than 20/40 in either eye, or previous vision therapy.
Interventions	 Intervention regimen #1: office-based therapy with supplemental home therapy Patients assigned to this group were scheduled for 24 weekly 45 minute office-based therapy sessions (some patients discharged earlier, once their treatment was successfully concluded; some patients required somewhat longer treatment periods). The office ther- apy procedures typically used include series of eye movement procedures and binocular fusion procedures. Procedures were assigned for practice at home to supplement office therapy. Intervention regimen #2: home therapy group Patients were seen for one office visit for instruction on the home therapy procedures. The home therapy procedures include four-corner oculomotor calisthenic fixations; Brock string; eccentric circles base-in and base-out; red-green lifesaver cards, base-in and base- out; and pointer-straw. Intervention regimen #3: control group Patients were given a handout "Care of Your Eyes" (which was also given to patients in the two treatment groups). This handout provided general information on ocular health, but provided no specific information relative to convergence insufficiency.
Outcomes	 Primary outcome: not explicitly specified, might be "success" and "failure" defined by the investigators on the basis of the improvement shown with respect to the asthenopia and functional criteria Secondary outcome:unclear

Birnbaum 1999 (Continued)

	• No harm was reported.
Notes	Funding sources: none reportedSubgroup analyses: none reported

Risk of bias

•		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not reported.
Allocation concealment?	Unclear	Not reported.
Blinding? Primary outcome	Unclear	Not reported.
Blinding? Secondary outcomes	Unclear	Not reported.
Incomplete outcome data addressed? Primary outcome	Yes	There was no lost to follow-up.
Incomplete outcome data addressed? Secondary outcomes	Yes	There was no lost to follow-up.
Free of selective reporting?	Unclear	No access to the protocol.
Intention-to-treat (ITT) analysis?	Yes	All participants were analyzed in the group they were assigned to.

CITT 2005a

Methods	 Study design: RCT Number randomized: 72 (36 assigned to base-in prism reading glasses; 36 assigned to placebo reading glasses) Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 65 (90%) (31 of 36 assigned to base-in prism reading glasses; 34 of 36 assigned to placebo reading glasses) Number of centers: 9 Date of first enrollment: July 21, 2003 Length of follow-up: planned: 6 weeks after initiation of treatment; actual: 6 weeks after initiation of treatment Sample size estimation: all sample size calculations were performed using PASS 2000 software assuming a two-sided test with α=0.05 and β=0.10 (90% power). Preliminary data from CITT 2005b were used to obtain estimates of variability to be used in the calculations. With 32 patients per group, the study would have 90% power to find differences in the mean near point of convergence as small as 3.7 cm.
Participants	 Country of recruitment: United States Mean age: 11.5±2.3 (SD) years in the base-in prism reading glasses group; 11.0±2.0 (SD) years in the placebo reading glasses group Sex: 63.9% were female in base-in prism reading glasses group; 47.2% were female in placebo reading glasses group Key inclusion criteria: age 9 to 18 years; best corrected visual acuity of 20/25 or better in both eyes at distance and near; willingness to wear eyeglasses to correct refractive error, if necessary; exophoria at near at least 4 D greater than at far; insufficient positive fusional convergence at near (fails Sheard's criterion); receded near point of convergence of > 6 cm break; appreciation of at least 500 seconds of arc on the forms part of the Randot Stereotest; Convergence Insufficiency Symptom Survey-V15 score > 16; informed consent and willingness to participate in the study and be randomized. Key exclusion criteria: convergence insufficiency previously treated with prism, pencil push ups, or office based vision therapy/orthoptics (no more than 2 months of treatment within the past year); amblyopia; constant strabismus; history of strabismus surgery; anisometropia > 1.50 D (spherical equivalent) difference between eyes; previous refractive surgery; vertical heterophoria greater than 1 D; systemic diseases known to affect accommodation, vergence, and ocular motility such as multiple sclerosis, Grave's thyroid disease, myasthenia gravis, diabetes, and Parkinsons disease; any ocular or systemic medication known to affect accommodation or vergence; monocular accommodative amplitude less than 4 D in either eye as measured by the push up method; manifest or latent nystagmus; attention deficit hyperactivity disorder or learning disability diagnosis by parental report that, in the investigator's opinion, would interfere with treatment.
Interventions	• Intervention regimen #1: base-in prism reading glasses Patients in this group received glasses that corrected for the patient's refractive error, if necessary, and base-in prism. The amount of prism was based on the minimum amount necessary to meet Sheard's criterion with no less than 1 D prescribed. To determine the amount of prism necessary to achieve this relationship he proposed the following formula: prism to be prescribed = 2/3 phoria -1/3 compensating fusional vergence. The amount of prism was rounded up to the nearest half prism diopter and split equally

CITT 2005a (Continued)

	 between the two eyes if the magnitude exceeded 1 D. The patient was asked to wear these glasses for all reading and near tasks requiring more than 5 minutes. Intervention regimen #2: placebo reading glasses Patients in this group received glasses that corrected their refractive error, or plano lenses were prescribed for those who did not require a refractive correction. The patient was asked to wear these glasses for all reading and near tasks requiring more than 5 minutes.
Outcomes	 Primary outcome: convergence insufficiency symptoms measured using Convergence Insufficiency Symptom Survey V-15 after 6 weeks of therapy. Key secondary outcomes: near point of convergence, and positive fusional vergence at near at 6 weeks of therapy. No harm was reported.
Notes	Funding sources: grants from the Pennsylvania and Ohio Lions.Subgroup analyses: none reported

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"The data coordinating centre randomly assigned eligible patients with equal proba- bility to either base-in prism reading glasses or placebo reading glasses. Randomization was accomplished with the study's web site using a permuted block design stratified by site."
Allocation concealment?	Yes	"Allocation to treatment group was achieved using a secure web site. Re- searchers entered eligibility data and were then given the group membership infor- mation (personal communication with the lead investigator)".
Blinding? Primary outcome	Yes	"Neither the patient nor the examiner per- forming testing at the outcome examina- tion was aware of the treatment assignment. To prevent potential examiner unmasking by observation of the glasses, the study co- ordinator placed Tac 'N Stik reusable adhe- sive around the edges of the eyeglasses. The edges of the lenses were therefore obscured, making it impossible for the examiner to see the edge thickness of the lenses."
Blinding? Secondary outcomes	Yes	See above.

CITT 2005a (Continued)

Incomplete outcome data addressed? Primary outcome	Unclear	"Thirty one of the 36 patients (86%) as- signed to receive base-in prism reading glasses and 34 of the 36 (94%) assigned to placebo reading glasses completed their 6 week outcome examination. There was no statistically significant difference in the per- centage loss to follow up between the two treatment groups (p=0.43)." "Statistical analyses techniques were em- ployed which allowed for incomplete data. No imputation or sensitivity analyses were performed (personal communication with the lead investigator)".
Incomplete outcome data addressed? Secondary outcomes	Unclear	See above.
Free of selective reporting?	Yes	All outcomes listed in the study protocol were reported.
Intention-to-treat (ITT) analysis?	Yes	Not reported in the article. The lead in- vestigator described through personal com- munication "All subjects were analyzed in the group to which they were randomized. There were no subjects switch groups."

Methods	 Study design: RCT Number randomized: 47 (15 assigned to pencil push-ups; 17 assigned to vision therapy/orthoptics; 15 assigned to placebo vision therapy/orthoptics) Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 38 (81%) (11 of 15 assigned to pencil push-ups; 15 of 17 assigned to vision therapy/orthoptics; 12 of 15 assigned to placebo vision therapy/ orthoptics) Number of centers: 6 Date of first enrolment: October 2000 Length of follow-up: planned: 12 weeks after initiation of treatment; actual: 12 weeks after initiation of treatment Sample size estimation: no formal sample size calculations were performed <i>a priori</i> because one goal of this pilot trial was to estimate the variability in the Convergence Insufficiency Symptom Survey, with α=0.05, assuming a 2-sided test, and assuming the post treatment mean of the most effective treatment group would approximate the mean among patients with normal binocular vision, the mean for the placebo group would decrease 20% from its baseline value, and the mean for the other treatment group would fall in the middle of these two groups, the sample size of 47 yields a power of 92.8%.
Participants	 Country of recruitment: United States Mean age: 11.2±2.2 (SD) years Sex: 57% were female Key inclusion criteria: ages 9 to 18 years inclusive; best-corrected visual acuity of 20/25 OU at distance and near; willingness to wear eyeglasses or contact lenses to correct refractive error, if necessary; exophoria at near at least 4 Δ greater than at far; insufficient positive fusional convergence (i.e., failing Sheard's criterion or < 15-Δ break on positive fusional vergence testing using a prism bar); receded near point of convergence of greater than or equal to 6 cm break; appreciation of at least 500s of arc on the forms part of the Randot Stereotest; Convergence Insufficiency Symptom Survey-V13 (original 13-item version) score > 9; informed consent and willingness to participate in the study and be randomized. Key exclusion criteria: convergence insufficiency previously treated with pencil push-ups (no more than 2 mo of treatment within the past year); convergence insufficiency previously treated with office-based vision therapy/orthoptics (no more than 2 mo of treatment within the past year); and of strabismus surgery; anisometropia > 1.50-D difference between eyes; prior refractive surgery; vertical heterophoria > 1Δ; systemic diseases known to affect accommodation, vergence, and ocular motility, such as multiple sclerosis, Graves thyroid disease, myasthenia gravis, diabetes, and Parkinson disease; any ocular or systemic medication known to affect accommodation or vergence; monocular accommodative amplitude < 4 D in either eye as measured by the Donder push-up method; manifest or latent nystagmus; attention-deficit/hyperactivity disorder or learning disability diagnosis by parental report; household member or sibling already enrolled in the CITT; any eye care professional, technician, medical student, or optometry student.

Interventions Intervention regimen #1: pencil push-ups Patients in the pencil push-ups group were taught a pencil push-up procedure that included monitoring for suppression. Patients were instructed to hold a pencil at arm's length directly between their eyes, and an index card, serving as a suppression control, was placed on the wall 6 to 8 feet away. Patients were instructed to look at the very tip of the sharpened pencil and to try and keep the pencil point single while moving it toward their nose. If one of the cards in the background disappeared, patients were instructed to stop moving the pencil and blink their eyes until both cards were present. Patients were told to continue moving the pencil slowly toward their nose until it could no longer be kept single and then to try and get the pencil point back into one. If patients were able to regain single vision, they were asked to continue moving the pencil closer to their nose. If patients could not get the pencil back to one, they were instructed to start the procedure again. Patients were instructed to do three sets of 20 pencil push-ups per day at home, 5 days per week for 12 weeks, and this treatment required an average of 15 minutes per day. Prior to doing the procedure at home, children had to demonstrate their understanding and ability to perform the procedure according to protocol. • Intervention regimen #2: office-based vision therapy/orthoptics The vision therapy/orthoptics group received therapy administered by a trained therapist during a weekly, 60-minute office visit, with additional procedures to be performed at home for 15 minutes a day, five times per week for 12 weeks. The items are listed in the article. In addition, treatment procedures were practiced at home. During a typical office-based treatment session, the patient practiced four to five procedures with constant supervision and guidance from the therapist. There were no diagnostic tests performed during these sessions. The therapist followed a very detailed and specific CITT protocol from the manual of procedures, which described the proper treatment technique, amount of time the technique was to be used, expected performance, and criteria for ending the procedure and advancing to a more difficult level. • Intervention regimen #3: placebo office-based vision therapy/orthoptics Like the vision therapy/orthoptics group, the placebo vision therapy/orthoptics group received therapy administered by a trained therapist during a 60-minute office visit and was prescribed procedures to be performed at home for 15 minutes, five times per week for 12 weeks. The procedures for placebo vision therapy/orthoptics were designed to simulate real vision therapy/orthoptics procedures without the expectation of affecting vergence, accommodation, or saccadic function. Outcomes • Primary outcome: convergence insufficiency symptoms measured using Convergence Insufficiency Symptom Survey V-15 after 12 weeks of therapy. A symptom score of 16 or higher differentiated children with symptomatic convergence insufficiency from those with normal binocular vision (sensitivity = 95.7%; specificity = 85.7%). The primary outcome was also measured at 4 and 8 weeks of therapy. • Key secondary outcomes: near point of convergence measured with the Astron International Accommodative Rule; positive fusional vergence at near measurements: measured with a horizontal prism bar while the patient viewed a 20/30-size column of letters held at 40cm. The secondary outcomes were measured at 4, 8 and 12 weeks of therapy. • No harms were reported.

CITT 2005b (Continued)

Notes	 Funding sources:National Eye Institute, National Institutes of Health, Bethesda, MD USA. Subgroup analyses: none reported

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"The data-coordinating center for the study, randomly assigned eligible patients with equal probability to either pencil push-ups, vision therapy/orthoptics, or placebo vision therapy/orthoptics. Ran- domization was accomplished with the study's Web site using blocks of 6 so that the investigator could not predict the sequence of treatment assignments. To ensure ap- proximately equal numbers of patients in each treatment arm, randomization was performed separately for each site."
Allocation concealment?	Yes	See above.
Blinding? Primary outcome	Yes	"At these follow-up visits, an examiner who was masked to the patient's treat- ment group administered the Convergence Insufficiency Symptom Survey V-15, the cover test, and near point of convergence and positive fusional vergence at near mea- surements."
Blinding? Secondary outcomes	Yes	See above.
Incomplete outcome data addressed? Primary outcome	Unclear	"The completion rate was not related to treatment assignment (p =.59). Of the nine patients not completing the primary out- come examination, four were lost to follow- up, two parents decided after randomiza- tion that they preferred to have their chil- dren treated outside of the study, and three did not complete the outcome examination within the visit window." "There were no statistically significant or clinically relevant differences in demo- graphic or clinical measures at eligibility found between these patients and those who completed the study within the treat-

CITT 2005b (Continued)

		ment window." "Statistical analyses techniques were em- ployed which allowed for incomplete data. No imputation or sensitivity analyses were performed (personal communication with the lead investigator)".
Incomplete outcome data addressed? Secondary outcomes	Unclear	See above.
Free of selective reporting?	Yes	All outcomes listed in the study protocol were reported.
Intention-to-treat (ITT) analysis?	Yes	Not reported in the article. The lead in- vestigator described through personal com- munication "all participants were analyzed in the group to which they were random- ized. No participants switched groups."

CITT 2005c

Methods	 Study design: RCT Number randomized: 46 (17 assigned to pencil push-ups; 15 assigned to vision therapy/orthoptics; 14 assigned to placebo vision therapy/orthoptics) Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 40 (87%) (15 of 17 assigned to pencil push-ups; 12 of 15 assigned to vision therapy/orthoptics; 13 of 14 assigned to placebo vision therapy/ orthoptics) Number of centers: 6 Date of first enrolment: Novermber 2000 Length of follow-up: planned: 12 weeks after initiation of treatment; actual: 12±2 weeks after initiation of treatment Sample size estimation: no formal sample size calculations were performed <i>a priori</i> because one goal of this pilot trial was to estimate the variability of the outcome measure. At the study completion, using the observed variability in the Convergence Insufficiency Symptom Survey, with α=0.05, assuming a 2-sided test, and assuming the post treatment mean of the most effective treatment group would approximate the mean among patients with normal binocular vision at 12 weeks, the mean for the other treatment group would fall in the middle of these two groups, the sample size of 46 yields a power of 99.6%.
Participants	 Country of recruitment: United States Mean age: 24.4±3.4 (SD) years in the pencil push-ups group; 23.7±3.9 (SD) years in the vision therapy/orthoptics group; 25.1±3.5 (SD) years in the placebo vision therapy/orthoptics group Sex: 70.6% were female in the pencil push-ups group; 73.3% were female in the

CITT 2005c (Continued)

vision therapy/orthoptics group; 71.4% were female in the placebo vision therapy/ orthoptics group

• Key inclusion criteria: age 19 to 30 years; best corrected visual acuity of 20/25 or better in both eyes at distance and near; willingness to wear eyeglasses or contact lenses to correct refractive error, if necessary; exophoria at near at least 4 D greater than at far; insufficient positive fusional convergence at near (i.e., failing Sheard's criterion 21 or less than 15 break); receded near point of convergence of ≥ 6 cm break; appreciation of at least 500 seconds of arc on the forms part of the Randot Stereotest; Convergence Insufficiency Symptom Survey V-13 score > 9; informed consent and willingness to participate in the study and be randomized.

• Key exclusion criteria: convergence insufficiency previously treated with pencil push ups, or office-based vision therapy/orthoptics (no more than 2 months of treatment within the past year); amblyopia; constant strabismus; history of strabismus surgery; anisometropia > 1.50 D (spherical equivalent) difference between eyes; prior refractive surgery; vertical heterophoria greater than 1 D; systemic diseases known to affect accommodation, vergence, and ocular motility such as multiple sclerosis, Grave's thyroid disease, myasthenia gravis, diabetes, and Parkinsons disease; any ocular or systemic medication known to affect accommodation or vergence; monocular accommodative amplitude less than 4 D in either eye as measured by the push up method; manifest or latent nystagmus; household member already enrolled in the CITT; any eye care professional, ophthalmic technician, medical student, or optometry student.

Intervention regimen #1: pencil push-ups

Patients in the pencil push-ups group were taught a pencil push-up procedure that included monitoring for suppression. Patients were instructed to hold a pencil at arm's length directly between their eyes, and an index card, serving as a suppression control, was placed on the wall 6 to 8 feet away. Patients were instructed to look at the very tip of the sharpened pencil and to try and keep the pencil point single while moving it toward their nose. If one of the cards in the background disappeared, patients were instructed to stop moving the pencil and blink their eyes until both cards were present. Patients were told to continue moving the pencil slowly toward their nose until it could no longer be kept single and then to try and get the pencil point back into one. If patients were able to regain single vision, they were asked to continue moving the pencil closer to their nose. If patients could not get the pencil back to one, they were instructed to start the procedure again. Patients were instructed to do three sets of 20 pencil push-ups per day at home, 5 days per week for 12 weeks, and this treatment required an average of 15 minutes per day. Prior to doing the procedure at home, the patient had to demonstrate their understanding and ability to perform the procedure according to protocol.

• Intervention regimen #2: office-based vision therapy/orthoptics

The vision therapy/orthoptics group received therapy administered by a trained therapist during a weekly, 60-minute office visit, with additional procedures to be performed at home for 15 minutes a day, five times per week for 12 weeks. The items are listed elsewhere. In addition, treatment procedures were practiced at home. During a typical office-based treatment session, the patient practiced four to five procedures with constant supervision and guidance from the therapist. There were no diagnostic tests performed during these sessions. The therapist followed a very detailed and specific CITT protocol from the manual of procedures, which described the proper treatment technique, amount of time the technique was to be used, expected performance, and criteria for ending the

Interventions

CITT 2005c (Continued)

	 procedure and advancing to a more difficult level. Intervention regimen #3: placebo office-based vision therapy/orthoptics Like the vision therapy/orthoptics group, the placebo vision therapy/orthoptics group received therapy administered by a trained therapist during a 60-minute office visit and was prescribed procedures to be performed at home for 15 minutes, five times per week for 12 weeks. The procedures for placebo vision therapy/orthoptics were designed to simulate real vision therapy/orthoptics procedures without the expectation of affecting vergence, accommodation, or saccadic function.
Outcomes	 Primary outcome: convergence insufficiency symptoms measured using Convergence Insufficiency Symptom Survey V-15 after 12 weeks of therapy. The primary outcome was also measured at baseline, 4 and 8 weeks of therapy. Key secondary outcomes: near point of convergence, and positive fusional vergence at near. The secondary outcomes were measured at baseline, 4, 8 and 12 weeks of therapy. No harms were reported.
Notes	 Funding sources: Grant EY13164-01, National Eye Insititute, National Insitutes of Health, Bethesda, MD USA. Subgroup analyses: none reported

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"The data-coordinating center for the study, randomly assigned eligible patients with equal probability to either pencil push-ups, vision therapy/orthoptics, or placebo vision therapy/orthoptics. Ran- domization was accomplished with the study's Web site using blocks of 6 so that the investigator could not predict the sequence of treatment assignments. To ensure ap- proximately equal numbers of patients in each treatment arm, randomization was performed separately for each site."
Allocation concealment?	Yes	See above.
Blinding? Primary outcome	Yes	"Examiners were masked to the treatment assignment (personal communication with the lead investigator)."
Blinding? Secondary outcomes	Yes	See above.

CITT 2005c (Continued)

Incomplete outcome data addressed? Primary outcome	Unclear	"All results are reported for only those pa- tients with data at the 12-week visit. Fur- ther analyses were performed after imput- ing outcome values for those patients lost to follow-up. That is, the value at the last available examination was used for each pa- tient who did not complete the study. For 5/6 patients, the only data available were collected at the eligibility visit. When dif- ference in statistical analyses were found, the results from analyses with imputed data are also reported."
Incomplete outcome data addressed? Secondary outcomes	Unclear	See above.
Free of selective reporting?	Yes	All outcomes listed in the study protocol were reported.
Intention-to-treat (ITT) analysis?	Yes	Not reported in the article. The lead in- vestigator described through personal com- munication "All participants were analyzed in the group to which they were random- ized. No participants switched groups."

|--|

0111 2000	
Methods	 Study design: RCT Number randomized: 221 (54 assigned to home-based pencil push-ups (HBPP); 53 assigned to home-based computer vergence/accommodative therapy and pencil push-ups (HBCVAT+); 60 assigned to office-based vergence/accommodative therapy with home reinforcement (OBVAT); 54 assigned to office-based placebo therapy with home reinforcement (OBPT)) Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 219 (99%) (53 of 54 assigned to HBPP; 52 of 53 assigned HBCVAT+; 59 of 60 assigned to OBVAT; 54 of 54 assigned to OBPT) Number of centers: 9 Date of first enrolment: July 2005 Length of follow-up: planned: 1 year after initiation of treatment; actual: this article reported outcomes at 12 weeks after initiation of treatment Sample size estimation: all sample size calculations were performed using PASS 2000 software35 and assuming a 2-sided test with 90% power. For a given outcome measure, the common standard deviation (SD) obtained from the CITT pilot study was used as an estimate of variability. To control for multiple comparisons (4 groups, with 2 compared at a time [6 pair-wise comparisons]), the α level used for determining sample size was set at 0.0083 (0.05/6). The sample size of 52 children per group was based on the required sample size for the 3 outcome variables and adjusted for a 10% loss to follow-up.
Participants	 Country of recruitment: United States Mean age: 11.9±2.2 (SD) years in the HBPP group; 11.6±2.3 (SD) years in the HBCVAT+ group; 12.0±2.6 (SD) years in the OBVAT group; 11.8±2.2 (SD) years in the OBPT group Sex: 27% were female in the HBPP group; 31% were female in the HBCVAT+ group; 41% were female in the OBVAT group; 32% were female in the OBPT group Key inclusion criteria: aged 9 to 17 years; exodeviation at near of at least 4 prism diopters greater than at far; receded near point of convergence (NPC) break (≥ 6 cm); insufficient positive fusional vergence at near (PFV) (i.e., failing Sheard's criterion; Convergence Insufficiency Symptom Survey score of 16 or greater; best-corrected visual acuity of 20/25 or better in both eyes at distance and near; willingness to wear eyeglasses or contact lenses to correct refractive error, if necessary; exodeviation at near at least 4Δ greater than at far; insufficient positive fusional convergence; receded near point of convergence of ≥ 6 cm break; appreciation of at least 500 seconds of arc on the forms part of the Randot Stereotest; Convergence Insufficiency Symptom Survey score ≥ 16. Key exclusion criteria: convergence insufficiency previously treated with pencil push-up therapy (> 2 wks of treatment), home- or office-based vergence/ accommodative therapy/orthoptics; amblyopia; constant strabismus; history of strabismus surgery; high refractive error; prior refractive surgery; vertical heterophoria >1∆; systemic diseases known to affect accommodation, vergence and ocular motility; accommodative amplitude < 5 D in either eye as measured by the Donders' push-up method Manifest or latent nystagmus; developmental disability; family or household member or sibling already enrolled in the CITT; family or household member of an eye care professional, ophthalmic technician, ophthalmology or optometry resident, or optometry student; convergence insufficiency secondary to acquired brain injury or any other neurological disorder.

Interventions Intervention regimen #1: home-based pencil push-ups The pencil push-ups procedure involved using a pencil with 20/60 reduced Snellen letters and a white index card placed in the background to provide a suppression check by using physiological diplopia awareness. The goal of the procedure was to move the pencil to within 2 to 3 cm of the brow, just above the nose on each push-up while trying to keep the target single and clear. Patients were instructed to perform the pencil pushups procedure 15 minutes per day, 5 days per week. They maintained home therapy logs, recording the closest distance that they could maintain fusion after each 5 minutes of therapy. • Intervention regimen #2: home-based computer vergence/accommodative therapy and pencil push-ups Patients in this group were taught to perform the pencil push-up procedure as well as procedures on the Home Therapy System/Computerized Vergence System (HTS/CVS) computer software system (Computer Orthoptics, Gold Canyon, Arizona). Using this program, they performed fusional vergence and accommodative therapy procedures, including vergence base-in, vergence base out, autoslide vergence, and jump ductions vergence programs using random-dot stereopsis targets. The accommodative rock program was used for accommodative therapy. Much like a clinician would do at each followup visit, this computer program automatically modified the therapy program after each session based on the patient's performance. Patients were instructed to do pencil pushups 5 minutes per day, 5 days per week, and the HTS software program for 15 minutes per day, 5 days per week, and to save their data on a disk provided by the study and to bring the disk to each follow-up visit. • Intervention regimen #3: office-based vergence/accommodative therapy with home reinforcement The OBVAT group received a weekly 60-minute in-office therapy visit with additional prescribed procedures to be performed at home for 15 minutes a day, 5 days per week. The therapy procedures are described in detail elsewhere (CITT 2008). At each officebased therapy session, the patient performed 4 to 5 procedures with constant supervision and guidance from the therapist. There were no diagnostic tests performed during these sessions. The therapist followed a detailed and specific protocol from the CITT manual of procedures (http://optometry.osu.edu/research/CITT/4363.cfm); this document describes each procedure, amount of time procedure was performed, expected performance, and criteria for ending the procedure and advancing to a more difficult level. • Intervention regimen #4: office-based placebo therapy with home reinforcement Patients in the OBPT group received therapy during a weekly 60-minute office visit and were prescribed procedures to be performed at home for 15 minutes per day, 5 days per week. The placebo therapy program consisted of 16 in-office therapy procedures and 4 home therapy procedures, which were designed to look like real vergence/accommodative therapy procedures yet not to stimulate vergence, accommodation, or fine saccadic eye movement skills beyond normal daily visual activities. The therapist followed a detailed protocol from the CITT manual of procedures. Five procedures were performed during each office therapy visit and 2 procedures were assigned for home therapy each week. Objectives and goals were established for each placebo procedure to simulate real therapy. For motivational purposes, the therapist told the patient the objective of each procedure before beginning the technique.

CITT 2008 (Continued)

Outcomes	 Primary outcome: convergence insufficiency symptoms measured using Convergence Insufficiency Symptom Survey V-15 after 12 weeks of therapy. The CI symptoms was also measured at baseline, 4 and 8 weeks of therapy. Key secondary outcomes: near point of convergence, and positive fusional vergence at near. The secondary outcomes were measured at baseline, 4, 8 and 12 weeks of therapy. Harms were reported.
Notes	 Funding sources: National Eye Institute, National Institutes of Health, Bethesda, MD USA. Subgroup analyses: none reported

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Randomization was achieved using a secure web site created and managed by the data coordinating center. The web site generated the patient's group assignment and assigned the patient a unique study identification number using a pre-determined list gener- ated by the data coordinating center. The randomization algorithm assigned patients to the four treatment groups with equal probability using a randomized permuted block design so investigators could not pre- dict the sequence of treatment assignments. To ensure approximately equal numbers of patients in each treatment arm, random- ization was performed separately for each clinical site.
Allocation concealment?	Yes	Access to the list was limited to the pro- grammer and principal investigator of the data coordinating center (personal commu- nication with the lead investigator).
Blinding? Primary outcome	Yes	The examiners responsible for obtaining the outcome measures were masked to pa- tient treatment assignment. None of the examiners felt that they could identify the patients' group assignment at the 4 or 8 week masked examinations, and only one examiner felt that he could iden- tify the group assignment at outcome. One third of the examiners responded that their patient was assigned to the OBVAT group,

CITT 2008 (Continued)

		24% responded that he/she was assigned to HBCVAT+, 21% said their patient was as- signed to HBPP, and 21% said their patient was assigned to the OBPT group. Exam- iners, when asked to guess, were correct in identifying the patient's group assignment only 34% of the time, which is less than is expected by chance. There was low agree- ment between the actual group assignment and the examiner's guess of assigned treat- ment group (0.11, 95% confidence inter- val, 0.04 to 0.20).
Blinding? Secondary outcomes	Yes	See above.
Incomplete outcome data addressed? Primary outcome	Unclear	"Statistical analyses techniques were em- ployed which allowed for incomplete data. No imputation or sensitivity analyses were performed (personal communication with the lead investigator)".
Incomplete outcome data addressed? Secondary outcomes	Unclear	See above.
Free of selective reporting?	Yes	All outcomes listed in the study protocol were reported.
Intention-to-treat (ITT) analysis?	Yes	All participants were analyzed in the group to which they were randomized.

Teitelbaum 2009

Methods	 Study design: RCT with cross-over design Number randomized: 29 Unit of randomization: individual participant (convergence insufficiency is a binocular vision disorder) Number analyzed: 29 Number of centers: 1 Date of first enrolment: not reported Length of follow-up: 3 weeks after initiation of each treatment (total study period was 6 weeks) Sample size estimation: estimated <i>post hoc</i> using data from the first 18 participants. "A sample size of 21 would be required to give 80% power at the 0.05 level, and 28 subjects are needed to given the 90% power."
Participants	 Country of recruitment: United States Mean age: 54.14±2.2 (SD) years

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Teitelbaum 2009 (Continued)

	 Sex: 86% female Key inclusion criteria: age ≥ 45 years; best-corrected visual acuity of 20/25 or better in each eye at distance and near; currently wearing progressive addition lenses; a minimum of 1.50 add in subjects' habitual prescription; a minimum of 2 hours spent on reading or close work on a daily basis; associated phoria at near ≥ 1∆ BI; no associated phoria with the potential BI prism at distance; exophoria at near at least 4∆ greater than at distance; Convergence Insufficiency Symptom Score ≥16; willingness to participate in the study and wear two pairs of eyeglasses consecutively. Key exclusion criteria: constant strabismus at distance or at near; convergence insufficiency previously treated with prism; vertical heterophoria greater than 1∆.
Interventions	 Intervention regimen #1: base-prism, using a novel progressive addition lens design which incorporates base-in prism in the near portion only Intervention regimen #2: progressive addition lenses
Outcomes	 Primary outcome: convergence insufficiency symptoms measured using Convergence Insufficiency Symptom Survey V-15 after 3 weeks of therapy. Key secondary outcomes: not reported No harms were reported.
Notes	 Funding sources: Signet Armorlite funded the study and provided the spectacle lenses. Subgroup analyses: none reported

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Patients were assigned two pairs of pro- gressive addition lenses (PAL) fabricated by Signet Armorlite with an updated lens pre- scription, in a randomized sequence."
Allocation concealment?	Unclear	Not reported.
Blinding? Primary outcome	Yes	"The study had a double-blind design as neither the examiner nor subject was aware of the glasses assignment."
Blinding? Secondary outcomes	Yes	See above.
Incomplete outcome data addressed? Primary outcome	Unclear	Unclear how many participants were ana- lyzed for the primary outcome.
Incomplete outcome data addressed? Secondary outcomes	Unclear	Not reported.

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Teitelbaum 2009 (Continued)

Free of selective reporting?	Unclear	Insufficient information to assess.
Intention-to-treat (ITT) analysis?	Unclear	Insufficient information to assess.

CITT: Convergence Insufficiency Treatment Trial HBPP: Home-based pencil push-ups HBCVAT+: Home-based computer vergence/accommodative therapy and pencil push-ups OBVAT: Office-based vergence/accommodative therapy with home reinforcement OBPT: Office-based placebo therapy with home reinforcement RCT: Randomized controlled trial SD: Standard deviation

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Al-Qurainy 1995	Not in patients with convergence insufficiency
Daum 1986	Not a RCT
Daum 1987	Not in patients with convergence insufficiency
Dragomir 2001	Not a RCT
Frantz 1993	Not a RCT
Gall 1998	Not a RCT
Gallaway 2002	Not a RCT
Granet 2005	Not a RCT
Grisham 1996	Unclear how many patients were affected by convergence insufficiency
Harele 2006	Not a RCT
Kerkhoff 1994	Not a RCT
Kommerell 2002	Not a RCT
Ludlam 1988	Not in patients with convergence insufficiency
O'Leary 2006	Not a RCT

Non-surgical interventions for convergence insufficiency (Review)

(Continued)

Rawstron 2005	Not a RCT
Rutstein 1988	Not in patients with convergence insufficiency
Stavis 2002	Not a RCT
Worrell 1971	Not a RCT

RCT: Randomized controlled trial

DATA AND ANALYSES

Comparison 1. Base-in prism reading glasses versus placebo reading glasses in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 6 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 Change in positive fusional vergence at near at 6 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Change in Convergence Insufficiency Symptom Survey (CISS) score at 6 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 2. Base-in prism reading glasses using a progressive addition lens design versus progressive addition lens alone in adults

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Convergence Insufficiency Symptom Survey (CISS) score at 3 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 3. Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
therapy				
1.1 Children	2	138	Mean Difference (IV, Fixed, 95% CI)	3.99 [2.11, 5.86]
1.2 Young adults	1	27	Mean Difference (IV, Fixed, 95% CI)	2.8 [-2.41, 8.01]
2 Change in positive fusional vergence at near at 12 weeks of therapy	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Children	2	138	Mean Difference (IV, Fixed, 95% CI)	13.13 [9.91, 16.35]
2.2 Young adults	1	27	Mean Difference (IV, Fixed, 95% CI) Mean Difference (IV, Fixed, 95% CI)	7.70 [0.82, 14.58]

Non-surgical interventions for convergence insufficiency (Review)

3 Change in Convergence Insufficiency Symptom (CISS)	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
score				
3.1 Children	2	138	Mean Difference (IV, Fixed, 95% CI)	9.86 [6.70, 13.02]
3.2 Young adults	1	27	Mean Difference (IV, Fixed, 95% CI)	4.70 [-1.45, 10.85]

Comparison 4. Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Change in positive fusional vergence at near at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Change in Convergence Insufficiency Symptom (CISS) score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Comparison 5. Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Change in positive fusional vergence at near at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Change in Convergence Insufficiency Symptom (CISS) score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Non-surgical interventions for convergence insufficiency (Review)

Comparison 6. Home-based pencil push-ups versus office-based placebo in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Change in positive fusional vergence at near at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Change in Convergence Insufficiency Symptom (CISS) score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Comparison 7. Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Change in positive fusional vergence at near at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Change in Convergence Insufficiency Symptom (CISS) score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Comparison 8. Vision therapy/orthoptics versus office-based placebo in children

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in near point of convergence at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2 Change in positive fusional vergence at near at 12 weeks of therapy	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Change in Convergence Insufficiency Symptom (CISS) score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Non-surgical interventions for convergence insufficiency (Review)

Analysis 1.1. Comparison I Base-in prism reading glasses versus placebo reading glasses in children, Outcome I Change in near point of convergence at 6 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: I Base-in prism reading glasses versus placebo reading glasses in children

Outcome: I Change in near point of convergence at 6 weeks of therapy

Study or subgroup	Prism reading glasses N	Mean(SD)	Placebo reading glasses N	Mean(SD)	Mean Difference IV,Fixed,95% Cl	Mean Difference IV,Fixed,95% CI
CITT 2005a	31	4.14 (9.99)	34	1.33 (8.25)		2.81 [-1.67, 7.29]
					10 -5 0 5 10	
				Fa	vours placebo Favours prism	

Analysis 1.2. Comparison I Base-in prism reading glasses versus placebo reading glasses in children, Outcome 2 Change in positive fusional vergence at near at 6 weeks of therapy.

N Mean(SD) N Mean(SD) IV,Fixed,95% CI IV,Fixed,95%	Study or subgroup	Prism reading glasse	s	Placebo reading	glasses			Me	an Diffe	rence	Mean Differenc
-4 -2 0 2 4						Mean(SD)		IV,Fixe	ed,95%	CI	IV,Fixed,95% C
	CITT 2005a	3	I I.97 (4.65)		34	2.66 (8.43)					-0.69 [-3.96, 2.58
Favours placebo Favours prism							-4	-2	0	2 4	
						F	Favours pla	.cebo	Fav	ours prism	

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Analysis I.3. Comparison I Base-in prism reading glasses versus placebo reading glasses in children, Outcome 3 Change in Convergence Insufficiency Symptom Survey (CISS) score at 6 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: I Base-in prism reading glasses versus placebo reading glasses in children

Outcome: 3 Change in Convergence Insufficiency Symptom Survey (CISS) score at 6 weeks of therapy

Study or subgroup	Prism reading glasses N	Mean(SD)	Placebo reading glasses N	Mean(SD)	Mean Difference IV,Fixed,95% Cl	Mean Difference IV,Fixed,95% CI
CITT 2005a	31	5. (.9)	34	10.84 (13.41)		4.26 [-1.90, 10.42]
					-20 -10 0 10 20	
				Fa	avours placebo Favours prism	

Analysis 2.1. Comparison 2 Base-in prism reading glasses using a progressive addition lens design versus progressive addition lens alone in adults, Outcome I Convergence Insufficiency Symptom Survey (CISS) score at 3 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 2 Base-in prism reading glasses using a progressive addition lens design versus progressive addition lens alone in adults

Outcome: I Convergence Insufficiency Symptom Survey (CISS) score at 3 weeks of therapy

Study or subgroup	Base-in prism glasses N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% Cl	Mean Difference IV,Fixed,95% Cl
Teitelbaum 2009	29	13.38 (9.44)	29	23.62 (10.76)		-10.24 [-15.45, -5.03]
				Favo	-20 -10 0 10 20 purs prism glasses Favours control	
Non-surgical interve	ntions for convergence	insufficiency (R	eview)			42

Analysis 3.1. Comparison 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults, Outcome I Change in near point of convergence at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults

Outcome: I Change in near point of convergence at 12 weeks of therapy

Study or subgroup	Vision therapy/orthoptics		Pencil push-ups		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
l Children							
CITT 2005b	15	9.2 (8.5)	11	5.4 (9.3)		→ 7.2 %	3.80 [-3.18, 10.78]
CITT 2008	59	10.4 (5.3)	53	6.4 (5.2)		92.8 %	4.00 [2.05, 5.95]
Subtotal (95% CI)	74		64		•	100.0 %	3.99 [2.11, 5.86]
Heterogeneity: Chi ² = 0.0	0, df = 1 (P = 0.96); $l^2 = 0.96$	0%					
Test for overall effect: Z =	4.17 (P = 0.000031)						
2 Young adults							
CITT 2005c	12	7.5 (8.2)	15	4.7 (4.7)		100.0 %	2.80 [-2.41, 8.01]
Subtotal (95% CI)	12		15			100.0 %	2.80 [-2.41, 8.01]
Heterogeneity: not applica	able						
Test for overall effect: Z =	1.05 (P = 0.29)						
						1	
				-	0 -5 0 5	10	

Favors pencil push-ups

Favors vison therapy

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Analysis 3.2. Comparison 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults

Outcome: 2 Change in positive fusional vergence at near at 12 weeks of therapy

Study or subgroup	Vision therapy/orthoptics		Pencil push-ups		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
I Children							
CITT 2005b	15	8.9 (.4)	11	2 (4.3)		→ 26.1 %	16.90 [10.60, 23.20]
CITT 2008	59	19.7 (10.2)	53	7.9 (10)		73.9 %	.80 [8.06, 5.54]
Subtotal (95% CI) 74		64		•	100.0 %	13.13 [9.91, 16.35]
Heterogeneity: Chi ² =	.86, df = 1 (P = 0.17); l ² =4	6%					
Test for overall effect: Z	= 7.99 (P < 0.00001)						
2 Young adults							
CITT 2005c	12	18.3 (9.2)	15	10.6 (8.9)		100.0 %	7.70 [0.82, 14.58]
Subtotal (95% CI) 12		15		-	100.0 %	7.70 [0.82, 14.58]
Heterogeneity: not appl	icable						
Test for overall effect: Z	= 2.19 (P = 0.028)						
						1	

-20 -10 0 10 20

Favours pencil push-ups Favours vision therapy

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Analysis 3.3. Comparison 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 3 Office-based vision therapy/orthoptics versus home-based pencil push-ups in children and young adults

Outcome: 3 Change in Convergence Insufficiency Symptom (CISS) score

Study or subgroup	Vision therapy/orthoptics		Pencil push-ups		Mea	n Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Fixe	d,95% Cl		IV,Fixed,95% CI
l Children								
CITT 2005b	15	22.6 (11.6)	11	3.4 (7.3)			18.8 %	19.20 [11.92, 26.48]
CITT 2008	59	14.8 (9.4)	53	7.1 (9.5)			81.2 %	7.70 [4.19, 11.21]
Subtotal (95% CI) 74		64			•	100.0 %	9.86 [6.70, 13.02]
Heterogeneity: Chi ² = 7	7.77, df = $ (P = 0.01); ^2 = 8$	7%						
Test for overall effect: Z	= 6.12 (P < 0.00001)							
2 Young adults								
CITT 2005c	12	15.8 (9.9)	15	. (5)	-		100.0 %	4.70 [-1.45, 10.85]
Subtotal (95% CI) 12		15		-	-	100.0 %	4.70 [-1.45, 10.85]
Heterogeneity: not appl	icable							
Test for overall effect: Z	= 1.50 (P = 0.13)							
							1	
				-20	0 -10 (D 10 2	20	
				Favours pen	icil push-ups	Favours visio	on therapy	

Analysis 4.1. Comparison 4 Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children, Outcome I Change in near point of convergence at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 4 Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children

Outcome: I Change in near point of convergence at 12 weeks of therapy

Study or subgroup	Vision therapy/orthoptics N	Mean(SD)	HBCVAT N	Mean(SD)			ean Difference xed,95% Cl		Mean Difference IV,Fixed,95% Cl
CITT 2008	59	10.4 (5.3)	52	7.5 (5.1)					2.90 [0.96, 4.84]
					-10 Favors HBC	5 SVAT	0 5 Favors v	10 rísion therapy	
	rentions for convergence in The Cochrane Collaboratio			& Sons, Ltd.					45

Analysis 4.2. Comparison 4 Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 4 Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children

Outcome: 2 Change in positive fusional vergence at near at 12 weeks of therapy

Study or subgroup	Vision therapy/orthoptics N	Mean(SD)	HBCVAT N	Mean(SD)		n Difference d,95% Cl	Mean Difference IV,Fixed,95% Cl
CITT 2008	59	19.7 (10.2)	52	12 (10)			7.70 [3.94, 11.46]
				Fa	-20 -10 (avours HBCVAT) 10 20 Favours vision th	пегару

Analysis 4.3. Comparison 4 Office-based vision therapy/orthoptics versus home-based computer assisted pencil push-ups in children, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

Review: Non-surgi	cal interventions for convergence	ce insufficiency					
Comparison: 4 Of	fice-based vision therapy/orthop	otics versus home-ba	ised compute	er assisted penc	il push-ups in chi	ldren	
Outcome: 3 Chang	ge in Convergence Insufficiency	Symptom (CISS) sco	ore				
Study or subgroup	Vision therapy/orthoptics		HBCVAT		٢	1ean Difference	Mean Difference
,	N	Mean(SD)	Ν	Mean(SD)	IV,F	ïxed,95% Cl	IV,Fixed,95% C
CITT 2008	59	14.8 (9.4)	52	6 (9.6)			8.80 [5.26, 12.34
					-20 -10	0 10 20	
					Favours HBCVAT	Favours vision the	rapy
	entions for convergence in						

Analysis 5.1. Comparison 5 Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children, Outcome I Change in near point of convergence at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 5 Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children

Outcome: I Change in near point of convergence at 12 weeks of therapy

Study or subgroup	Pencil push-ups N	Mean(SD)	HBCVAT N	Mean(SD)		Difference 1,95% Cl	Mean Difference IV,Fixed,95% Cl
CITT 2008	53	6.4 (5.2)	52	7.5 (5.1)			-1.10 [-3.07, 0.87]
					-10 -5 0 Favors HBCVAT	5 10 Favors pencil push-ups	

Analysis 5.2. Comparison 5 Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Review: Non-surgic	cal interventions for con-	vergence insufficiency	Ý				
Comparison: 5 Hor	me-based pencil push-up	os versus home-base	d computer assis	sted vision thera	py/orthoptics in chil	ldren	
Outcome: 2 Chang	e in positive fusional ver	rgence at near at 12 v	weeks of therapy	/			
Study or subgroup	Pencil push-ups		HBCVAT			an Difference	Mean Difference
	N	Mean(SD)	Ν	Mean(SD)	IV,Fixe	ed,95% Cl	IV,Fixed,95% CI
CITT 2008	53	7.9 (10)	52	12 (10)		-	-4.10 [-7.93, -0.27]
						<u> </u>	
					-20 -10	0 10 20	
					Favours HBCVAT	Favours pencil push-	ups

Analysis 5.3. Comparison 5 Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 5 Home-based pencil push-ups versus home-based computer assisted vision therapy/orthoptics in children

Outcome: 3 Change in Convergence Insufficiency Symptom (CISS) score

Study or subgroup	Pencil push-ups N	Mean(SD)	HBCVAT N	Mean(SD)		n Difference d,95% Cl	Mean Difference IV,Fixed,95% Cl
CITT 2008	53	7.1 (9.5)	52	6 (9.6)	_	·	1.10 [-2.55, 4.75]
					-20 -10	0 10 20	
					Favours HBCVAT	Favours pencil push-ups	

Analysis 6.1. Comparison 6 Home-based pencil push-ups versus office-based placebo in children, Outcome I Change in near point of convergence at 12 weeks of therapy.

N Mean(SD) N Mean(SD) IV,Fixed,95% CI IV,Fixed,95%	Outcome: I Char	nge in near point of co	onvergence at 12	weeks of therapy			
-10 -5 0 5 10	Study or subgroup		Mean(SD)		Mean(SD)		Mean Difference IV,Fixed,95% (
	CITT 2008	53	6.4 (5.2)	54	3.9 (5.2)		2.50 [0.53, 4.47

Analysis 6.2. Comparison 6 Home-based pencil push-ups versus office-based placebo in children, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 6 Home-based pencil push-ups versus office-based placebo in children

Outcome: 2 Change in positive fusional vergence at near at 12 weeks of therapy

Study or subgroup	Pencil push-ups N	Mean(SD)	Office-based placebo N	Mean(SD)		Me IV,Fix		fferen % Cl	ce		Mean Difference IV,Fixed,95% Cl
CITT 2008	53	7.9 (10)	54	6.9 (9.9)		-					1.00 [-2.77, 4.77]
					I			1			
					-20	-10	0	10	20		
					Favours	placebo	F	avours	pencil p	oush-ups	5

Analysis 6.3. Comparison 6 Home-based pencil push-ups versus office-based placebo in children, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

N Mean(SD) N Mean(SD) IV,Fixed,95% CI IV,Fi	
tudy or subgroup Pencil push-ups Office-based placebo Mean Difference Mean N Mean(SD) N Mean(SD) IV,Fixed,95% Cl IV,Fix CITT 2008 53 7.1 (9.5) 54 7.8 (9.6) - 0.70 [- -20 -10 0 10 20	
N Mean(SD) N Mean(SD) IV,Fixed,95% Cl IV,Fix CITT 2008 53 7.1 (9.5) 54 7.8 (9.6) -0.70 [- -20 -10 0 10 20	
CITT 2008 53 7.1 (9.5) 54 7.8 (9.6) -0.70 [- -20 -10 0 10 20	Differenc
-20 -10 0 10 20	xed,95% (
	4.32, 2.92
Favours placebo Favours pencil push-ups	

Analysis 7.1. Comparison 7 Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children, Outcome I Change in near point of convergence at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 7 Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children

Outcome: I Change in near point of convergence at 12 weeks of therapy

Study or subgroup	HBCVAT N	Mean(SD)	Office-based placebo N	Mean(SD)	Mean Difference IV,Fixed,95% CI		Mean Difference IV,Fixed,95% CI
CITT 2008	52	7.5 (5.1)	54	3.9 (5.2)			3.60 [1.64, 5.56]
					-10 -5 Favors placebo	0 5 10 Favors HBCVAT	

Analysis 7.2. Comparison 7 Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Outcome: 2 Chang	ge in positive fus	sional vergence at n	ear at 12 weeks of therapy			
Study or subgroup	HBCVAT		Office-based placebo		Mean Difference	Mean Differenc
CITT 2008	N 52	Mean(SD)	N 54	Mean(SD) 6.9 (9.9)	IV,Fixed,95% Cl	IV,Fixed,95% C
CITT 2000	52	12 (10)	JT	0.7 (7.7)		3.10 [1.31, 0.07
					-20 -10 0 10 20 Favours placebo Favours HBCVAT	-

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Analysis 7.3. Comparison 7 Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

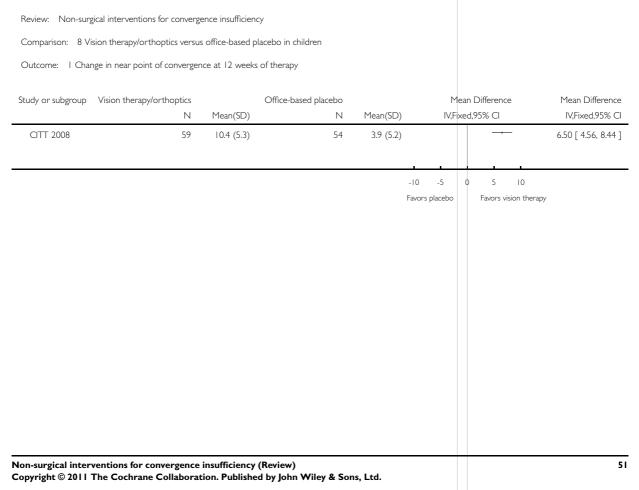
Review: Non-surgical interventions for convergence insufficiency

Comparison: 7 Home-based computer assisted vision therapy/orthoptics versus office-based placebo in children

Outcome: 3 Change in Convergence Insufficiency Symptom (CISS) score

Study or subgroup	HBCVAT N	Mean(SD)	Office-based placebo N	Mean(SD)		an Difference ed,95% Cl	Mean Difference IV,Fixed,95% Cl
CITT 2008	52	6 (9.6)	54	7.8 (9.6)	+	-	-1.80 [-5.46, 1.86]
					-20 -10 Favours placebo	0 10 20 Favours HBCVAT	

Analysis 8.1. Comparison 8 Vision therapy/orthoptics versus office-based placebo in children, Outcome I Change in near point of convergence at 12 weeks of therapy.



Analysis 8.2. Comparison 8 Vision therapy/orthoptics versus office-based placebo in children, Outcome 2 Change in positive fusional vergence at near at 12 weeks of therapy.

Review: Non-surgical interventions for convergence insufficiency

Comparison: 8 Vision therapy/orthoptics versus office-based placebo in children

Outcome: 2 Change in positive fusional vergence at near at 12 weeks of therapy

Study or subgroup	Vision therapy/orthoptics N	Mean(SD)	Office-based placebo N	Mean(SD)		n Difference :d,95% Cl	Mean Difference IV,Fixed,95% Cl
CITT 2008	59	19.7 (10.2)	54	6.9 (9.9)	11, 11		12.80 [9.09, 16.51]
					-20 -10 avours placebo	0 10 20 Favours vision th	erapy

Analysis 8.3. Comparison 8 Vision therapy/orthoptics versus office-based placebo in children, Outcome 3 Change in Convergence Insufficiency Symptom (CISS) score.

Sattorne. S Chan	ge in Convergence Ir	isamelency symp					
Study or subgroup	Vision therapy		Office-based placebo		Mean	Difference	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Fixed	1,95% CI	IV,Fixed,95% C
CITT 2008	59	14.8 (9.4)	54	7.8 (9.6)			7.00 [3.49, 10.51
					-20 -10 0	10 20	
					Favours placebo	Favours vision therapy	

APPENDICES

Appendix I. CENTRAL search strategy

#1 MeSH descriptor Ocular Motility Disorders #2 MeSH descriptor Convergence, Ocular #3 MeSH descriptor Accommodation, Ocular #4 MeSH descriptor Vision, Binocular #5 MeSH descriptor Exotropia #6 convergence near insufficiency* #7 heterophoria* #8 exotropi* #9 exophori* #10 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9) #11 prism* #12 pencil near push* #13 orthoptic* #14 (exercis* or therap* or treat*) near (home*) #15 (exercis* or therap* or treat*) near (office*) #16 vision therap* #17 sterogram* #18 (#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17) #19 (#10 AND #18)

Appendix 2. MEDLINE search strategy

1 randomized controlled trial.pt. 2 (randomized or randomised).ab,ti. 3 placebo.ab,ti. 4 dt.fs. 5 randomly.ab,ti. 6 trial.ab,ti. 7 groups.ab,ti. 8 or/1-7 9 exp animals/ 10 exp humans/ 11 9 not (9 and 10) 12 8 not 11 13 exp ocular motility disorders/ 14 exp convergence ocular/ 15 exp accommodation ocular/ 16 exp vision binocular/ 17 exp exotropia/ 18 (convergence adj3 insufficienc\$).tw. 19 heterophoria.tw. 20 exotropi\$.tw. 21 exophori\$.tw. 22 or/13-21 23 prism\$.tw. 24 (pencil adj2 push\$).tw. 25 orthoptics.tw. 26 ((exercise\$ or therap\$ or treat\$) adj10 home\$).tw. 27 ((exercise\$ ortherap\$ or treat\$) adj10 office\$).tw.

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28 vision therapy.tw.
29 sterogram\$.tw.
30 or/23-29
31 22 and 30
32 12 and 31
The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al (Glanville 2006).

Appendix 3. EMBASE search strategy

1 exp randomized controlled trial/ 2 exp randomization/ 3 exp double blind procedure/ 4 exp single blind procedure/ 5 random\$.tw. 6 or/1-5 7 (animal or animal experiment).sh. 8 human.sh. 97 and 8 10 7 not 9 11 6 not 10 12 exp clinical trial/ 13 (clin\$ adj3 trial\$).tw. 14 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw. 15 exp placebo/ 16 placebo\$.tw. 17 random\$.tw. 18 exp experimental design/ 19 exp crossover procedure/ 20 exp control group/ 21 exp latin square design/ 22 or/12-21 23 22 not 10 24 23 not 11 25 exp comparative study/ 26 exp evaluation/ 27 exp prospective study/ 28 (control\$ or prospectiv\$ or volunteer\$).tw. 29 or/25-28 30 29 not 10 31 30 not (11 or 23) 32 11 or 24 or 31 33 exp eye movement disorder/ 34 exp binocular convergence/ 35 exp accommodation/ 36 exp binocular vision/ 37 exp divergent strabismus/ 38 (convergence adj3 insufficienc\$).tw. 39 heterophoria.tw. 40 exotropi\$.tw. 41 exophori\$.tw. 42 or/33-41 43 prism\$.tw.

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44 (pencil adj2 push\$).tw.
45 orthoptics.tw.
46 ((exercise\$ or therap\$ or treat\$) adj10 home\$).tw.
47 ((exercise\$ or therap\$ or treat\$) adj10 office\$).tw.
48 vision therapy.tw.
49 sterogram\$.tw.
50 or/43-49
51 42 and 50
52 32 and 51

Appendix 4. metaRegister of Controlled Trials search strategy

convergence insufficiency

Appendix 5. ClinicalTrials.gov search strategy

Convergence Insufficiency

HISTORY

Protocol first published: Issue 4, 2007

Review first published: Issue 3, 2011

Date	Event	Description
19 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Conceiving the review: MS, JG, TL

Designing the review: MS, JG, TL

Coordinating the review: TL

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Data collection for the review

- Designing search strategies: CEVG Trials Search Co-ordinator, MS, JG
- Undertaking electronic searches: CEVG Trials Search Co-ordinator
- Undertaking manual searches: MS
- Screening search results: TL, MS, JG
- Organizing retrieval of papers: TL
- Screening retrieved papers against inclusion criteria: TL, MS, JG
- Appraising quality of papers: TL, MS, JG
- Extracting data from papers: TL, MS, JG
- Writing to authors of papers for additional information: TL, MS
- Providing additional data about papers: MS
- Obtaining and screening data on unpublished studies: MS, TL

Data management for the review

- Entering data into RevMan: TL, MS

Analysis of data: TL

Interpretation of data

- Providing a methodological perspective: TL
- Providing a clinical perspective: MS, JG
- Providing a policy perspective: MS
- Providing a consumer perspective: MS
- Writing the review: MS, TL, JG

Providing general advice on the review: MS, JG, TL

Securing funding for the review: TL

Performing previous work that was the foundation of the current study: MS, TL

DECLARATIONS OF INTEREST

Mitchell Scheiman, OD is the Study Chair of the Convergence Insufficiency Treatment Trial (CITT) Study Group. This group completed three of the clinical trials described in this paper and the group continues to investigate treatment of convergence insufficiency in children and adults.

SOURCES OF SUPPORT

Internal sources

• Johns Hopkins Bloomberg School of Public Health, USA.

External sources

- Contract N-01-EY-2-1003 and Grant 1 U01 EY020522-01, National Eye Institute, National Institutes of Health, USA.
- Grant EY11756, National Eye Institute, National Institutes of Health, USA.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

• Compliance to treatment is reported as an *ad hoc* secondary outcome because the success of treatment depends on compliance and three trials included in our review reported compliance data

• Cochrane methodology regarding assessments of the risk of bias in included studies have been modified and the review authors updated the 'Assessment of risk of bias in included studies' section of the methods to reflect updated methodological considerations