Visual Information Processing Evaluation and Orthoptic and Vision Therapy (for Louisiana Only)

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➲ Instructions for Use

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Application

This Medical Policy only applies to the state of Louisiana.

Coverage Rationale

The following are proven and medically necessary:

- Occlusion Therapy or Pharmacologic Penalization Therapy for treating Amblyopia
- Orthoptic Therapy or Vision Therapy for treating Convergence Insufficiency
- Prism Adaptation Therapy for treating Esotropia

The following are unproven and not medically necessary due to insufficient evidence of efficacy:

- Orthoptic Therapy or Vision Therapy for treating **all** other indications not listed above
- Virtual perception therapy for treating any type of learning disability or language disorder
- Vision Restoration Therapy (VRT) for treating visual field deficits following stroke or neurotrauma
- Visual information processing evaluation to diagnose reading or other learning disabilities
- Remote, online and/or digital therapy for Amblyopia

Definitions

Amblyopia: Amblyopia is a decreased vision in one or both eyes due to abnormal vision development in infancy and childhood. In the first few years of life, the brain must learn to see or interpret the images provided by the eyes. In Amblyopia, the brain receives a poor image from one eye and thus does not learn to see well. Vision loss occurs in this case because nerve pathways between the brain and the eye are not properly stimulated. Amblyopia is often referred to as lazy eye (American Association for Pediatric Ophthalmology and Strabismus [AAPOS], 2019).

Convergence Insufficiency: Inability to maintain binocular function (keeping the two eyes working together) while working at a near distance. Typically, one eye will turn outward (intermittent Exotropia) when focusing on a word or object at near distance (AAPOS, 2020).

Esotropia: A form of Strabismus (eye misalignment) characterized by an inwards turn of one or both eyes. It may be intermittent or constant and may occur with near fixation, distance fixation, or both. The crossing may occur mostly with one eye or may alternate between eyes. It is the opposite of crossed eyes, or Exotropia. Esotropia may occur at any age (AAPOS, 2019).

Exotropia: A form of Strabismus in which one or both eyes turn outward. It is the opposite of crossed eyes, or Esotropia. Exotropia may occur from time to time (intermittent Exotropia) or may be constant, and is found in every age group (AAPOS, 2019).

Occlusion Therapy: Patching or Occlusion Therapy is the mainstay of Amblyopia treatment. Patching the unaffected, or good eye provides monocular stimulation to the amblyopic eye, promoting visual development. Occlusion Therapy is prescribed to improve vision, and as a rule, does not eliminate Strabismus (AAPOS, 2021).

Orthoptic Therapy: A series of exercises, usually weekly over several months, performed in the optometric office. Orthoptic eye exercises (orthoptics), as used by pediatric ophthalmologists and orthoptists, are eye exercises to improve binocular function and are taught in the office and carried out at home. Orthoptics is a well-established profession performed by orthoptists who work within the sub-specialty of ophthalmology. Orthoptists evaluate and measure eye deviations, manage Amblyopia treatment and treat small intermittent symptomatic eye deviations (AAPOS, 2020). Also referred to as Vision Therapy. The profession of orthoptics includes the evaluation and treatment of disorders of the visual system, particularly involving binocular vision and eye movement (American Association of Certified Orthoptists [AACO], 2018).

Pharmacologic Penalization Therapy: The instillation of pharmacologic drops (e.g., atropine) to penalize the better seeing eye by forcing the brain to pay attention to the image coming from the weaker eye, prompting the brain to learn to see better from the weaker eye (AAPOS, 2021).

Prism Adaptation Therapy: The use of clear, triangular shaped objects that bend light to permit alignment of the visual axes, simulating the absence of Strabismus. It is also proposed to determine the angle of deviation or the target angle more accurately to

determine the angle of deviation or the target angle for Strabismus surgery (**American Academy of Ophthalmology [**AAO**]**, 2018).

Strabismus: Misalignment of the eyes. Strabismus is most commonly described by the direction of the eye misalignment such as Esotropia, Exotropia, and hypertropia (AAPOS, 2020).

Vision Restoration Therapy (VRT): An in-home computer-based program designed to strengthen the visual information processing of residual neuronal structures that have survived following acute lesions of the nervous system resulting from trauma, stroke, inflammation, or elective surgery for removal of brain tumors. It is argued that by repeated activation through the course of the therapy, patients use the program to train and improve their impaired visual functions, and thus regain useful vision in the visual field deficit (NovaVision, 2021).

Vision Therapy: Optometrists define Vision Therapy as an attempt to develop or improve visual skills and abilities; improve visual comfort, ease, and efficiency; and change visual processing or interpretation of visual information. An optometric Vision Therapy program consists of supervised in-office and at home reinforcement exercises performed over weeks to months. In addition to exercises, lenses ("training glasses"), prisms, filters, patches, electronic targets, or balance boards may be used (AAPOS, 2020).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
*0687T	Treatment of amblyopia using an online digital program; device supply, educational set-up, and initial session
*0688T	Treatment of amblyopia using an online digital program; assessment of patient performance and program data by physician or other qualified health care professional, with report, per calendar month
*0704T	Remote treatment of amblyopia using an eye tracking device; device supply with initial set-up and patient education on use of equipment
*0705T	Remote treatment of amblyopia using an eye tracking device; surveillance center technical support including data transmission with analysis, with a minimum of 18 training hours, each 30 days
*0706T	Remote treatment of amblyopia using an eye tracking device; interpretation and report by physician or other qualified health care professional, per calendar month
92065	Orthoptic training**; performed by a physician or other qualified health care professional**
92066	**Orthoptic training; under supervision of a physician or other qualified health care professional**
92499	Unlisted ophthalmological service or procedure

Codes labeled with an asterisk (*) are not on the State of Louisiana Medicaid Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program.

Description of Services

For purposes of this policy, Orthoptic or Vision Therapy does not include the use of refractive treatment including refractive lenses.

Vision Therapy is also referred to as eye exercise therapy, Visual Therapy, visual training, vision training, Orthoptic Therapy, orthoptics, orthoptic Vision Therapy, or optometric Vision Therapy. It is a term used by optometrists and is defined as an attempt to develop or improve visual skills and abilities; improve visual comfort, ease, and efficiency; and change visual processing or interpretation of visual information. An optometric Vision Therapy program consists of a series of supervised in-office and at home reinforcement exercises performed over weeks to months (AAPOS, 2020).

Behavioral/Visual perceptual therapy is a psychoeducational intervention intended to correct visual-motor or perceptual-cognitive deficiencies that are claimed to contribute to **a** delay in speech and language development in preschool children. It involves eye exercises to improve visual processing and perception (AAPOS, 2020).

Visual information processing evaluation (VIPE) identifies problems with **the** processing of information for enhanced school and/or social development. Visual processing refers to a group of skills used for interpreting and understanding visual information. The evaluation may include testing for visual spatial orientation skills, visual analysis skills, including auditory-visual integration, visual-motor integration skills and rapid naming.

Clinical Evidence

~~Occlusion or Pharmacologic Penalization for Amblyopia~~

~~Wang et al. (2021) conducted a single-center randomized clinical trial to compare the efficacy of combined atropine and patching therapy (CAPT) versus patching alone in children aged three to 12 years with severe amblyopia. Participants with severe amblyopia resulting from strabismus, anisometropia, or both were randomly assigned to CAPT or patching therapy. Change of the amblyopic eye visual acuity (VA) from baseline to six months was the primary outcome measure, and the VA examiner was masked to the treatment groups. Follow-up visits were conducted at three and six months. In total, 53 individuals were randomized to CAPT and 55 to patching therapy. The average baseline amblyopic eye VA was 0.95 (0.22) Log of Minimum Angle of Resolution (logMAR). At the three-month follow-up visit, the amblyopic eye VA in the CAPT group was more improved than in the patching alone group resulting in an average difference of 0.13 log MAR; 95% CI, 0.4-0.22 log MAR; p = 0.004. The six-month follow-up visit showed the CAPT group with an average improvement in amblyopic eye VA of 0.72 log MAR compared with 0.58 logMAR in the patching alone group resulting in a difference of 0.14 logMAR greater in the CAPT group; 95% CI, 0.05-0.22 logMAR; p = .002. Limitations of the study included a small sample size of children aged 7 to 12 years and the single center design. The study concluded that CAPT and patching alone were efficacious for children aged three to 12 years with severe amblyopia. The differences in improvement of amblyopic eye VA were relatively small; however, CAPT resulted in more significant improvement.~~

~~Li et al. (2020) conducted a systematic review and network meta-analysis (NMA) of 23 studies (n = 3279) to establish a comparative efficacy between refractive correction, patching, atropine, atropine weekly plus Plano lens, optical penalization, and binocular therapy for treatment of amblyopia. Only randomized control trials (RCTs) comparing two or three of the following treatments were included in the NMA: refractive correction, patching for two-hours a day, six hours a day, 12 hours a day and two-hours a day plus doing near activities, patching for two hours plus doing distant activities, atropine daily, atropine weekly, atropine weekly plus a Plano lens over the sound eye, optical penalization, and binocular therapy. Optical penalization was the least effective of all the treatments for the change of VA, refractive lenses (mean difference [MD], 2.9 Log MAR lines; 95% credibility interval [CrI], 1.8-4.0), patch two-hours (MD, 3.3; 95% CrI, 2.3-4.3), patching six hours (MD, 3.6; 95% CrI, 2.6-4.6), patch 12 hours (MD, 3.4; 95% CrI, 2.3-4.5), patching two hours plus near activities (MD, 3.7; 95% CrI, 2.5-5.0), patching two hours plus doing distant activities (MD, 3.5; 95% CrI, 2.1-5.0), atropine daily (MD, 3.2; 95% CrI, 2.2-4.3), atropine weekly (MD, 3.2; 95% CrI, 2.2-4.3), atropine weekly plus a Plano lens (MD, 3.7; 95% CrI, 2.7-4.7), binocular therapy (MD, 3.1; 95% CrI, 2.0-4.2). Patching six hours and patching two hours plus doing near activities were better than refractive correction ([MD, 0.73; 95% CrI, 0.10-1.40]; [MD, 0.84; 95% CrI, 0.19-1.50]). The authors concluded the clinical efficacy among various amblyopia treatments were comparable but did not determine any significant differences. Further high-quality RCTs are needed to determine efficacy between refractive correction, patching, atropine, atropine weekly plus Plano lens, optical penalization, and binocular therapy for treatments. The following publications, discussed in more detail below, were reviewed as part of this systematic review: Manh et al., 2018; Herbison et al., 2016; Wallace et al., 2013.~~

~~In a Cochrane Database Systematic Review, Li et al. (2019) aimed to synthesize the available evidence regarding the efficacy and safety of conventional occlusion therapy~~

~~compared to atropine penalization in treating amblyopia. Data was collected and analyzed by two reviewer authors who independently screened abstracts and full-text articles, abstracted data, and assessed the risk of bias. The review included five RCTs and two quasi-RCTs that compared conventional occlusion to atropine penalization for amblyopia. The trials were conducted in six countries with a total of 1,177 amblyopic eyes studied. The investigation resulted in evidence from six trials demonstrating that atropine penalization is as effective as conventional occlusion in improving VA. No evidence indicated a difference in ocular alignment, stereo acuity, or sound eye VA between occlusion and atropine penalization groups. The authors also discovered that both treatments are well tolerated, although atropine was associated with better adherence and quality of life. Atropine had a higher report of adverse events such as reduction in the VA of the good eye not requiring treatment and light sensitivity. Adverse events in the participants receiving patching were skin, lid, or conjunctival irritation, most commonly than those receiving atropine. Limitations of the search were the clinical heterogeneity and the methodological quality of the included trials, the small number of trials, and differing follow-up examination times. In conclusion, the investigation demonstrated improvements in VA in the amblyopic eye using both conventional occlusion and atropine penalization, and atropine penalization appeared to be as effective as conventional occlusion; however, the magnitude of improvement was different among the trials analyzed.~~

~~In a meta-analysis of part-time (PTO) versus full-time occlusion therapy (FTO) for treatment of amblyopia, Yazdani et al. (2017) included six studies (3 RCTs and 3 non-RCTs). Pooled standardized difference in the mean changes in the VA was 0.337 (lower and upper limits: 0.009, 0.683) higher in the FTO as compared to the PTO group; however, this difference was not statistically significant (p = 0.056, Cochrane Q value = 20.4 (p = 0.001), I2 = 75.49%). Egger's regression intercept was 5.46 (p = 0.04). The pooled standardized difference in means of VA changes was 1.097 [lower and upper limits: 0.68, 1.513] higher in the FTO arm (p < 0.001), and 0.7 [lower and upper limits: 0.315, 1.085] higher in the PTO arm (p < 0.001) compared to PTO less than two hours. The authors concluded that this meta-analysis showed no statistically significant difference between PTO and FTO in treatment of amblyopia. However, their results suggest that the minimum effective PTO duration, to observe maximal improvement in VA is six hours per day.~~

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~~Repka et al. (2014) published a follow up study of a randomized trial using atropine vs. patching for treatment of moderate amblyopia. The VA of patients at 15 years of age who were younger than 7 years when enrolled in a treatment trial for moderate amblyopia was reported in the original multicenter clinical trial, 419 children with amblyopia (VA, 20/40 to 20/100) were randomly assigned to patching (minimum of 6 h/d) or pharmacologic penalization with atropine sulfate eyedrops, 1% (1 drop daily), for 6 months. Treatment after 6 months was at the discretion of the investigator. Two years after enrollment, an unselected subgroup of 188 children were enrolled into long-term follow-up. At 15 years of age, most children treated for moderate amblyopia when younger than 7 years had good VA, although mild residual amblyopia was common. The authors found the outcome to be~~

~~similar regardless of initial treatment with atropine or patching. Better VA at the 15-year examination was achieved in those who were younger than 5 years at the time of entry into the RCT (mean logMAR, 0.09) compared with those aged 5 to 6 years (mean logMAR, 0.18; p < .001). When the authors compared subgroups based on original treatment with atropine or patching, no significant differences were observed in VA of amblyopic and fellow eyes at 15 years of age (p = .44 and p = .43, respectively). The authors concluded that the results indicate that improvement occurring with amblyopia treatment is maintained until at least 15 years of age.~~

~~In a prospective, multicenter RCT, the Pediatric Eye Disease Investigator Group (PEDIG) evaluated the effectiveness of increasing prescribed daily patching from 2 to 6 hours in children with stable residual amblyopia. The study group consisted of 169 children aged 3 to < 8 years (mean, 5.9 years) with stable residual amblyopia (20/32-20/160) who had received 2 hours of daily patching for at least 12 weeks. The main outcome measure was best-corrected-visual acuity (BCVA) in the amblyopic eye after 10 weeks. Ten weeks after randomization, amblyopic eye VA had improved an average of 1.2 lines in the 6-hour group and 0.5 line in the 2-hour group (difference in mean VA adjusted for acuity at randomization = 0.6 line; 95% , 0.3-1.0; p = 0.002). Improvement of 2 or more lines occurred in 40% of participants patched for 6 hours versus 18% of those who continued to patch for 2 hours (p = 0.003). The authors concluded that when amblyopic eye VA stops improving with 2 hours of daily patching, increasing the daily patching dosage to 6 hours results in more improvement in VA after 10 weeks compared with continuing 2 hours daily (Wallace et al., 2013).~~

~~In an RCT, Rutstein et al. (2010a) evaluated whether VA improvement with Bangerter filters is similar to improvement with patching as initial therapy for children with moderate amblyopia. The study enrolled 186 children, 3 to < 10 years old, with moderate amblyopia. Children were randomly assigned to receive either daily patching or to use a Bangerter filter on the spectacle lens in front of the fellow eye. Study visits were scheduled at 6, 12, 18, and 24 weeks. At 24 weeks, amblyopic eye improvement averaged 1.9 lines in the Bangerter group and 2.3 lines in the patching group. The authors concluded that because the average difference in VA improvement between Bangerter filters and patching was less than half a line and there was lower burden of treatment on the child and family, Bangerter filter treatment is a reasonable option to consider for initial treatment of moderate amblyopia. The authors indicated that although the mean difference between groups was only 0.38 line, the end of the confidence interval on the difference was 0.76 line, and thus, treatment with Bangerter filters did not quite meet the prespecified definition of non-inferiority to patching when initiating therapy for moderate amblyopia. However, the authors also did not find that patching was statistically superior to Bangerter filters. Therefore, the authors could not conclude that the Bangerter filter treatment effect is similar to that seen with patching (based on our predefined definition of non-inferiority).~~

~~In a prospective, RCT, Agervi et al. (2010) compared spectacles plus patching 8 hours or more daily 6 days a week with spectacles plus patching 8 hours or more on alternate days to treat amblyopia in 40 children 4 to 5 years of age. The main outcome measure was median change in BCVA of the amblyopic eye after 1 year. The median change in BCVA of the amblyopic eye did not differ significantly between the 2 groups. Binocular function improved in both groups with no significant differences between the groups at 1 year. The investigators concluded that the magnitude of change in the BCVA 1 year after spectacles plus prescribed alternate-day patching was not significantly different than that after spectacles plus prescribed daily patching to treat amblyopia in children 4 to 5 years~~

~~old. The effect of patching was not separate from that of optical correction with a period of refractive adaptation. Thus, the improvement in VA is a combined effect of spectacle wear and occlusion therapy.~~

~~A 2009 multicenter RCT by PEDIG compared weekend atropine sulfate use augmented by a Plano lens for the sound eye (optical penalization/study group) with weekend atropine use alone (pharmacologic penalization/control group) for moderate amblyopia in 180 children aged 3 years to younger than 7 years. Primary outcome measured was masked assessment of amblyopic eye VA using the Amblyopia Treatment Study HOTV testing protocol at 18 weeks. The researchers concluded that optical penalization was not substantially better than pharmacologic penalization in this patient population.~~

Occlusion or Pharmacologic Penalization for Amblyopia

Wang et al. (2021) conducted a single-center randomized clinical trial to compare the efficacy of combined atropine and patching therapy (CAPT) versus patching alone in children aged three to 12 years with severe amblyopia. Participants with severe amblyopia resulting from strabismus, anisometropia, or both were randomly assigned to CAPT or patching therapy. Change of the amblyopic eye visual acuity (VA) from baseline to six months was the primary outcome measure, and the VA examiner was masked to the treatment groups. Follow-up visits were conducted at three and six months. In total, 53 individuals were randomized to CAPT and 55 to patching therapy. The average baseline amblyopic eye VA was 0.95 (0.22) Log of Minimum Angle of Resolution (logMAR). At the three-month follow-up visit, the amblyopic eye VA in the CAPT group was more improved than in the patching alone group resulting in an average difference of 0.13 log MAR; 95% CI, 0.4-0.22 log MAR; p = 0.004. The six-month follow-up visit showed the CAPT group with an average improvement in amblyopic eye VA of 0.72 log MAR compared with 0.58 logMAR in the patching alone group resulting in a difference of 0.14 logMAR greater in the CAPT group; 95% CI, 0.05-0.22 logMAR; p = .002. Limitations of the study included a small sample size of children aged 7 to 12 years and the single center design. The study concluded that CAPT and patching alone were efficacious for children aged three to 12 years with severe amblyopia. The differences in improvement of amblyopic eye VA were relatively small; however, CAPT resulted in more significant improvement.

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Remote, Online and/or Digital Therapies or Vision Therapy (VT) for Amblyopia

~~**Remote, Online and/or Digital Therapies or Vision Therapy (VT) for Amblyopia**~~

Only limited quality clinical evidence with appropriate length of follow-up was found to support the use of remote, online, or digital orthoptic or ~~vision therapy~~**VT** for amblyopia.

In the 2023 prospective, multicenter, randomized, masked, controlled, noninferiority pivotal clinical trial conducted by Wygnanski-Jaffe and colleagues, the authors compared visual outcomes after the use of binocular eye-tracking based home treatment (CureSight; NovaSight Ltd) with patching. Children aged four to less than nine years with anisometropic, small-angle strabismic, or mixed-mechanism amblyopia (N=103) were randomized 1:1 to a group getting either CureSight or patching treatment. In the CureSight group, the participants utilized the device for 90 minutes/day, five days/week for 16 weeks (120 hours), while the patching group received two hours of patching seven days a week for 224 hours. The primary outcomes measured were the improvement in the amblyopic eye visual acuity (VA), modeled with a repeated measures analysis of covariance, stereo acuity, binocular VA, and treatment adherence rates, which were evaluated by a 1-sample Wilcoxon test in each group and a 2-sample Wilcoxon test that compared the two groups. The safety results were calculated by the frequency and severity of the study-related adverse events (AE). The trial resulted in the CureSight group VA improvement found to be noninferior to the patching group improvement (0.28 ± 0.13 logarithm of the minimum angle of resolution [logMAR] [P < 0.0001] and 0.23 ± 0.14 logMAR [P < 0.0001], respectively; 90% CI of difference, - 0.008 to 0.076). Stereoacuity improvement of 0.40 log arcseconds (P < 0.0001) and improved binocular VA (0.13 logMAR; P < 0.0001) were observed in the binocular treatment group, with similar improvements in the patching group in stereoacuity (0.40 log arcseconds; P < 0.0001) and binocular VA (0.09 logMAR; P < 0.0001), with no significant difference between improvements in the two groups in either stereoacuity (difference, 0; 95% CI, - 0.27 to - 0.27; P = 0.76) or binocular VA (difference, 0.041; 95% CI, - 0.002 to 0.085; P = 0.07). The binocular treatment group had a significantly higher adherence than the patching group (91% vs. 83%; 95% CI, - 4.0% to 21%; P = 0.011). No severe AEs were found. The limitations of the study include most individuals having anisometropic amblyopia, lack of generalizability between strabismic and mixed amblyopia populations, and lack of evaluation on the impact of dosing for the rapidity of visual improvement, durability, and effect of subgroups for treatment effectiveness. The authors concluded that the binocular treatment was well tolerated after a 16-week trial period and showed higher regimen adherence rates and parent preferences, though non-inferior to patching for children with amblyopia. Improvements were seen in stereopsis and binocular visual acuity.

In 2023, Roy et al. performed a prospective, randomized, interventional study to evaluate smartphone-based dichoptic video games versus occlusion therapy for children with anisometropic amblyopia. Children aged 5 to 15 with anisometropic amblyopia were included

in the study (N=55) and randomized into two groups: the video game group (N=27) and the patching group (N=28). The video game group played a dichoptic video game with adjusted contrast for two hours a day, and the patching group received occlusion therapy of the non-amblyopic eye for six hours a day. The outcomes measured were the best corrected visual acuity (BCVA), near vision, contrast sensitivity (CS), and near and distance stereoacuity at baseline, at one, two, and three months. The study's results showed that the mean distance BCVA improved from 0.74 ± 0.19 and 0.70 ± 0.18 logarithm of the minimum angle of resolution (logMAR) in the video game and patching groups, respectively, at baseline to 0.53 ± 0.19 and 0.49 ± 0.19 logMAR, at three months (P < .001 for both). The mean near vision was 0.82 ± 0.19 and 0.81 ± 0.17 logMAR in the video game and patching groups, respectively, at baseline and improved to 0.60 ± 0.16 and 0.63 ± 0.17 logMAR at three months (P < .001 for both). There was no sizable difference in distance and near vision among the two groups at baseline and the last follow-up visit. CS was 1.41 ± 0.20 and 1.38 ± 0.20 in the video game and patching groups, respectively, at baseline and 1.74 ± 0.18 and 1.61 ± 0.21 at three months (P < .001 for both). At the final follow-up visit, CS was better in the video game group compared to the patching group (P = .01). Near stereoacuity notably progressed only in the video game group (P = .006); in contrast, distance stereoacuity did not improve in either group. The limitations of the study include the small sample size and lack of long-term follow-up. The authors concluded that dichoptic video game therapy showed better outcomes in terms of improved CS and near stereoacuity and comparable results for distance and near vision compared to patching for children with anisometropic amblyopia. The accessibility of exciting games is necessary to support children's interests.

In a systematic review and meta-analysis, Shao, and colleagues (2023) sought to uncover how virtual reality (VR) technology varies from conventional patching therapy's efficacy. The meta-analysis consists of eight studies and ten trials with 459 participants. The results of the review and analysis showed that overall, VR technology treatment considerably improved visual acuity (VA) by 0.07 logMAR (95% CI, −0.11 to −0.02; P < 0.001; I2 = 94.4%) versus traditional patching therapy. In addition, subgroup analyses also exposed that treatment with VR technology was more efficient when the child was younger than seven years old or when the intervention was no more than twenty hours. The studies limitations include a high degree of heterogeneity, lack of analysis on the effect of VR technology on stereo acuity, and the meta-analysis only included studies published in English. Furthermore, most included studies were of short duration (2-12 weeks), and it is unclear whether the observed benefit would be sustained after the initial interest of the child. The authors concluded that VR technology treatment substantially improved VA for children seven years of age or younger with amblyopia.

In a 2023 systematic review and meta-analysis, Yeh et al. investigated the efficacy of the Cambridge Stimulator with grating element stimulation of VA, grating acuity (GA), and CS for individuals with amblyopia. The search uncovered 1221 studies, with 24 of those studies encompassing 900 individuals included in the review. The results of the review suggested that the outcome measure of all visual indexes (VA: Hedges' g of - 0.43, 95% CI = - 0.81 to - 0.05, I2 = 86%, p = 0.02; GA: Hedges' g of 3.79, 95% CI = 1.05 to 6.54, I2 = 98%, p = 0.01; CS: Hedges' g of 0.64, 95% CI = 0.19 to 1.09, I2 = 41%, p = 0.00) significantly favored in the grating group. The limitations of the study include high risk of bias and the lack of varying methodologies in the study designs. The authors concluded that grating stimulation may positively benefit visual functions for individuals with amblyopia.

In a retrospective interventional comparative study, 36 children with unilateral amblyopia were enrolled to determine the efficacy of ~~vision therapy (~~VT~~)~~ for unilateral refractive amblyopia in children aged 7-10. For the study, the participants were divided into a case group and a control group. The case group received VT, optical correction, and part-time patching of the weaker eye, and the control group received optical correction and part-time patching of the weaker eye. Outcomes of VA were measured at baseline, three months, six months, nine-month visits, and three months after completion of treatment. The case group consisted of 19 individuals and 17 individuals in the control group. The study showed a mean improvement in the case group from 0.39 ±0.24 logMAR at baseline to 0.10 ±0.23 logMAR after treatment. The results for the control group demonstrated an improvement from 0.64 ±0.30 logMAR at baseline to 0.52 ±0.27 logMAR after treatment. All participants underwent follow-up examinations within six to 12 months, with no regression of VA seen in the case group three months after completion of therapy. Individuals in the case group who received VT demonstrated improved VA versus those who received optical correction and patching. A limitation of the study is the retrospective design which restricts the ability to control and randomize the participants into case and control groups. The authors concluded from the study that for children aged 7-10 with unilateral refractive amblyopia, VT combined with conventional treatment such as optical correction and part-time patching are more effective than traditional treatment alone. Furthermore, the therapy provided more significant vision gain and a shorter duration of treatment when compared to conventional treatment (Hsieh et al., 2022).

In a retrospective comparative study, individuals aged 7-10 years were enrolled to determine the effects of VT on bilateral amblyopia unresponsive to conventional treatment. The control group consisted of 16 cases with age and visual acuity-matched bilateral amblyopes; 15 cases were included in the treatment group. The study showed no improvement in either group for VA for more than three months with part-time patching and full refraction correction. Of 22 eyes, 68.7% showed no improvement in the control group versus the treatment group, which exhibited better VA in every eye. The treatment group revealed significant improvement in BCVA, with an average gain of 0.32 ±0.15 logMAR vs. 0.003 ±0.19 logMAR in the control group. The benefits of treatment are most significant in the first three months of treatment and continue until the endpoint. Results of stereoacuity showed improvements from 190.00 ±163.34 to 85.00 ±61.24 arc seconds (a 55.26% improvement). Limitations of the study are the retrospective design, which restricts the ability to control and randomize the participants, small subject size, and lack of completed stereoacuity data. The authors conclude that a VT program comprising orthoptic therapy, perceptual learning, and dichoptic training successfully increases VA and stereoacuity in 7–10-year-old individuals with bilateral amblyopia that is unresponsive to conventional treatment (Huang et al., 2022).

In 2022, Jost et al. conducted a randomized clinical trial to evaluate the effectiveness of dichoptic movies versus patching for treating amblyopia in children aged three to seven. After inclusion and exclusion criteria were met, 65 children were considered eligible and were enrolled in the trial, and 60 participants completed the study through the four-week visit. Children were randomized to a movie group and a patching group. During the first two weeks, the movie group watched 5.7± 0.7 movies, and the patching group averaged 30.0 ±11.0 hours of patching. At the two-week primary outcome visit, the movie and patching groups found a similar improvement in amblyopic eye BCVA (0.07 vs. 0.06 logMAR). Treatment with movie and patching significantly improved VA (0.07 ±0.05 logMAR and 0.06 ±0.05 logMAR, respectively). VA continued to advance in the movie group after the two-week primary outcome visit, with enhancements of 0.13 ±0.11 logMAR by four

weeks and 0.15 ±0.10 logMAR by six weeks. The patching group exhibited comparable improvements after crossing over to movies at two weeks. By week eight, the patching group who crossed over at two weeks gained 0.18 ±0.07 logMAR. The choice to remain in the movie treatment past the four weeks visit for up to six weeks of the movie treatment was chosen by 35 (58%) participants. After six weeks of watching contrast re-balanced dichoptic movies (six-week visit for the movie group and eight weeks visit for the patching group), 26% of children had ≤ 0.1 logMAR interocular difference in VA. The authors concluded that the at-home binocular movie treatment effectively improves amblyopic eye BCVA. Additional improvements were seen with up to six weeks of treatment, making repeated binocular visual experience with contract re-balanced dichoptic movies an additional treatment option for amblyopia. Limitations of the study include short treatment duration, the difference in VA tests, and lack of objective adherence monitoring **(Included in the Shao et al. 2023 systematic review)**.

Xiao et al. (2022) evaluated the safety and efficacy of a dichoptic digital therapeutic for amblyopia. This phase three **randomized controlled trials (**RCT**)** consisted of 105 children aged four to seven with amblyopia and enrolled at 21 academic and community sites in the United States. Individuals were randomized to the treatment or comparison group in a 1:1 ratio and stratified by site. The treatment group consisted of 51 participants and 54 in the comparison group. Individuals in the comparison group continued to wear ~~classes~~ **glasses** on a full-time basis while the treatment group used the therapeutic at home for one hour a day, six days a week, and wore glasses full-time. To determine efficacy, the change in amblyopic eye VA from baseline to 12 weeks was measured by masked examiners. The authors evaluated the frequency and severity of study-related adverse events **(AEs)** (anticipated and unanticipated) to determine the therapy's safety. The intention-to-treat population was utilized to develop a primary analysis. In the treatment group at 12 weeks, amblyopic eye VA improved by 1.8 lines [95% ~~confidence interval (~~CI~~)~~, 1.4-2.3 lines; n = 45]; and in the comparison group, there was an improvement by 0.8 lines (95% CI, 0.4-1.3 lines; n = 45). The difference between groups was significant 1.0 line (0.10 logMAR; 96.14% CI, 0.33-1.63 lines; p = 0.0011). Individuals sustained high adherence to the therapeutic throughout the study, and adherence was associated with overall satisfaction. No serious ~~adverse events~~**AEs** were reported, and the study was stopped early per protocol due to success. Limitations include the lack of comparison between patching and atropine penalization, short follow-up time, and risk of bias. The authors support the value of the therapeutic in clinical practice as an effective treatment. Additional independent studies with longer follow-up and sham interventions are warranted to confirm the long-term value of this approach over or in addition to standard treatments **(Included in the Shao et al. 2023 systematic review)**.

In 2021, Roda et al. conducted a systematic review and meta-analysis of ~~randomized clinical trials~~**RCTs** to summarize the available evidence to determine if binocular treatment is more effective than patching in children with amblyopia. VA and stereopsis were assessed as primary outcome measures. Out of five ~~randomized clinical trials~~**RCTs**, no significant difference in VA between individuals treated with binocular treatment and patching was demonstrated at -0.12 (95% CI: -0.45–0.20; p = 0.464). Additionally, no significant difference in stereopsis was found between individuals treated with binocular treatment versus patching -0.07 (95% CI: -0.61–0.48; p = 0.809). Limitations to the study include the high heterogeneity in effect estimation, inconsistency between studies, and the lack of consideration regarding cost and availability of treatment. The authors concluded that this meta-analysis uncovered no substantial evidence that supports the efficacy of binocular therapy as an alternative to traditional patching. Although

binocular treatment can be considered a good complementary therapy in particular cases, it cannot fully replace conventional treatment. The following publications, discussed in more detail below, were reviewed as part of this systematic review: Manh et al., 2018; Rajavi et al., 2019.

Elhusseiny et al. (2021) conducted pilot, prospective, randomized, double-masked, crossover clinical trial at a single center site using (n = 20) children and young adult participants. The participants had unilateral anisometropic and/or strabismic amblyopia with amblyopia treatment failure. Eleven participants underwent eight weeks of binocular treatment using ~~virtually reality~~**VR** headset that contained a therapeutic software application. The sham-crossover group (n = 9) underwent four weeks of sham treatment followed by four weeks of binocular treatment. Both groups underwent one hour of treatment per day. Participants and clinicians were masked to prescribed treatment. The devices were loaned to the participants and devices used were Apple iPhone 6 Plus smartphone, preloaded with the prototype therapeutic software, and a Zeiss VR One Plus virtual reality headset that delivered the visual input to each eye dichotically. Outcomes in the full-treatment group (n = 11), the mean amblyopic eye logMAR VA at 16 weeks was 0.49 ±0.26, compared with 0.47±0.20 at baseline. Compared to the sham-crossover group, it was 0.51 ±0.18 at 16 weeks, compared with 0.53 ±0.21 at baseline. Stereoacuity (log arcsec) was significantly improved, from 7.3 – 2 at baseline to 6.6 – 2.3 at 8 weeks ($p < 0.001$) and 6.7 – 2.6 at 16 weeks ($p < 0.001$). No significant ~~adverse events~~**AEs** (diplopia, asthenopia, or worsening strabismus) were noted in either group. The authors concluded that virtual reality-based prototype binocular amblyopia therapy did not significantly improve VA. Stereoacuity did improve compared to baseline measurements when all participants were combined. The current study is limited by its small sample size and short follow-up. The authors report that they did not achieve the target sample size due to participant attrition **(Included in the Shao et al. 2023 systematic review).**

Birch et al. (2020) conducted an RCT with (n = 48) children diagnosed with amblyopia. The children were randomly divided into two groups. Group one (n = 24) received binocular amblyopia game treatment for one hour a day, five days a week. Group two (n = 24) received patching treatment two hours per day, seven days a week. The outcomes measured were changes in the amblyopic eye best-corrected VA at the two-week visit. Baseline factors examined were age at enrollment, VA, stereoacuity, and suppression. At baseline, the mean amblyopic eye best-corrected VA± **standard deviation (**SD**)** was 0.49 ±0.16 logMAR (~20/63 ±1.6 lines), range = 0.3-0.8 logMAR (20/40-20/125). VA was 0.3-0.6 logMAR (20/40-20/80) in 38 (79%) children and 0.7-0.8 logMAR (20/100-20/125) in 10 (21%) children. After two weeks, the measurements for group one, who received binocular amblyopia game treatments showed improvement which ranged from 0.0 to 0.4 logMAR; 21 children (87.5%, CI 95% = 69%-96%) improved by 0.1 logMAR or more (2 improved 0.3-0.4 logMAR, 10 improved 0.2 logMAR, 9 improved 0.1 logMAR), and three children did not improve (12.5%, CI 95% = 4%-31%). Group two, who received patching treatment, showed improvement which ranged from -0.1 to 0.2 logMAR; 12 children (50%, 95% CI = 31%-69%) improved by 0.1 logMAR or more (5 improved 0.2 logMAR, 7 improved 0.1 logMAR), and 11 children (46%, CI 95% = 28%-65%) did not improve, and one child (4%, CI 95% = 1%-20%) decreased by -0.1 logMAR. At the 2-week visit, 35% (95% CI: 19% - 55%) of children playing the binocular game had recovered normal VA for age (≤ 0.2 logMAR; 20/32 or better). Only 8% (CI 95% = 2%-26%) of the children in the patching group had recovered normal VA for age at the 2-week visit. The authors concluded that after two weeks of treatment, VA improvement was significantly greater with the binocular game treatment than patching. Children with moderate amblyopia and orthotropia had more VA improvement with binocular game play than those with severe amblyopia. Limitations of this trial include small sample size, short time duration and

inability to monitor the number of hours of patching objectively, authors relied on a calendar log completed by the parents.

Rajavi et al. (2019) conducted a randomized control trial with 38 children diagnosed with unilateral amblyopia who received amblyopia therapy via interactive binocular treatment (I-BiT™) and others received standard patching of the dominant eye with a placebo I-BiT. Children who had BCVA less than 20/30 (0.3 logMAR) in one eye or a difference of two lines of Snellen between their two eyes were included in this study and randomly divided into the case study group (n = 19) and control group (n = 21). The case study group was recommended to play the I-BiT games using red-green glasses, 20 to 30 minutes per a day for at least five days a week for one month (total hours = 6). The control group underwent two- and four-hour patching of dominant eye per a day and to play I-BiT games with no red-green glasses, 20 to 30 minutes per a day for at least five days a week for one month. The authors concluded that BCVA improved significantly in both groups after one-month treatment (case: $p = 0.003$, control: $p < 0.001$). There was not a significant difference between the two groups ($p = 0.52$). Stereopsis improved in the case study group by ($p < 0.001$) and control group by ($p < 0.001$), but they did not identify large difference between the two groups pre- and post-therapy. The children engaged in playing I-BiT game for six hours total during one month in both groups. Compliance in case study group was 87.5% and 76% in the control group. Limitations of this study include a small sample size, the short study duration and lack of monitoring for recurrence of decreased BCVA. Additionally, some participants were excluded after randomization due to lack of compliance, which could introduce biases in the findings **(Included in the Shao et al. 2023 systematic review)**.

Manh et al. (2018) conducted an RCT to compare VA improvement of 100 participants aged 13 to < 17 years (mean 14.3 years) with amblyopia who were treated with either part-time eye patching or a binocular game on a tablet device. Participants were randomly assigned to treatment for 16 weeks of either the binocular game prescribed for 1 hour per day (n = 40) or patching of the fellow eye prescribed for 2 hours per day (n = 60). The main outcome measure was change in amblyopic eye VA from baseline to 16 weeks. Mean amblyopic eye VA improved from baseline by 3.5 letters [2-sided 95% ~~confidence interval (~~CI~~)~~: 1.3-5.7 letters] in the binocular group and by 6.5 letters (2-sided 95% CI: 4.4-8.5 letters) in the patching group. After adjusting for baseline VA, the difference between the binocular and patching groups was -2.7 letters (95% CI: -5.7 to 0.3 letters, p = .082) or 0.5 lines, favoring patching. In the binocular group, treatment adherence data from the device indicated that only 13% of participants completed > 75% of prescribed treatment. In this patient population, eye patching was favored over the binocular group; however, it remains unclear whether the minimal response to binocular treatment was due to poor treatment adherence or lack of treatment effect.

In 2016 Herbison et al. conducted a three-arm RCT was performed on children (n = 75) with Amblyopia. The (n = 75) children were randomized and assigned one of three treatments I-BiT game (n = 26), Non-I-BiT game (n = 25) and I-BiT **digital video disc (**DVD**)** (n = 24). The I-BiT game being used is a ~~virtual reality~~**VR** technology that uses either DVD footage or computer games that present a common background both eyes and a foreground that contains imagery of interest for the amblyopic eye only. The assigned groups received treatment for 30 minutes weekly for six weeks. The primary outcome is the difference in VA between the group treated with I-Bit game versus non-I-Bit game which I measured by using a logMAR VA test at pretreatment (baseline), and after three, six and final treatment over 10 weeks. The secondary outcomes included changes in stereoacuity (Frisby test), safety, acceptability, and compliance during treatment. The authors concluded

there was modest VA improved in all three arms by approximately 0.07 logMAR in the amblyopic eye at 6 weeks. There was not a significant difference between I-BiT DVD and non-I-BiT games compared with I-BiT games in terms of improvement of vision. Limitations of the trial are short treatment times, trial was hospital based during work and school hours with limited the duration and frequency of treatment sessions, a high number of participants with previous amblyopia treatment failures, and a high number of participants with strabismus created disadvantages for dichoptic stimulation. An adverse effect reported of diplopia which led to decreased VA and participant withdrawal from the trial. Further, I-BiT game multicenter and longer duration studies are needed with the amblyopic population. Lack of comparison with conventional amblyopia therapy is another limitation of this study **(Included in the Shao et al. 2023 systematic review)**.

Prism Adaptation Therapy for Esotropia

In a 2022 single-center retrospective study, Gietzelt et al. aimed to evaluate the effects of the p~~P~~rism adaptation test (PAT) on the angle of squint (AOS) in decompensated esophoria (decEPH) and decompensated microesotropia (decMET). The medical records of individuals at least 12 years of age diagnosed with decEPH or decMET and treated with strabismus surgery for the first time were reviewed. To measure outcomes, the maximum AOS for far (F) and near (N) fixation, PAT results, AOS (F) and AOS (N) after surgery, and results of binocular function tests were utilized. A total of 182 participants were included in the study; 100 were included in the decEPH group and 82 in the decMET group. Results from the decEPH group AOS before surgery were 25.5 ±8.8 pdpt (F) and 23.5 ±9.8 pdpt (N). During PAT, the AOS increased significantly by 2.7 ±4.3 to 28.2 ±8.6 pdpt (F) and by 4.9 ±4.5 to 28.3 ±9.5 pdpt (N). As a whole, 82% of individuals with decEPH showed AOS (F) and/ or AOS (N) in or decreased by at least 3 pdpt. In the decMET group, AOS before surgery was 28.6 ±10.8 pdpt (F) and 30.9 ±11.8 pdpt (N). During PAT, the AOS increased significantly by 4.2 ±5.8 to 32.5 ±9.5 pdpt (F) and by 3.7 ±6.1 to 34.4 ±9.5 pdpt (N). Altogether, 51% of individuals with decMET showed AOS (F) and/ or AOS (N) increased by at least 10 pdpt. A limitation of the study is the difficulty of diagnosing decEPH and decMET due to the young age of individuals with unreliable results of orthoptic and stereo function tests. PAT demonstrated remarkable changes in AOS in both decEPH and decMET. The authors concluded that for individuals with decEPH preoperative assessment of "true AOS" utilizing PAT is essential for successful strabismus surgery (82% had dose-relevant angle changes ≥ 3 pdpt), and preoperative PAT is of great diagnostic value for individuals with decMET (51% had changes in AOS beyond the expected microtropic angle, ≥ 10 pdpt, or even a dose relevant angle decrease, ≥ 3 pdpt).

In ~~2022~~**2021**, Crouch et al. conducted a prospective observational study to describe 10-week and 12-month outcomes following treatments for adult-onset divergence insufficiency-type esotropia. The study consisted of 110 adults with divergence insufficiency-type esotropia initiating a new treatment and enrolled at 28 sites. The participants had a distance esodeviation measuring 2 to 30 D and at least 25% larger at a distance than near, and binocular diplopia present at least "sometimes" at a distance. At enrollment, 10-weeks and 12-month follow-ups, diplopia was assessed using a standardized diplopia questionnaire (DQ). A successful outcome was defined as having DQ responses of 'rarely' or 'never' when looking straight ahead in the distance, with no alternative treatment introduced. The study resulted in 32 (29%) individuals being prescribed base-out prism; none had received prior treatment for esotropia. At 10 weeks, 22 of 30 participants met success criteria (73%; 95% CI, 54%-88%), and 16 of 26 at 12 months (62%; 95% CI, 41%-80%). Success criteria were met by 69 of the 74 participants who underwent strabismus surgery at ten weeks (93%; 95% CI, 85%-98%) and by 57 of 72 at 12 months (79%; 95% CI,

68%-88%). The authors concluded that strabismus surgery and base-out prism as initial therapy successfully treated diplopia for most adults with divergence insufficiency-type esotropia at a 12-month follow-up. Limitations to the study included the lack of untreated controls and **lack of** randomization, short follow-up period, and the risk of misclassification.

In a 2019 retrospective case control study, Choe et al. aimed to investigate the long-term outcome of prism glasses after full hypermetropic correction for partially accommodative esotropia (PAET). 124 children aged 10 or younger with a residual esotropia of ≤ 20 prism diopters (PD) after full hypermetropic correction who were fitted with prism glasses and followed for 3 or more years were included. Clinical characteristics and the angle of esodeviation were obtained at each follow-up examination. Successful motor outcome after 3 years of prismatic correction was determined if the residual angle of esotropia after full hypermetropic correction was ≤ 10 PD. Patients who eventually weaned off prism glasses were noted. The results showed 30.6% success with 7.3% weaned off prism glasses after three years of prism-wear. Smaller amount of latent esodeviation ($p = 0.001$) revealed by prism adaptation (PA) and good fusional response at near with the Worth 4-dot test were significant prognostic factors of success by multivariate analysis ($p = 0.033$). After 3 years of wearing prism glasses, the rate of improvement in stereoacuity was higher in the Success group (60.5% vs. 27.9%) ($p = 0.001$), however, there was no significant difference between the prism-weaned group and prism-wearing group within the Success group ($p > 0.05$). The authors concluded that prism glasses for small angle PAET can be a treatment option for patients who have a small angle of latent esodeviation revealed by PA and good sensory function at near, but early surgery may be better as the majority of patients showed suboptimal outcomes even after long-term wearing of prism glasses.

In a retrospective review, Quigley et al. (2017) evaluated the PAT response and postoperative outcomes in a cohort of children with accommodative esotropia who underwent bilateral medial rectus recession. The authors reported that 36% of patients showed a requirement for increase of prism dosage to maintain orthotropia during PAT; these patients did better than those whose deviation was stable, with postoperative rate of motor success (defined as ≤ 10Δ esotropia) of 100% versus 56%. PAT may be a useful positive prognostic test, and it also identifies a substantial patient population who may avoid under correction, the prism builders. The authors suggest that additional randomized studies are required to demonstrate definitive benefit of PAT.

The National Eye Institute sponsored the Prism Adaptation Study (PAS), a multicenter RCT to determine the overall effect of PA. The study randomized 333 eligible patients who were at least 3 years of age, had no previous eye surgery, and had acquired deviations of 12 to 40 ~~prism diopters~~**PD**. All patients had 20/40 or better VA in each eye, and amblyopic patients underwent occlusion therapy before entry. Two levels of randomization were used. Sixty percent of the patients (n = 199) underwent PA and 40% (n = 134) did not. Those who did not have PA underwent conventional surgery for their entry angle of deviation. Of those who responded to prisms with motor stability and sensory fusion (n = 131), half (n = 67) underwent a conventional amount of surgery, i.e., surgery for angle at entry, and half (n = 64) underwent augmented surgery based on the prism-adapted angle of deviation. A successful outcome was defined as a deviation of less than or equal to 8 PD of esotropia or exotropia. Success rates 6 months after surgery were highest in PA responders who underwent augmented surgery and lowest in patients who did not undergo PA (89% versus 72%). The estimated overall rate of success for patients who went through the PA process was significantly better than the success rate of patients who did not undergo

PA but underwent surgery for their deviation at entry into the study (83% versus 72%). The investigators concluded that there was a beneficial overall effect of the PA process for patients with acquired esotropia (PAS Research Group, 1990).

Vision Therapies for Convergence Insufficiency (CI)

The 2023 Hayes Health Technology Assessment on Vision Therapy (VT) for Accommodative Dysfunction evaluated VT for treating children and younger adults with accommodative dysfunction with or without concomitant convergence insufficiency. The assessment concluded that there is an overall low-quality body of evidence indicating VT is safe and expected to correct the symptoms and measures of accommodative dysfunction compared with baseline and alternative treatments. However, only some studies considered results beyond the end of VT to see if outcomes were sustained, and only two studies gauged an individual's symptoms, with most counting on intermediate/surrogate results of accommodative function to assess success. In addition, there was sizable variation in the precise indications for therapy and the types of VT provided. There is a need for additional well-designed studies to outline the modes and treatment schedules that would be most effective and address the comparative efficiency of VT with clinical alternatives.

In 2022, Li et al. conducted a pilot **randomized control trial (**RCT**)** to compare the effectiveness of virtual reality-based VT and office-based vergence/accommodative therapy in young adults with CI or accommodative dysfunction. Individuals were randomly assigned in a 1:1 ratio to participate in one of two groups, the virtual reality-based VT group**,** or the office-based vergence/accommodative therapy group. Both groups received 12 weeks (one hour a week) of VT. A subjective questionnaire-based assessment was performed at baseline and after six and 12 weeks of therapy, and binocular vision (BV) functions were also measured. After 12 weeks of treatment, 33 participants with CI and 30 with accommodative dysfunction completed the study. The study demonstrated significant improvements in both groups after 12 weeks of therapy with a Convergence Insufficiency Symptom Survey (CISS) score of ($F = 13.704$, $p < 0.001$), near point of convergence (NPC) ($F = 21.774$, $p < 0.001$), positive fusional vergence (PFV) ($F = 71.766$, $p < 0.001$), and near horizontal phoria ($F = 16.482$, $p < 0.001$). Furthermore, improvements in the monocular accommodative amplitude ($F = 22.154$, $p < 0.001$) and monocular accommodative facility ($F = 86.164$, $p < 0.001$). Between the two groups a statistically significant difference was seen in monocular accommodative facility ($F = 8.140$, $p = 0.009$), however not in other vergence and accommodative functions ($0.098 < p < 0.687$). The study's limitations included the lack of a placebo/sham control group, small sample size, and short follow-up. From the trial, the authors concluded that virtual reality-based VT significantly improved BV functions and symptoms for individuals with CI and accommodative dysfunction, suggesting the therapy as a new optional or additional treatment for young adults with these conditions **(Included in the 2023 Hayes Technology Assessment)**.

In 2021, the American Academy of Ophthalmology (AAO) conducted an Ophthalmic Technology Assessment on the efficacy of vergence and accommodative therapies in treating symptomatic CI in children and young adults. The AAO reviewed home- and office-based vergence and accommodative therapies for the treatment of CI through a literature search. The exploration yielded 12 full-text articles appropriate for inclusion in the assessment. Out of the 12 studies, two RCTs discovered that office-based vergency and accommodative therapies effectively improved motor results in children with symptomatic CI. The limitations of the two trials are the conflicting results on the efficacy of

office-based therapy for treating symptoms of CI. The evidence found on home-based treatments was inconclusive compared to placebo in relieving symptoms of CI. The authors concluded that the evidence suggests that both therapies improve motor outcomes; however, the data is inconsistent regarding symptomatic relief. Additionally, the evidence on the efficacy of home-based treatments is insufficient (Chang et al., 2021).

In 2021, Chen et al. conducted a randomized control trial to determine the effectiveness of office-based vergence accommodative therapy (OBVAT) for improving accommodative amplitude and accommodate facility in children with symptomatic CI and accommodative dysfunction. The trial consisted of 115 participants in vergence/accommodative therapy and 65 in placebo therapy for those with decreased accommodative amplitude. There were 71 participants in the vergence/accommodative therapy for those with decreased accommodative facility and 37 in placebo therapy. After four, eight, 12, and 16 weeks of treatment, the primary analysis was conducted using analyses of variance models comparing the mean change in amplitude and facility between the vergence/accommodative and placebo groups. Results of the study show that from baseline to 16 weeks, the mean improvement in amplitude was 8.6 dioptres (D) and 5.2 D in the vergence/accommodative and placebo therapy groups, respectively [MD = 3.5 D, 95% ~~confidence interval (~~CI~~)~~: 1.5 to 5.5 D; p = 0.01]. The mean improvement in facility was 13.5 cycles per minute (cpm) and 7.6 cpm in the vergence/accommodative and placebo therapy groups, respectively (MD = 5.8 cpm, 95% CI: 3.8 to 7.9 cpm; p < 0.0001). Significantly superior amounts of individuals treated with vergence/accommodative therapy attained a normal amplitude (69% vs. 32%, difference = 37%, 95% CI: 22 to 51%; p < 0.0001) and facility (85% vs. 49%, difference = 36%, 95% CI: 18 to 55%; p < 0.0001) than those who received placebo therapy. Amplitude increased at an average rate of 1.5 D per week during the first four weeks (p < 0.0001), then reduced to 0.2 D per week (p = 0.002) from weeks four to 16 in the vergence/accommodative therapy group. Likewise, facility improved at an average rate of 1.5 cpm per week throughout the first four weeks (p < 0.0001), then decelerated to 0.6 cpm per week from weeks four to 16 (p < 0.0001). From this study, the authors concluded that office-based vergence/accommodative therapy effectively improves accommodative function in children with symptomatic CI and coexisting accommodative dysfunction **(Included in the 2023 Hayes Technology Assessment)**.

In a double-masked randomized clinical trial conducted in 2021, Sangoi et al. aimed to compare changes in phoria adaption between young adult binocular normal controls (BNCs) and individuals with symptomatic CI. Those with BNC (50 participants) and CI (50 participants) were randomized to an OBVAT group or office-based placebo therapy (OBPT) group. Participants received therapies for 12 one-hour office sessions utilizing a 6Δ base-out, and 6Δ base-in phoria adaptation experiment at near (40 cm) using the flashed Maddox rod technique at baseline and the outcome. The results showed that both individuals with BNC and CI had significantly different rates and magnitudes of base-in and base-out phoria adaption (p < 0.001). Additionally, significant main effect differences in longitudinal measurements were demonstrated for the magnitude and the rate of phoria adaption for both base-in and base-out experiments (p < 0.05). Post hoc analyses using paired t-tests for the magnitude and rate of phoria adaption revealed that the CI group which received OBVAT exhibited a significant increase compared to baseline for both base-in and base-out phoria adaption (p < 0.01) and not for those who received OBPT. The longitudinal study of the therapeutic interventions using paired t-tests showed that the CI group which was administered OBVAT had a significant improvement in NPC, with results showing a baseline of 10.5 ±3.7 cm compared to an outcome of 4.5 ±1.6 cm [t(24) = 7.6, p < 0.0001]; PFV demonstrated baseline of 12.2 ±3.2Δ compared to the outcome of 28.9 ±10.4Δ [t(24) = 6.4, p < 0.0001]; and results of the CI Symptom Survey (CISS) were

baseline of 34 ±9 points compared to the outcome of 21.6 ±8 points [t(24) = 5.6, p < 0.0001). The authors concluded there are significant differences at baseline between individuals with normal BV and those with symptomatic CI. Treatment with OBVAT significantly improves the rate and magnitude at near compared to OBPT for both base-in and base-out phoria adaptation.

Alvarez et al. (2020) conducted a double-masked, ~~randomized control trial~~**RCT** to study the neuro mechanism of CI in (n = 50) adult participants. The participants were randomized into two groups. Group one received office-based vergence/accommodative therapy and group two received OBPT. Office-based therapy was administered by a trained therapist during a biweekly, 60-minute office visit. The participants were prescribed additional procedures to be performed at home for 10 minutes a day, three times per week during the duration of the therapy. Home therapy was to be conducted on days when office-based therapy was not conducted. The objective was for participants to attend two 60-minute therapy sessions per week for 6 weeks. The home therapy was all computer based through (HTS, visiontherapysolutions.net). The HTS program was used for the vergence/accommodative therapy group and a custom designed HTS program was used by the placebo. Outcomes measured were near point convergence, PFV and self-reported symptoms through a CISS score. The mean NPC improved by 6.0 and 3.1 cm in both the office-based vergence/accommodative and OBPT groups. With a ~~mean difference~~**MD** of −2.9 cm; 95% ~~confidence interval (~~CI~~)~~, −4.6 to −1.0 cm; p < .01. The mean PFV increased by 17.3 and 7.4Δ in both the office based vergence/accommodative and OBPT groups. With a ~~mean difference~~**MD** of 9.9Δ; 95% CI, 4.9 to 16.0Δ; p < .001. The mean CISS score improved by 12.4 and 10.1 points in both the office-based vergence/accommodative and OBPT groups. With a ~~mean difference~~**MD** of 2.3 points; 95% CI, −8.3 to + 4.6 points; p = .56. The authors concluded that after twelve one-hour sessions that the office-based vergence/accommodative therapy group outcomes were significantly more effective than group of OBPT for improving clinical outcomes of NPC and PFV in the participants. However, the CISS measurements were not significantly different between the two groups.

In a Cochrane Database Systematic Review and NMA, Scheiman et al. (2020) analyzed twelve RCTs that included both children and adults (n = 1,289) with symptomatic CI. The study measured the effectiveness of non-surgical interventions for CI. The outcomes measured required both clinical measures of convergence to be normal~~,~~ and show a pre-specified degree of improvement. The seven interventions measured were as follows: 1.) office-based vergence/accommodative therapy with home reinforcement; 2.) home-based pencil/target push-ups; 3.) home-based computer vergence/accommodative therapy; 4.) office-based vergence/accommodative therapy alone; 5.) placebo vergence/accommodative therapy or other placebo intervention; 6.0 prism reading glasses; and 7.0 placebo reading glasses. This systematic review and NMA found with a high-certainty of evidence that office-based vergence/accommodative therapy with home reinforcement increases the chance of a successful outcome, compared with home-based computer vergence/accommodative therapy [risk ratio (RR) 1.96, 95% ~~confidence interval (~~CI~~)~~ 1.32 to 2.94], home-based pencil/target push-ups (RR 2.86, 95% CI 1.82 to 4.35); and placebo (RR 3.04, 95% CI 2.32 to 3.98). However, there was no evidence of any treatment difference between home-based computer vergence/accommodative therapy and home-based pencil/target push-ups (RR 1.44, 95% CI 0.93 to 2.24; low-certainty evidence), or between either of the two home-based therapies and placebo therapy to be considered effective treatment. The authors concluded that office-based vergence/accommodative therapy with home reinforcement is more effective than home based pencil/target push-ups or home-based computer vergence/accommodative therapy for children. The evidence is unclear in adults as to which of the therapies is more effective.

An RCT, (CITT-ART Investigator Group, 2019) was designed to determine whether treating symptomatic CI would lead to better reading fluency and comprehension. Three hundred eleven children aged 9 to 14 years with symptomatic CI were randomly assigned to 16 weeks of office-based vergence/accommodative therapy or to placebo therapy. Improvements in (1) NPC, (2) PFV, and (3) self-reported symptoms CISS score were compared after 16 weeks of treatment. The results showed mean NPC improvement of 10.4 cm in the vergence/accommodative group, and 6.2 cm in the placebo therapy, mean PFV increased 23.2 and 8.8 in the vergence/accommodative and placebo therapy groups, respectively as well as a mean CISS score improvement of 11.8 and 10.4 points in the vergence/accommodative and placebo therapy groups, respectively. The authors concluded that these results demonstrate that office-based vergence/accommodative therapy is effective for improving the NPC and PFV in children with symptomatic CI. However, given that both treatment groups had a similar reduction in self-reported symptoms, it may not be prudent to use the CISS alone as a measure of successful treatment **(Included in the Scheiman et al. 2020 systematic review and network meta-analysis)**.

In a systematic review of the literature on orthoptic therapy for CI, Rucker, and Phillips (2018) reported that convergence exercises reduce symptoms and improve signs of CI in otherwise healthy patients. Patients with learning disabilities (LD), poor reading ability, dyslexia, or Attention Deficit Hyperactive Disorder (ADHD) do not consistently have unique ocular motor deficits, nor do patients who acquire ocular motor deficits develop these conditions, and there is insufficient evidence that shows treatment consisting of repetitive ocular motor tasks improves LD, reading, dyslexia, or ADHD. The most efficacious convergence tasks and the optimal duration and frequency of these tasks remain unknown.

In an RCT, Scheiman et al. (2011) assessed the effectiveness of various types of VT for improving accommodative amplitude or accommodative facility in 221 children with deficiencies in these measures at baseline. All types of VT (i.e., office-based VT, HBCVAT +, and HBPP) were superior to office-based placebo vision treatment for improving mean accommodative amplitude. Regarding accommodative facility, only the office-based VT group exhibited a significantly greater improvement than the placebo group. This study did not report the results of symptoms or other clinical signs. One year after completion of therapy, reoccurrence of decreased accommodative amplitude was present in only 12.5% and accommodative facility in only 11%. The authors concluded that ~~vision therapy~~**VT**/orthoptics is effective in improving accommodative amplitude and accommodative facility in school-aged children with symptomatic CI and accommodative dysfunction **(Included in the 2023 Hayes Technology Assessment)**.

Shin et al. (2011) conducted a prospective controlled trial comparing office-based VT with no VT treatment. The study included 57 children aged 9-13 years who were diagnosed with symptomatic CI (n = 27) or combined symptomatic CI and accommodation insufficiency (AI) (n = 30). They were independently divided into a treatment and a control group, matched by age and gender. Office-based VT significantly improved symptoms and clinical signs including NPC, PFV, mean accommodative amplitude, and mean accommodative facility relative to no treatment in children with CI and AI. Of the patients with concurrent CI and AI who received VT, 77% were considered improved and 61% were considered cured. Of the 11 patients who completed the 1-year follow-up, symptom scores had deteriorated to abnormal levels in 2 children and 1 child also showed regression of the NPC. The authors concluded that this study supports the use of VT as a successful method of treating CI and CI combined with AI.

The National Eye Institute sponsored the Convergence Insufficiency Treatment Trial (CITT) study, an RCT comparing the effectiveness of different treatment options for the condition in 221 children (age 9 to 17 years). Three types of VT were compared with a placebo therapy intervention. VT included: (1) office-based VT with at-home exercises; (2) home-based pencil push-ups with additional computer vision therapy (HBCVAT +); and (3) home-based pencil push-up (HBPP) therapy alone. The placebo therapy group was given placebo vision activities that simulated office-based therapy. The study found that after 12 weeks of treatment, nearly 75% of children who received office-based VT with at-home reinforcement achieved normal vision or had significantly fewer symptoms of CI. In comparison, only 43% of patients who completed home-based therapy alone showed similar results, as did 33% of patients who used HBCVAT + and 35% of patients who underwent OBPT (Convergence Insufficiency Treatment Trial Study Group, 2008).

Vision Therapy for Convergence Excess or Nystagmus

No well-designed clinical trials evaluating the use of vision therapy for convergence excess or nystagmus were identified.

Vision Therapy for Divergence Excess or Insufficiency

No well-designed clinical trials evaluating the use of vision therapy for divergence excess or divergence insufficiency were identified.

Orthoptic or Vision Therapy (VT) for Exotropia or Esotropia

Only limited quality clinical evidence was found to support the use of orthoptic or ~~vision therapy~~**VT** for exotropia.

In a randomized controlled trial (RCT) by Liang et al. (2023), the authors assessed the effectiveness of binocular vision training (BVT) and Fresnel press-on prism (FPP) for children with esotropia combined with amblyopia. Registered for the trial were children aged 3-9 years with esotropia and amblyopia (N=101). Two random groups were formed, the combined group (N=48) and the prism group (N=53). The children in the prism group received FPP treatment, while those in the combined group received a combination of therapy, BVT, and FPP. The primary outcomes measured were the visual acuity (VA), binocular function, and strabismic therapeutic effects. The results demonstrated a sizable improvement in both groups for VA versus before treatment (P=0.0079). The binocular-monocular function, plus synoptophore visual function and the Titmus stereopsis, in both groups, was considerably better compared with those before treatment (P < 0.05), and it was more substantial in the combined group versus the prism group (P < 0.05). The cure rate of strabismus was 87.50% (42/48) and 30.19% (16/53) in the combined group and the prism group, respectively, and there was a significant difference between groups (P = 0.0036). The cure time was decreased with the lower degree of esotropia. The study is limited by the small sample size. Larger, multi-center, and multi-disciplinary, high-quality research should be performed for further investigation. The authors concluded that BVT combined with FPP can efficiently promote the healing of binocular vision in children with esotropia combined with amblyopia, and some children can attain a complete cure for strabismus.

Through a randomized controlled trial (RCT), Zhang et al. investigated the effect of virtual reality (VR) technology on children after surgery for concomitant strabismus. Included in the trial were 200 children with concomitant exotropia or concomitant

esotropia who were randomly divided into two groups: the training group (N=100) and the control group (N=100). In the training group, participants received VR intervention training within a week after surgery. Those in the control group did not receive training. The results of the trial demonstrated that six months after the surgery, the orthophoria (the far or near strabismus degree was ≤8Δ) rate was meaningfully higher in the training group than in the control group (P = 0.001). In contrast, the eye position regression rate (versus the strabismus degree within one-week post-surgery, the amount of regression >10Δ) was notably lower in the training group versus the control group (P = 0.001). Six months post-surgery, the number of children with simultaneous vision and remote stereovision was substantially higher in the training group compared to the control group (P = 0.017 and 0.002, respectively). The differences in the quantity of children with peripheral stereopsis, macular stereopsis, and stereopsis in macular fovea centralis at one, three-, and six-months post-surgery among the training and the control groups were not statistically significant (P = 0.916, 0.274, and 0.302, respectively). The authors concluded that the intervention of VR technology after strabismus correction efficiently enhanced children's visual function and cure rate post-surgery and sustained their eye position.

In a 2023 meta-analysis of randomized clinical trials, Song and associates sought to compare the efficiency of part-time occlusion therapy (PTO) and the observation of intermittent exotropia (IXT) therapy. The exploration uncovered four articles with 617 individuals that could be included in the meta-analysis. The pooled outcomes exhibited PTO with higher effects versus observation, with more substantial reduction in exotropia control at distance and near (MD=0.38, 95% CI: -0.57 to -0.20, P<0.001; MD=-0.36, 95%CI, -0.54 to -0.18, P<0.001), those subjected to PTO therapy had a more noteworthy reduction in distance deviations (MD=-1.95, 95% CI: -3.13 to -0.76, P=0.001). And there was a more substantial increase in near stereoacuity among the PTO group versus the observation group (P<0.001). The limitations of the study include a limited number of participants included leading to possible selection bias, limited data from included studies, and different classes of deviation control scale contributing to clinical heterogeneity. The authors concluded that PTO improved control and near stereopsis and reduced distance exodeviation angle of children with IXT compared with observation. PTO therapy is superior to observation for improving stereopsis at near. Studies are necessary to investigate if the advantage of PTO treatment is stable after the completion of therapy, the relationship among compliance and treatment results, and the effect of increasing occlusion duration on results.

In a 2023 randomized clinical trial, Hatt et al. evaluated the effect of part-time patching versus observation on distance exodeviation control in a post hoc analyses of 3- to < 11-year-olds with IXT formerly reported in a randomized clinical trial. This trial analyzes 306 participants who, at a distance fixation, naturally manifested either a constant or IXT or had continued recovery after monocular occlusion at baseline. The authors measured the change in control at distance and near fixation, from baseline to three months and baseline to six months. The results showed a more significant improvement in the distance control score with patching than with observation at three months (MD, 0.4 points; 95% CI, 0.1-0.7) and six months (MD, 0.3 points; 95% CI, 0.02-0.6). The limitations of this trial consist of the analyses being conducted post hoc with 75% of the cohort for which treatment group differences in distance exodeviation control did not achieve statistical significance. Additionally, multiple comparisons were made, which can cause a greater likelihood that some are significant by chance. The authors concluded that part-time patching may result in improved distance control and reduced

exodeviation in this subgroup of children. Due to the post hoc nature of the analysis, added studies are required to confirm the above results and decide the sustainability of the results.

In a Cochrane Database Systematic Review, Pang et al. (2021) analyzed the effects of various surgical and non-surgical treatments located in RCTs consisting of individuals with ~~intermittent exotropia (~~IXT~~)~~. Additional aims of the review were to report intervention criteria and determine whether the treatment effect varies by age and subtype of IXT. The exploration uncovered six RCTs with a total of 890 individuals with basic or distance IXT. A meta-analysis of two RCTs comparing patching (n = 249) with active observation (n = 252) was completed. Further meta-analysis could not be undertaken due to clinical and methodological heterogeneity in the remaining trials. The evidence shows patching was clinically more effective than active observation for improving motor alignment at near and distance fixation. The results were measured by a prism and alternate cover test (PACT) at six months; results for patching: MD-2.23, 95% CI -4.02 to -0.44, and for active observation, MD -2.00, 95% CI -3.40 to -0.61. The results showed little to no difference in stereoacuity at near fixation (MD 0.00, 95% CI -0.07 to 0.07). The authors concluded from the evidence that patching offers a clinical benefit in children 12 months to 10 years of age who have basic-or distance-type IXT compared with active observation. From the literature, there is not enough evidence to determine if interventions such as bilateral lateral rectus recession (BLR) vs. unilateral rectus recession with medical rectus resection; PAT before eye muscle surgery versus eye muscle surgery alone; and lateral rectus recession and medial rectus plication versus lateral rectus recession and medial rectus resection offer any benefit.

Feng et al. (2021) conducted a~~n randomized control trial~~**RCT** in (n = 60) participants with IXT to determine the efficacy of using over minus lenses combined with prisms to improve control of IXT. Group one (n = 30) was the observation group, and they wore lenses if refractive error met any of the following criteria: **spherical equivalent (**SE**)** anisometropia ≥ 1.00 D; astigmatism ≥ 1.00 D in either eye; or SE hyperopia ≥ + 1.00 D. Group two (n = 30) was treatment group, and they were prescribed over minus lenses of -2.50 D combined with the two **prism diopters (**PD**)** base-in prism on each side. Any participant who did not need refractive correction were prescribed Plano lens to be worn at each follow-up visit, but not to be worn in the during the trial. Ocular alignment, status of BV and refraction were measured at one, three, six and 12 months for both groups. After 12 months, the mean refractive error was 1.42 ±1.25 D, and 1.43 ±1.12 D for the observation and the treatment group, with a (95% CI: − 0.61 to 0.62); the mean exotropia control score was 5.72 ±1.28 and 1.75 ±1.18 in the observation and the treatment group, with a (95% CI: − 4.63 to − 3.33); the mean near stereoacuity was 2.16 ±0.42 log arcsec and 1.91 ±0.26 log arcsec in the observation and the treatment group, respectively (95% CI: − 0.44 to − 0.06). The authors concluded that over minus lenses combined with prisms significantly improved the control of IXT and stereopsis. It reduced the angle strabismus in children with IXT. Limitations of the study small population size and no long-term monitoring after treatment to see control of IXT remains.

In 2019, Ma et al. designed a single-arm, prospective, unmasked, single-center pilot study to evaluate changes in the office control score after office-based vergence/accommodative therapy for IXT. Enrolled were 14 individuals aged six to 18 years with a diagnosis of IXT (excluding the CI type). All participants received 60 minutes of therapy, including vergence, accommodation, saccades, and pursuits, anti-suppression, and monocular fixation in binocular field techniques for 12 weeks. At the 13-week outcome visit, the primary outcome measure was the change in office control score from the

baseline visit. The office control score at distance changed by -1.0 [95% ~~confidence interval (~~CI~~)~~ = -1.6 to -0.4; p = .005; Cohen's d effect size, 0.93]. The distant Look And Cover, then Ten seconds Observation Scale for Exotropia score and distant Newcastle control score **(NCS)** total score changed by -0.7 (95% CI, -1.2 to -0.2; p = .02; Cohen's d effect size, 0.55) and -1.9 (95% CI, -2.8 to -1.0; p < .001; Cohen's d effect size, 1.37), respectively. There was no significant change in the angle of distance exodeviation [-1.8 prism diopter (DELTA) less exodeviation; 95% CI, -3.74 to 0.14 (DELTA); p = .11], but a substantial change was detected in the near angle [-4.4 (DELTA) less exodeviation; 95% CI, -7.3 to -1.5 (DELTA); p = .01; Cohen's d effect size, 0.79). There was no considerable variation in stereopsis or the Chinese ~~intermittent exotropia~~**IXT** ~~Q~~questionnaire score. Limitations of the study included the lack of a control group, lack of masking of other examiners and participants, and the relatively small sample size. The results demonstrated a statistical and clinical improvement in the distance control of exodeviation and the near exodeviation magnitude after 12 weeks of office-based vergence/accommodative therapy with home reinforcement. There is a need for a randomized clinical trial intending to determine the effectiveness of VT as a treatment for IXT **(Included in the 2023, Hayes Technology Assessment)**.

Shin et al. (2017) conducted a retrospective review to determine the effect of preoperative part time occlusion **(PTO)** therapy on long-term surgical success in early-onset exotropia in 51 consecutive patients. The mean duration of preoperative occlusion therapy was 10.2 ±5.4 months (range, 6 to 28 months). The mean follow-up duration after surgery for exotropia was 78.0 ±28.1 months (range, 36 to 135 months). Overall, the final success rate of surgery for early-onset exotropia was 66.7%. Five patients (9.8%) showed persisting consecutive esotropia and eventually underwent surgical correction for these consecutive esotropia at a mean age of 18.8 months (range, 8 to 40 months) after the primary surgery for exotropia. A higher long-term success and lower recurrence rate was found in patients who were deemed as compliant (≥ 50%) than in the group of patients who were deemed to be non-compliant (< 50%). These findings are limited by the observational design of the study.

Joyce et al. (2015) conducted a systematic review of RCTs, quasi-experimental and cohort studies with a comparison group examining interventions for divergence excess, simulated divergence excess or basic type exotropia in children, up to and including 18 years of age, followed for at least 6 months. Eleven studies satisfied the eligibility criteria. Seven examined the comparative effectiveness of two surgical procedures: four compared surgeries with other interventions, including botulinum toxin A therapy, orthoptic exercises, occlusion, BV training and watchful waiting. The evidence retrieved was of limited extent and quality with differences across studies in terms of outcome assessment and most appropriate time-point for measuring long-term outcomes. There were mixed outcomes when comparing unilateral recession/resection (R&R) with BLR on improving angle of deviation, which makes it difficult to recommend either surgical option with confidence. While non-surgical interventions appear less effective in terms of improving angle of deviation, they are rarely associated with adverse outcomes. The authors concluded that given the limited evidence base, better designed studies are required to address the question of the most effective management for treatment of childhood exotropia. Importantly, consensus is required on what constitutes a successful outcome as well as agreement on how this should be measured.

An RCT was designed to compare part-time patching with observation for previously untreated IXT in children 12-35 months old (n = 201). Participants were randomly assigned to either observation (no treatment for 6 months) or patching prescribed for 3 hours

daily for 5 months, followed by 1 month of no patching. The authors reported deterioration (defined as constant exotropia measuring at least 10Δ at distance and near or receipt of non-protocol treatment for IXT) over 6 months was uncommon, with or without patching treatment. There was insufficient evidence for the authors to recommend part-time patching for the treatment of IXT in children in this age group (Mohney et al., 2015).

~~In a 2013 Cochrane systematic review, Hatt and Gnanaraj analyzed the effects of various surgical and non-surgical treatments in randomized trials of people with IXT, to report intervention criteria and determine the significance of factors such as age with respect to outcome. The authors searched for RCTs of any surgical or non-surgical treatment. One randomized trial was eligible for inclusion in the review. This trial showed that unilateral surgery was more effective than bilateral surgery for correcting basic IXT. According to the authors, measures of severity and criteria for intervention were poorly validated for all identified studies. The authors concluded that there is a need for improved measures of severity, a better understanding of the natural history and carefully planned clinical trials to improve the evidence base for the management of this condition.~~

Buck et al. (2012) investigated the current patterns of management and outcomes of intermittent distance exotropia in an observational cohort study which recruited 460 children aged < 12 years of age with previously untreated distance exotropia. Data collected included angle, near stereoacuity, VA, control of distance exotropia measured with the ~~Newcastle Control Score (~~NCS~~)~~, and treatment. The main outcome measures were change in clinical outcomes in treated and untreated distance exotropia, 2 years from enrolment (or, where applicable, 6 months after surgery). At follow-up, data were available for 371 children (81% of the original cohort). Of these, 53% (195) had no treatment; 17% (63) had treatment for reduced VA only (pure refractive error and amblyopia); 13% (50) had no- surgical treatment for control (spectacle lenses, occlusion, prisms, exercises) and 17% (63) had surgery. Only 0.5% (2/371) children developed constant exotropia. The surgically treated group was the only group with clinically significant improvements in angle or NCS, but rates of overcorrection were high. Non-surgical treatment of intermittent distance exotropia had less significant impact on angle of deviation or scores on the NCS.

Orthoptic or Vision Therapy (VT) for Stroke and Traumatic Brain Injury

Only limited quality clinical evidence was found to support the use of orthoptic or ~~vision therapy~~**VT** for stroke and traumatic brain injury.

In 2023, Longley and colleagues studied prisms and therapy in attention loss after stroke (SPATIAL) via a feasibility randomized controlled trial (RCT). The trial contained those with inattention (spatial neglect) early after a stroke. The trial was conducted with a 3:1 stratified allocation to standard occupational therapy with or without intervention and nested process evaluation. The participants were those who were positive for inattention for more than a week post-stroke. The occupational therapy sessions were for three weeks altogether. The outcome measures included recruitment and retention rates, intervention fidelity, and attrition. The outcomes were measured at three and 12 weeks, involving the Nottingham Extended Activities of Daily Living (ADLs) Scale. The acceptability was explored through qualitative interviews and structured questions. The results of the trial showed that 80 (31%) subjects were eligible, 57 (71%) consented, 54 were randomized (40:13, +1 exclusion), and 39 (74%) completed 12-week outcomes. Treatment

fidelity was good: participants received a median of eight intervention sessions (IQR: 5, 12) for a duration of 4.7 min (IQR: 4.1, 5.0). All six serious adverse events (AE)s were not related. There was no indication that those allocated to the intervention did better than controls. Recruited caregivers (25/35) offered results with excellent data totality. Therapists, participants, and caregivers found prism adaptation (PA) training adequate. Limitations of the study include participants remained in the hospital at 12 weeks, limiting the number of ADLs reported on the primary outcome. The authors concluded that conducting a high-quality definitive trial of PA training within occupational therapy early after stroke in a standard care setting is conceivable and acceptable. However, it is challenging to justify given no sign of value over standard occupational therapy.

Through a 2022 comprehensive systematic review, Cinnera and associates explored the prospective of immersive virtual reality (IVR) for treating unilateral spatial neglect (USN) due to stroke. The authors uncovered 436 articles, with ten having a heterogeneous study design involving 77 individuals with USN from low to moderate methodological quality. Out of the studies, five assessed the usability of IVR for measuring or treating visual perception deficits in USN and compared those outcomes with 134 healthy individuals. The other studies testing IVR displayed three statistically positive results ($P<0.05$) for visual perception outcomes. The literature to date shows a possibility of benefit from using IVR for impending visual perception disorders in USN. The limitations of the study include reviews based on studies with research designs other than RCTs, and the difference between the studies in terms of study design, interventions, type, and techniques of IVR does not allow for a meta-analysis to be conducted. Also, the selected studies had a limited sample size. The authors found that IVR encourages individuals during the rehabilitation process to increase compliance and interest. Progress in visual perception and head movement, with good adherence, was conveyed frequently. Future studies are necessary due to the heterogeneity in the study design and IVR treatments.

Hazelton et al. (2022) assessed the effectiveness of interventions aimed at perceptual disorders after stroke compared to no intervention or control on performance measures in ADL. The results of their exploration uncovered 18 eligible RCTs involving 541 participants. The trials addressed touch (three trials, 70 participants), somatosensory (seven trials, 196 participants), and visual perception disorders (seven trials, 225 participants), with one (50 participants) investigating mixed touch-somatosensory conditions. All but one explored the efficiency of rehabilitation interventions; the exception assessed non-invasive brain stimulation. The limitations of the assessment include the variation of interventions, low quality of evidence examined, and lack of trials focusing on the main parallels of intervention versus no treatment or control assessed as a primary outcome at follow-up. Furthermore, there was limited reporting of performance in ADLs. The authors concluded that there is little RCT evidence of the efficacy of interventions for perceptual disorders after a stroke. Inadequate evidence advocates for or refutes the proposal that perceptual interventions are beneficial. Higher-quality trials of interventions for perceptual disorders in stroke are necessary. The authors further conclude that people with impaired perception after a stroke should continue to receive neurorehabilitation.

In a 2022 RCT, Batool et al. examined the effects of visual scanning exercises and a task-specific approach on balance and ADL for individuals post-stroke with eye movement disorders. Recruitment of 64 individuals took place at the University of Lahore Teaching Hospital, where the participants were randomized into either an experimental (N=32) or a control group (N=32). The experimental group was treated with visual scanning exercises and a task-specific approach, and the control group was treated with a task-specific

approach alone. The outcomes measured were pre- and post-balance and ADL assessed on the Berg balance scale and Barthel index scale at baseline and the fourth week. The trial results demonstrated an Intra-group analysis of BERG BALANCE SCALE in the experimental group and showed statistically significant results (p<0.05) in all items except items four, 13, and 14, respectively. Intra-group analysis of BERG BALANCE SCALE in the control group showed statistically significant results (p<0.05) in items three, five, eight, and 12, respectively, while all remaining items showed statistically insignificant results. Intra-group analysis of BARTHEL INDEX SCALE in the experimental group showed statistically significant results in all items (p<0.05) except in items nine and 10, respectively. Intra-group analysis of BARTHEL INDEX in the control group showed statistically significant results (p<0.05) in items one, three, four, and eight, respectively, while all outstanding items showed statistically insignificant results. Inter-group analysis displayed statistically significant findings in total scores of BERG BALANCE SCALE (p=0.000) and BARTHEL INEX SCALE (p=0.033). The limitations of the study include small sample size and the lack of assessment of both therapies at follow-up. The authors concluded that visual scanning exercises and a task-specific approach were more effective than a task-specific approach alone. Visual scanning exercises and a task-specific approach can be used to train balance and ADLs for individuals with stroke and eye movement disorders.

Qiu et al. (2021) performed a meta-analysis of seven RCTs including (n=211) participants reviewing the efficacy of PA treatment in unilateral neglect post-stroke. Of the seven studies included, one study investigated the effects of PA in acute post-stroke neglect and another study examined the chronic stage of stroke rehabilitation. Four studies reviewed terminal PA, two studies reviewed concurrent PA—, and another singular study reviewed both treatments combined. Only one trial used no goggles as the control treatment, but neutral goggles (sham adaptation) were used in control groups of other studies. Visual deviation toward the right varied from six to twelve degrees. One trial adopted prism goggles with 11.4-degree rightward shift of visual field, and other trials used the goggles with 10-degree rightward deviation. The duration of PA treatment ranged from four days to four weeks, and most of the studies conducted two weeks of treatment. The results of the present meta-analysis show that PA did not have significant short-term or long-term beneficial effects which showed significant improvement in neglect symptoms of unilateral stroke patients. These outcomes were measured by using the Behavioral Inattention Test (BIT) or Catherine Bergego Scale (CBS) and compared with neutral goggles (sham adaptation) and standard care alone (no adaptation). The results were highly consistent and evaluated by the I^2 statistic ($I^2 \leq 15.9\%$) between studies regardless of the variability in treatment duration, type of PA, parameter of visual shift, and follow-up duration. The authors concluded the application of PA, compared to using a placebo or no treatment, lacked significant data which demonstrated much improvement in neglect symptoms of participants diagnosed with unilateral post-stroke. The meta-analysis and systematic review findings do not support routine use of PA therapy for unilateral post-stroke participants.

Cavanaugh et al. (2020) published the results of an RCT evaluating the efficacy of motion discrimination training as a potential therapy for stroke-induced hemianopia visual field defects. Forty-eight subjects with stroke-induced homonymous hemianopia were randomized into two training arms, an intervention, and a control. Subjects were between 21-75 years of age and presented with no ocular issues. Subjects were randomized with equal allocation to receive training in either their sighted or deficit visual fields. Training was performed at home for six months, consisting of repeated visual discriminations at a

single location for 20-30 minutes per day. Pre- and post-training testing was identical, consisting of Humphrey Visual Fields, Macular Integrity Assessment Perimetry, Ocular Coherence Tomography, motion discrimination performance, and visual quality of life questionnaires. Primary outcome measures were changes in perimetric mean deviation (PMD) on Humphrey Visual Field Analyzer in both eyes. The results showed mean PMDs improved over 6 months in Deficit-trained subjects, and no improvement was observed in Sighted-trained subjects. However, there were no significant differences between the alternative training modalities. It was concluded that while there is no widely accepted therapy available to treat homonymous hemianopia, this study evaluated the efficacy of visual perceptive training as a potential therapy.

In a 2019 Cochrane systematic review, Pollock et al. sought to determine the effects of various interventions for people with visual field defects following a stroke. Randomized trials in adults after a stroke were selected if the intervention was specifically targeted at improving the visual field or improving the ability of the participant to cope with the vision loss. The primary outcome was functional ability in ~~activities of daily living~~**ADL** and secondary outcomes included functional ability in other ~~activities of daily living~~**ADL**, including reading ability, visual field measures, balance, falls, depression and anxiety, discharge destination or residence after stroke, quality of life and social isolation, visual scanning, ~~adverse events~~**AE**, and death. There were 20 studies that evaluated the effect of treatments for visual field defects, however only 10 of them compared the effect of a particular treatment with no treatment. Of these, four studies investigated a type of eye movement training designed to improve the lost visual field (a 'restitutive' intervention), four studies investigated the effect of scanning training, which involves training people to 'scan' across the space in front of them and into the 'lost' visual field, in order to better cope with their lost vision (a 'compensatory' intervention), and three studies investigated the effect of wearing a special prism on a pair of glasses, which increases the amount a person can see on their affected side (a 'substitutive' intervention). One of the studies investigated the effect of specialized assessment by an orthoptist (a hospital-based vision specialist), compared to standard care. Only two studies presented data relating to how treatment can improve stroke survivors' abilities in ~~activities of daily living~~**ADLs**, and there was a lack of consistency across studies that limited our ability to draw clear conclusions. There was insufficient evidence to draw any conclusions about the effectiveness of restitutive interventions as compared to control. There was low or very low-quality evidence that scanning training may help improve quality of life but may have no effect on other outcomes (including ~~adverse events~~**AEs**). There was low or very-low quality evidence that prisms may have an effect on ability to scan (look) for objects but may cause a range of minor ~~adverse events~~**AEs** (particularly headache) and may have no effect on other outcomes. Limitations with the evidence meant that we could not draw any conclusions about the benefits of assessment interventions.

Hunt et al. (2016) conducted a systematic review of evidence regarding the use of oculomotor-based vision assessment to identify and monitor recovery from mild traumatic brain injury (mTBI). Their objectives were to (1) identify changes in oculomotor-based vision following mTBI; (2) distinguish methods of assessment; (3) appraise the level and quality of evidence; and, if warranted, (4) determine clinical recommendations for assessment. Articles were included if study populations were clearly identified as having mTBI and used an assessment of oculomotor-based vision. Twenty articles met their inclusion criteria. Exploratory findings suggest that measurements of saccades, smooth pursuit, and vergence are useful in detecting changes associated with mTBI. The authors noted that the strength of this evidence is not yet sufficient to warrant clinical

recommendations. Research using rigorous methods is required to develop reliable, valid, and clinically useful assessment protocols.

In a systematic review of interdisciplinary literature, Klinke et al. (2015) identified rehabilitation interventions that can be integrated into ward-based nursing for patients with hemi-spatial neglect following stroke in the right brain hemisphere. Using 41 original studies, 11 interventions were identified. The selected studies were graded according to the strength of their evidence (Levels 1-5); the proposed interventions were given recommendation grades (Grades A-D). The interventions included right half-field eye patching (Grade D), smooth pursuit eye-movement training (Grade B) and visual scanning training (Grade D). The authors noted that there was general low level of evidence and the diversity of interventions which made it difficult to endorse specific priorities and combinations for implementation and interventions should be applied after careful evaluation of each patient's unique capacities and problems. The authors also emphasized the need to integrate evidence-based interventions to stimulate rehabilitation outcomes and further research.

Van Wyk et al. (2014) evaluated the effect of saccadic eye movement training with visual scanning exercises (VSEs) integrated with task-specific activities on ~~unilateral spatial neglect (~~USN~~)~~ post stroke. A matched-pair RCT was conducted. Subjects were matched according to their functional activity level and allocated to either a control (n = 12) or an experimental group (n = 12). All patients received task-specific activities for a 4-week intervention period. The experimental group received saccadic eye movement training with VSE integrated with task specific activities as an "add on" intervention. Assessments were conducted weekly over the intervention period. Statistically significant differences were noted on the King-Devick Test (p = .021), Star Cancellation Test (p = .016), and Barthel Index (p = .004). The authors concluded that intensive saccadic eye movement training with VSE integrated with task-specific activities has a significant effect on USN in patients post stroke. Long-term follow-up and further studies with larger patient populations are needed to verify these results.

Orthoptic or Vision Therapy (VT) for Dyslexia and Other Learning Disabilities (LD)

Only limited quality clinical evidence was found to support the use of orthoptic or ~~vision therapy~~**VT** for dyslexia and other ~~learning disabilities~~**LDs**.

In ~~2016~~**2018**, Hussaindeen et al. carried out a study at a center for LD to report the frequency of BV anomalies in children with specific learning disorders (SLD) and to assess the efficacy of VT in children with a non-strabismic BV anomaly (NSBVA). The study consisted of 94 children with a diagnosis of SLD. Children with **best corrected visual acuity (**BCVA**)** of ≥ 6/9 - N6, who are cooperative for examination and free from any ocular pathology, were assessed for BV. Participants diagnosed with NSBVA (n = 46) 24 of 46 were randomized to VT, with no intervention for 22 participants placed in the experimental control. Each group received ten sessions of VT, with a BV assessment performed for both the intervention and non-intervention groups. The results showed BV anomalies in 59 children (62.8%); of the 59 children, 13 (22%) had strabismic binocular vision anomalies (SBVA) and 46 participants (78%) had NSBVA. Most seen in individuals with NSBVA was accommodative infacility (AIF), found in 67%, followed by CI in 25%. The intervention group showed significant improvement post-VT and met all the BV parameters (Wilcoxon signed rank test, $p < 0.05$) apart from negative fusional vergence.

Hall et al. (2013) conducted a randomized, double-blind trial with 73 delayed readers to compare changes in reading and spelling as well as irregular and non-word reading skills after 3 months of wearing either the Harris or the Dyslexia Research Trust (DRT) filters. Reading improved significantly after wearing either type of filter, with 40% of the children improving their reading age by 6 months or more during the 3-month trial. However, spelling ability and non-word reading improved significantly more with the DRT than with the Harris filters. The authors concluded that education and rehabilitation professionals should consider colored filters as an effective intervention for delayed readers experiencing visual stress. According to the authors, this research will help to support the use of colored filters for visual reading capacity, but further rigorous research is needed. The study is limited by lack of comparison group undergoing a non-filter intervention or no intervention.

In a double-masked, placebo crossover **randomized control trial (**RCT**)**, Ritchie et al. (2011) tested the efficacy of Irlen colored overlays for alleviating reading difficulties thought to have been caused by Irlen syndrome, a proposed perceptual disorder with controversial diagnostic status. Sixty-one school children (aged 7-12 years) with reading difficulties were included in the study. Based on the study results, the authors concluded that Irlen colored overlays do not have any demonstrable immediate effect on reading in children with reading difficulties.

Visual Information Processing Evaluation

Limited clinical evidence was found to support the use of visual information processing evaluations for diagnosing learning-related or other types of visual deficits.

Hopkins et al. (2019) conducted a study to evaluate the association between performance on visual information processing tests and academic performance in 222 second grade school children, with a mean age of 8-8.5 years. The Progressive Achievement Tests in Reading (PAT-R) and Mathematics (PAT-M) were used as assessment tools. Both tests are timed, paper based, standardized tests, referenced against the Australian national curriculum used in schools across Australia to monitor student progress, typically across testing sessions 9–12 months apart. The results showed that visual information processing assessed using the Visual- Motor Integration (VMI) and Developmental Eye Movement (DEM) measures were significantly associated with academic performance. However, given that the VMI task involves visual spatial, visual analysis and visual motor skills, it may be more relevant than the DEM test in capturing the diverse range of activities (e.g., reading, writing and mathematics) carried out by children in a classroom. In a clinical setting, a child's academic performance can play an important role in the optometric management of conditions such as hyperopia, thus tests, such as the VMI, can provide clinicians with insight into a child's potential overall academic performance and support clinicians regarding their management decisions. Limitations of this study include the potential for normal developmental differences in children of the same age or year in school, as well as the authors did not include assessment of refractive error, accommodation, or general IQ tests. It is important that future research include these parameters to assess if the provision of optometric interventions can improve academic performance in longitudinal studies.

Goldstand et al. (2005) compared visual and visual-information processing skills between children with and without mild reading and academic problems and examine the incidence of visual deficits among them. A total of 71 seventh graders classified as proficient (n = 46) and non-proficient (n = 25) readers were compared with respect to scores on an

accepted vision screening, on tests of visual-perception, visual-motor integration, and academic performance. Further, academic performance and visual-information processing were compared between children who failed and passed the vision screening. Visual deficits were found in 68% of the participants, and among significantly more boys than girls. Non-proficient readers had significantly poorer academic performance and vision-screening scores than the proficient readers. Participants who passed the visual screening performed significantly better in visual perception than those who failed. According to the investigators, visual function significantly distinguishes between children with and without mild academic problems, as well as on visual-perception scores. The investigators concluded that the high occurrence of visual deficits among participants warrants consideration of vision deficits among school children with academic performance difficulties. These findings require confirmation in a larger study.

Visual Perceptual Therapy

Only limited quality clinical evidence was found to support the use visual perceptual therapy.

In 2022, Zhong et al. conducted a randomized controlled trial (RCT) to evaluate the therapeutic efficacy of perceptual learning (PL) in improving contrast sensitivity (CS) function (CSF) and visual acuity (VA). Children with limbal dermoid (LD) (N=25) and children without LD were compared regarding CSF and VA. The LD group was randomized to two arms: PL combined with patching (N=9) and patching only (N=8). The outcomes measured were the area under log CSF (AULCSF) and best corrected VA (BCVA). The results showed a reduction in the LD group compared to controls. After six months of training, the difference in the changes in the AULCSF between the PL and patching groups was 0.59 (95% CI: 0.32, 0.86, p < 0.001), and the between-group difference in VA at six months was -0.30 (95% CI: -0.46, -0.14, p < 0.001). The limitations of the study were the small sample size and short-term following up. The authors concluded that those suffering from LD with amblyopia simultaneously showed CSF deficits and VA loss. According to the results, PL could improve CSF and VA in the amblyopic eye better than patching.

Choi (2022) developed a pilot study to investigate the effects of task-oriented training on upper-limb functioning, visual perception, and activities of daily living (ADL)~~s~~ for individuals following acute stroke. The study enrolled 20 participants, randomly assigned to either a control group or an experimental group in a 1:1 ratio. For six weeks, task-oriented training and table-top activity training were employed. The Manual Function Test (MFT) was applied to evaluate changes in upper limb functioning. The Motor-Free Visual Perception Test-Vertical (MVPT-V) was employed to assess visual perceptual skills, and the Korean Modified Barthel Index (K-MBI) was used to gauge ADL performance. The results of the study showed that the group effect was not significant ($p > 0.05$); however, there was a significant interaction in the MFT and MBI score between group and time ($p < 0.05$). After the intervention, both groups demonstrated a substantial increase in MFT and MBI scores ($p < 0.001$), although the effect size was more significant in the task-oriented training group versus the table-top activity training group. The MVPT-V score demonstrated no significant interaction between the group and time ($p > 0.05$); additionally, the results showed no significant group difference ($p > 0.05$). After the intervention, both groups demonstrated significant improvement in MVPT-V scores ($p < 0.001$). The authors concluded from the pilot study that both trainings effectively recover upper-limb function, visual perception, and ADLs for individuals following acute stroke.

In a prospective study, Yalcin and Balci (2014) evaluated the efficacy of neural **vision therapy (**VT**)**, also known as perceptual ~~vision therapy~~**VT**, in enhancing BCVA and ~~contrast sensitivity~~**CS** function in amblyopic patients. The study enrolled 99 subjects (age 9 to 50 years) previously diagnosed with unilateral hypermetropic amblyopia. The subjects were divided into two groups, with 53 subjects (53 eyes) in the perceptual VT group and 46 subjects (46 eyes) in the control group. Study phases included a baseline screening, a series of 45 training sessions with perceptual VT, and an end-of-treatment examination. BCVA and ~~contrast sensitivity~~**CS** function at 1.5, 3, 6, 12, and 18 cycles per degree spatial frequencies were obtained for statistical analysis in both groups. All subjects had follow-up examinations within 4-8 months. Except for one subject from the study group and two subjects from the control group, all subjects had occlusion during childhood. The study was not masked. The results for the study group demonstrated a mean improvement of 2.6 logarithm of the minimum angle of resolution (logMAR) lines in VA (from 0.42 to 0.16 logMAR). ~~Contrast sensitivity~~**CS** function improved at 1.5, 3, 6, 12, and 18 cycles per degree spatial frequencies. The control group did not show any significant change in VA or ~~contrast sensitivity~~**CS** function. None of the treated eyes showed a drop in VA. The authors concluded that the results of the study demonstrate the efficacy of perceptual VT in improving VA. According to the authors, long-term follow-up and further studies are needed to verify these results **(Included in the Yeh et al. 2023 systematic review and meta-analysis)**.

Vision Restoration Therapy (VRT)

Only limited quality clinical evidence was found to support the use of vision restoration therapy.

Alber et al. 2017 conducted an open-label pilot study in a rehabilitation center, which included seven individuals receiving transcranial direct current stimulation (tDCS)/VRT vs. a convenience sample of seven individuals in the control group. All participants suffered from homonymous visual field defects following a posterior cerebral artery stroke. The combined therapy of tDCS and VRT was employed for 50 days post-stroke in the form of 10 sessions for seven individuals with homonymous hemianopia. Following treatment, visual field recovery was compared with retrospective data from seven controls matching the defect sizes and age of lesions and matched to those in the experimental group who had received standard rehabilitation with compensatory eye movement and exploration training. Safety and acceptance from the participants were exceptional, although individuals reported occasional itchy skin under the electrodes. Both the treatment and control groups demonstrated improvements in visual fields confirmed by an increased mean sensitivity threshold in decibels shown in standard static perimetry. For the tDCS/VRT group, recovery was significantly greater (36.73% 37.0%) than the control group (10.74% 8.86%). From the study, the authors concluded that treating tDCS/VRT for individuals following an acute stroke is safe with excellent applicability and acceptance of the treatment. Data suggested tDCS/VRT is superior to standard vision training procedures. Larger-sample, controlled, randomized and double-blinded trials are underway and necessary to determine real tDCS vs. sham tDCS supported visual field training in the early vision rehabilitation phase.

In a prospective, double-blind, placebo-controlled **randomized controlled trial (**RCT**)**, Sabel and Gudlin (2014) determined if behavioral activation of areas of residual vision using daily 1-hour VRT for glaucoma for 3 months improved detection accuracy compared with placebo. The study participants included a volunteer sample of patients with glaucoma (mean age, 61.7 years) with stable visual fields and well-controlled intraocular

pressure. Study interventions included computer based VRT for glaucoma (n = 15) or visual discrimination placebo training in the intact visual field (n = 15). After randomization, 4 patients withdrew from the trial because of mild headaches (n = 2) or lack of time to complete the schedule (n = 2). The primary end point was change in detection accuracy in high-resolution perimetry. VRT for glaucoma led to significant detection accuracy gains in high-resolution perimetry, which were not found with white-on-white or blue-on-yellow perimetry. Furthermore, the pre-post differences after VRT for glaucoma were greater compared with placebo in all perimetry tests, and these results were independent of eye movements. VRT for glaucoma (but not placebo) also led to faster reaction time. Vision-related quality of life (QOL) was unaffected, but the health-related quality-of-life mental health domain increased in both groups. The authors concluded that visual field defects caused by glaucoma can be improved by repetitively activating residual vision through training the visual field borders and areas of residual vision, thereby increasing their detection sensitivity. According to the authors, this trial revealed evidence that visual field loss is in part reversible by behavioral, computer-based, online controlled vision training, comprising a new rehabilitation treatment option in glaucoma. These findings require confirmation in a larger study with long-term follow-up.

Jung et al. (2008) evaluated the effects of VRT on the visual function of 10 patients with anterior ischemic optic neuropathy in a double-blind pilot RCT. All patients were evaluated before VRT and after 3 and 6 months of treatment by Early Treatment Diabetic Retinopathy Study (ETDRS) **visual acuity (**VA**)**, contrast sensitivity **(CS)**, reading speed, 24-2 SITA-standard Humphrey visual field (HVF), High Resolution Perimetry (HRP) (perimetry obtained during VRT), and vision-based QOL questionnaire. Patients were randomized between two VRT strategies (5 in each group): I) VRT in which stimulation was performed in the seeing VF of the affected eye ("seeing field-VRT"); II) VRT in which stimulation was performed along the area of central fixation and in the ARV (areas of residual vision) of the affected eye ("ARV-VRT"). The results of the HRP, HVF, and clinical assessment of visual function were compared for each patient and between the two groups at each evaluation. VA qualitatively improved in the ARV-VRT group; however, the change was not statistically significant. Binocular reading speed significantly improved in the ARV-VRT group. HVF foveal sensitivity increased mildly in both groups. HRP analysis showed a similar increase in stimulus accuracy in both groups (mean improvement of about 15%). All patients reported functional improvement after VRT. A small study population limits the conclusions that can be reached from this study.

Mueller et al. (2007) performed a case series including observational analysis of visual fields of 302 patients before and after being treated with computer--based VRT for a period of 6 months. The visual field defects were due to ischemia, hemorrhage, head trauma, tumor removal or anterior ischemic optic neuropathy. Primary outcome measure was a visual field assessment with super-threshold perimetry. VRT improved patients' ability to detect super-threshold stimuli in the previously deficient area of the visual field by 17.2% and these detection gains were not significantly correlated with eye movements. Notable improvements were seen in 70.9% of the patients. Efficacy was independent of lesion age and etiology, but patients with larger areas of residual vision at baseline and patients older than 65 years benefited most. Conventional perimetry validated visual field enlargements and patient testimonials confirmed the improvement in every day visual functions. The lack of a control group limits the validity of the results of this study.

Clinical Practice Guidelines

American Academy of Pediatrics (AAP)/ Section on Ophthalmology, Council on Children with Disabilities/American Academy of Ophthalmology (AAO)/American Association for Pediatric Ophthalmology and Strabismus (AAPOS)/American Association of Certified Orthoptists (AACO)

~~According to a joint policy statement issued by the AAP, AAO, AAPOS, and AACO, diagnostic and treatment approaches for dyslexia that lack scientific evidence of efficacy such as behavioral VT, eye muscle exercises, or colored filters and lenses are not endorsed or recommended. The ophthalmologist should identify and treat any significant visual defect according to standard principles of treatment. Strabismus, amblyopia, and refractive errors may require glasses, eye patching, eye drops, or eye-muscle surgery. In addition, the ophthalmologist should discuss the lack of efficacy of VT and other "alternative treatments" with the parents (AAP, 2009).~~

A 2011 joint technical report by the **AAP, AAO, AAPOS, and AACO** ~~same societies~~ indicates that vision problems can interfere with the process of reading, but children with dyslexia or related **learning disabilities (**LD**)** have the same visual function and ocular health as children without such conditions. LD constitute a diverse group of disorders in which children who generally possess at least average intelligence have problems processing information or generating output. Their etiologies are multifactorial and reflect genetic influences and dysfunction of brain systems. Currently, there is inadequate scientific evidence to support the view that subtle eye or visual problems cause or increase the severity of LD. According to the report, scientific evidence does not support the claims that visual training, muscle exercises, ocular pursuit-and-tracking exercises, behavioral/perceptual **vision therapy (**VT**)**, "training" glasses, prisms, and colored lenses and filters are effective direct or indirect treatments for LD. There is no valid evidence that children who participate in VT are more responsive to educational instruction than children who do not participate (Handler and Fierson, 2011).

According to a joint policy statement issued by the AAP, AAO, AAPOS, and AACO, diagnostic and treatment approaches for dyslexia that lack scientific evidence of efficacy such as behavioral VT, eye muscle exercises, or colored filters and lenses are not endorsed or recommended. The ophthalmologist should identify and treat any significant visual defect according to standard principles of treatment. Strabismus, amblyopia, and refractive errors may require glasses, eye patching, eye drops, or eye-muscle surgery. In addition, the ophthalmologist should discuss the lack of efficacy of VT and other "alternative treatments" with the parents (AAP, 2009).

American Academy of Ophthalmology (AAO)

In the 2022 AAO preferred practice pattern for Amblyopia, the recommendations are as follows:

- **Treatment of refractive error alone can improve visual acuity (VA) in children with anisometropic, strabismic, or combined Amblyopia. Visual acuity of children with bilateral refractive Amblyopia also can substantially improve with refractive correction alone.**
- **Most children who have moderate amblyopia (20/40 to 20/80) respond to initial treatment consisting of 2 hours of daily patching or weekend atropine.**
- **Following treatment of Amblyopia caused by strabismus, anisometropia, or both, continued monitoring is necessary, and additional treatment, if needed, is associated with the long-term durability of the VA improvement.**

- **Suitable treatment options for Amblyopia include optical correction, patching, pharmacological treatment, optical treatment, Bangerter (translucent) filters, digital therapeutics, and managing the underlying cause of Amblyopia.**
- **Amblyopia treatment may be effective in older children and adolescents, particularly if they have not previously been treated (Cruz et al., 2023).**

The AAO's 2021 Preferred Practice Pattern guidelines for pediatric ophthalmology/strabismus summary benchmarks for treating amblyopia:

- All children with amblyopia should be offered an attempt at treatment regardless of age.
- Choose treatment based on patient's age; VA; adherence with previous treatment; and physical, social, and psychological status.
- Treatment goal is equal VA between two eyes.
- Once maximal VA has been obtained, treatment should be tapered and eventually stopped.

Exotropia:

- All forms of exotropia should be monitored, and some will require treatment.
- Young children with **intermittent exotropia (**IXT**)** and good fusional control can be followed without surgery.
- Deviations that are present most or all the time require treatment.
- Prescribe corrective lenses for any clinically significant refractive error.
- Optimal modes of therapy are not well established.

Esotropia:

- Consider all forms of esotropia for treatment and re-establish binocular alignment as soon as possible.
- Prescribe corrective lenses for any clinically significant refractive error as initial treatment.
- If eyeglasses and amblyopia management are ineffective in aligning the eyes, then surgical correction is indicated
- Start amblyopia treatment before surgery because surgical treatment of esotropia in the presence of moderate to severe amblyopia has a lower success rate than in the presence of mild or no amblyopia.

The AAO esotropia and exotropia preferred practice pattern (Wallace et al. 2018) states the potential benefits of treatment for esotropia include promoting BV and normal visual function in each eye. If binocularity is achieved, the number of surgical procedures over a lifetime may be reduced. Treatment should be considered for all forms of esotropia, and binocular alignment should be established as soon as possible, especially in young children, to maximize binocular potential to prevent or facilitate treatment of amblyopia and to restore normal appearance.

The following are included in the list of current treatment practices for esotropia:

- Correction of refractive errors
- Bifocal eyeglasses
- Prism therapy
- Amblyopia treatment

The AAO includes the following in its list of current treatment practices for exotropia:

- Correction of refractive errors
- Stimulating accommodative convergence (overcorrection of myopia or under-correction of hyperopia)
- Patching (anti-suppression) therapy
- Amblyopia treatment
- Prism therapy
- Convergence exercises for CI exotropia

The AAO's amblyopia preferred practice pattern (Repka et al. 2017) states that timely treatment of amblyopia usually improves VA and binocularity, and it decreases the likelihood of severe visual handicap if there is loss of vision in the fellow eye later in life. The prognosis for attaining normal vision in an amblyopic eye depends on many factors, including the age of onset; the cause, severity, and duration of amblyopia; the history of and response to previous treatment; adherence to treatment recommendations; and concomitant conditions. Several strategies are used in the treatment of amblyopia:

- Treatment of refractive error alone is the initial step in care of children 0 to 17 years of age with amblyopia (moderate quality, strong recommendation).
- Patching is an appropriate choice for treatment for children who do not improve with eyeglasses alone or who experience incomplete improvement (moderate quality, strong recommendation).
- Patching as initial therapy after refractive correction should be considered for children with moderate amblyopia (20/40 to 20/80) (moderate quality for treatment of amblyopia, strong recommendation) with a prescribed dose of 2 hours of daily patching or weekend atropine (moderate quality for amount of time treatment, discretionary recommendation).
- There is insufficient evidence to recommend VT techniques.

Additional strategies for treatment of amblyopia, such as pharmacologic therapy, are also addressed in this preferred practice pattern.

~~In a separate policy statement, the AAO (2013) maintains that children with possible or diagnosed LD, such as dyslexia, should undergo a comprehensive eye examination so that any undiagnosed vision impairment can be identified and treated. Such children should be referred for appropriate medical, psychological, and educational evaluations and treatment of any learning disability. The organization states that there is insufficient evidence to conclude that "defective eye teaming" and "accommodative disorders" can be underlying causes of educational impairment.~~

~~The AAO esotropia and exotropia preferred practice pattern (Wallace et al. 2018) states the potential benefits of treatment for esotropia include promoting BV and normal visual function in each eye. If binocularity is achieved, the number of surgical procedures over a lifetime may be reduced. Treatment should be considered for all forms of esotropia, and binocular alignment should be established as soon as possible, especially in young children, to maximize binocular potential to prevent or facilitate treatment of amblyopia and to restore normal appearance.~~

~~The following are included in the list of current treatment practices for esotropia:~~
~~Correction of refractive errors~~
~~Bifocal eyeglasses~~
~~Prism therapy~~

~~Amblyopia treatment~~

~~The AAO includes the following in its list of current treatment practices for exotropia:~~
~~Correction of refractive errors~~
~~Stimulating accommodative convergence (overcorrection of myopia or under-correction of hyperopia)~~
~~Patching (anti-suppression) therapy~~
~~Amblyopia treatment~~
~~Prism therapy~~
~~Convergence exercises for CI exotropia.~~

American Association for Pediatric Ophthalmology and Strabismus (AAPOS)/American Academy of Ophthalmology (AAO)

In 2022, the AAPOS and AAO created a joint statement on vision screening for infants and children. The recommendations for community and school screening programs state that in community and school-based screening programs, screeners should have specific training in vision screening techniques and protocols as recommended by the Academy and AAPOS. Children who do not pass these screenings should be referred for an additional ocular assessment performed by the primary care provider or an eye care provider with training and experience in treating children.

In the primary care setting, the Academy and AAPOS recommend that an ocular assessment be performed whenever questions arise about the health of the visual system of a child of any age. In addition, even without specific signs or symptoms, they recommend that infants and children be routinely screened for vision problems and that any child who does not pass one or more of these screening tests have an ophthalmological examination.

- **A pediatrician, family physician, or other appropriately trained health care provider should examine a newborn's eyes for general eye health and perform a red reflex test in the nursery. Any baby with an abnormal red reflex requires urgent consultation. An ophthalmologist should be asked to examine all high-risk infants (i.e., those at risk of developing retinopathy of prematurity (ROP); those with a family history of retinoblastoma, glaucoma, or cataracts in childhood; those with a family history of retinal dystrophy/degeneration; those with systemic diseases or neurodevelopmental delays associated with eye problems; those with any opacity of the ocular media; or those with nystagmus).**
- **From 1 month to 4 years of age, infants and toddlers should have their ocular health assessed at each routine well-child visit, including an external inspection, pupillary examination, corneal light reflection, and fixation, and following behavior assessment. This assessment should address any concerns raised by the family or noted by the primary care provider.**
- **Emphasis should be placed on checking VA when a child is cooperative enough to complete the assessment. Generally, this occurs between ages 3 ½ and four years. This assessment can be performed by a pediatrician, family practitioner, ophthalmologist, optometrist, orthoptist, nurse, or other appropriately trained individual. Screeners should not have a vested interest in the screening outcome. A child referred from a vision screening or uncooperative at a second attempt at vision testing should be referred for a comprehensive eye evaluation. It is essential that formal testing of VA be performed by the age of 5 years.**
- **Photo screening and handheld autorefraction may be electively performed in children 12 months to 3 years of age, allowing earlier detection of conditions that may lead to amblyopia. Photo screening and handheld automated refraction are recommended as an**

alternative to VA screening with vision charts (typically used for children 3 through 5 years of age) and in children who are unable or unwilling to cooperate with routine acuity screening with vision charts (but are not superior to vision chart testing for children able to participate). Using vision charts to assess amblyopia in children 3 to 5 years of age remains a viable practice.

- **Additional screening on each child should be done at routine school checks or well-child visits every 1-2 years after age five. Regular comprehensive professional eye examinations performed on normal asymptomatic children have no proven medical benefit.**
- **Children with possible or diagnosed learning disabilities, such as dyslexia, should undergo a comprehensive eye examination to identify and treat any undiagnosed vision impairment. Such children should be referred for appropriate medical, psychological, and educational evaluations and treatment of any learning disability. There is inadequate scientific evidence to suggest that "defective eye teaming" and "accommodative disorders" are common causes of educational impairment. Hence, routine screening for these conditions is not recommended.**

Many serious ocular conditions are treatable if identified through screening during the preschool and early school-aged years. Many of these conditions are associated with a positive family history. Therefore, additional emphasis should be directed to screening high-risk infants and children, and when necessary, screeners should readily refer such children to an ophthalmologist for a comprehensive eye evaluation.

In a joint policy statement, the AAPOS and the AAO state that amblyopia is a medical condition and requires treatment. Amblyopia is typically a preventable and treatable form of vision loss caused by developmental abnormalities of the brain's vision centers. Unless amblyopia is treated promptly during childhood, permanent structural changes occur in the brain, resulting in decreased visual function; recovery of vision in this instance is rarely achieved.

Current methods of preschool vision screening can identify risk factors (primarily high levels of refractive error and anisometropia) that, if untreated, increase the likelihood of amblyopia developing. Therefore, these amblyopia risk factors should also be considered medical conditions.

Optical correction such as eyeglasses and contacts may be medically indicated as a part of amblyopia treatment in addition to other modalities, such as patching and/or pharmacologic treatment (AAPOS, AAO; 2002, revised and reaffirmed 2017).

American Optometric Association (AOA)

~~The AOA (2009) issued a clinical care publication on the definition of optometric VT. The document states that research has demonstrated VT can be an effective treatment option for:~~

- ~~Ocular motility dysfunctions (eye movement disorders)~~
- ~~Non-strabismic binocular disorders (inefficient eye teaming)~~
- ~~Strabismus (misalignment of the eyes)~~
- ~~Amblyopia (poorly developed vision)~~
- ~~Accommodative disorders (focusing problems)~~
- ~~Visual information processing disorders, including visual-motor integration and integration with other sensory modalities~~
- ~~Visual sequelae of acquired brain injury~~

According to the AOA's revised guideline on the care of the patient with strabismus: esotropia and exotropia, VT is successful in the treatment of many forms of strabismus. The AOA states that VT or orthoptics involves active training procedures to improve the patient's fixation ability and oculomotor control, to help eliminate amblyopia, to improve sensory and motor fusion, and to increase facility and the range of accommodation and vergence responses. They note that the prognosis is most favorable for patients with intermittent strabismus, especially IXT, who have sensorimotor fusion at some point in space and those with recently developed strabismus (Rutstein et al., 2010b).

In their guideline on care of the patient with accommodative and vergence dysfunction, the AOA states that improvement in both accommodative and vergence adaptation systems is the basis of the success of VT. According to the guideline, data is lacking for the efficacy of home-based VT by itself. Home-based VT may be less effective than office-based therapy, as there is no therapist available to provide motivation or correct inappropriate procedures. Therefore, preferred clinical management involves office-based VT in combination with home therapy. They note that therapy combining diplopia awareness with operant-conditioning technique to reinforce alignment in the absence of visual cues has been advocated for divergence excess, and that VT is usually successful in patients with divergence insufficiency (Cooper et al., 2010).

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- **Ocular motility dysfunctions (eye movement disorders)**
- **Non-strabismic binocular disorders (inefficient eye teaming)**
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- **Amblyopia (poorly developed vision)**
- **Accommodative disorders (focusing problems)**
- **Visual information processing disorders, including visual-motor integration and integration with other sensory modalities.**
- **Visual sequelae of acquired brain injury.**

The AOA clinical practice guideline on care of the patient with learning related vision problems describes these as deficits in two broads visual system components: visual efficiency and visual information processing.

- **Visual efficiency comprises the basic visual physiological processes of VA (and refractive error), accommodation, vergence, and ocular motility.**
- **Visual information processing involves higher brain functions including the non-motor aspects of visual perception and cognition, and their integration with motor, auditory, language, and attention systems. Learning related vision problems are the manifestation of deficits in visual efficiency and visual information processing.**
- **Visual efficiency problems include uncorrected refractive error, dysfunction of accommodation and vergence control systems and the interaction of these systems, and ocular motility. Accommodative and vergence dysfunctions can be primary deficits or can occur secondary to uncorrected refractive error. Isolated visual efficiency deficits are relatively uncommon; most patients present with multiple deficits.**

This guideline also notes that correction of refractive error and treatment of visual efficiency dysfunctions can result in improved visual information processing. The

treatment of vision information processing deficits usually requires VT, which can begin during the later stages of visual efficiency therapy. This is dependent on associated conditions such as accommodative and vergence dysfunction (Garzia et al., 2008).

In their clinical guideline on the care of the patient with amblyopia, the AOA states that the rationale for using occlusion is that occluding the better eye stimulates the amblyopic eye, decreasing inhibition by the better eye. Occlusion enables the amblyopic eye to enhance neural input to the visual cortex. It is also important in eliminating eccentric fixation. However, noncompliance with occlusion represents a significant factor in occlusion failures, especially in patients over 8 years of age in whom up to 50 percent noncompliance is common. They also note that active VT for amblyopia is designed to remediate deficiencies in four specific areas: eye movements and fixation, spatial perception, accommodative efficiency, and binocular function. The goal of VT is remediation of these deficiencies, with subsequent equalization of monocular skills and, finally, integration of the amblyopic eye into binocular functioning. Untreated amblyopic patients are at a greater risk for loss of vision in the better eye (Rouse et al., 1994; revised 2004).

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National Institute for Health and Care Excellence (NICE)

A National Institute for Health and Care Excellence (NICE) guidance document states that eye movement therapy can be offered to people who have persisting hemianopia after stroke and who are aware of the condition. This recommendation was based on 3 **randomized controlled trials (**RCTs**)**, the confidence level of results ranging from very low to moderate (2013).

United States Preventative Services Task Force (USPSTF)

The USPSTF (2017) recommends the primary treatment for amblyopia as the correction of any underlying refractive error with the use of corrective lenses, occlusion therapy (eye

patching, atropine eye drops, or Bangerter occlusion foils), or a combination of treatments.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Vision therapy is a procedure and, as such, is not subject to FDA regulation. Devices used in vision training programs may be classified under several different product codes. Some of these devices may be exempt from the 510(k)-clearance process. For information on a specific device or manufacturer refer to the following website: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed **July 31, 2023** ~~August 10, 2022~~)

NovaVision™, an attention task performance recorder, consists of two software programs, one for healthcare professionals for precise diagnosing of visual deficiencies, develop patient specific therapies and analyze results of therapy. The other software is intended for patients in their homes to train and improve impaired visual functions. It is intended for the diagnosis and improvement of visual functions in patients with impaired vision that may result from trauma, stroke, inflammation, surgical removal of brain tumors or brain surgery, and may also be used to improve visual function in patients with amblyopia. Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf2/K023623.pdf. (Accessed **July 31, 2023** ~~August 10, 2022~~)

Luminopia One, Luminopia Inc. was granted **d**~~D~~e **n**~~N~~ovo classification (DEN210005) on February 26, 2021. According to the FDA website, Luminopia is a software-only digital therapeutic designed to be used with commercially available Head-Mounted Displays (HMDs), which are compatible with the software application. Luminopia One is indicated for improvement in **VA** ~~visual acuity~~ in amblyopia patients, aged 4-7, associated with anisometropia and/or mild strabismus, having received treatment instructions (frequency and duration) as prescribed by a trained eye-care professional. Luminopia One is intended for both previously treated and untreated patients. Luminopia One is intended to be used as an adjunct to full-time refractive correction, such as glasses, which should also be worn under the HMD during Luminopia One therapy. Luminopia One is intended for prescription use only in an at-home environment. Additional information is available at: https://www.accessdata.fda.gov/cdrh_docs/pdf21/DEN210005.pdf. (Accessed **July 31, 2023** ~~August 10, 2022~~)

The RevitalVision technology 510K: K012530 was originally FDA cleared in 2001 (originally branded as the NeuroVision AA-1 system) for treating amblyopia in patients aged ≥ 9 years. Additional information is available at: https://www.accessdata.fda.gov/cdrh_docs/pdf/K012530.pdf. (Accessed **July 31, 2023** ~~August 10, 2022~~)

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Policy History/Revision Information

Date	Summary of Changes
TBD	**Applicable Codes** • **Added CPT code 92066** • **Revised description for CPT code 92065** **Supporting Information** • **Updated *Clinical Evidence* and *References* sections to reflect the most current information**

	• **Archived previous policy version CS131LA.K**

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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