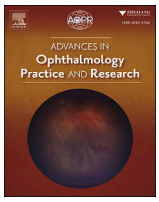
Advances in Ophthalmology Practice and Research 6 (2026) 341–354

Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

journal homepage: www.journals.elsevier.com/advances-in-ophthalmology-practice-and-research



Review

Beyond monocular acuity: Resolving the amblyopia treatment paradox with mechanism-targeted outcomes and modern testing methods

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ARTICLE INFO

Keywords:
Amblyopia
Binocular therapy
Multi-level visual disorders
Visual function assessment
Occlusion

ABSTRACT

Background: Amblyopia is a neurodevelopmental disorder affecting approximately 1%–5% of the population and has traditionally been treated based on reduced monocular visual acuity. However, growing evidence indicates that amblyopia involves broader deficits spanning low- and high-level visual processing, many of which persist even after successful acuity restoration and cannot be explained solely by acuity loss of the poor eye.

Main text: Despite the expanded understanding and the development of binocular (dichoptic) therapies designed to rebalance interocular suppression, clinical trials over the past decade comparing binocular and occlusion therapies have remained largely focused on monocular visual acuity gains. Measures of binocular function were typically limited to coarse clinical stereoacuity tests, which lack the sensitivity needed to detect subtle yet meaningful functional improvements. This therapeutic paradox—targeting binocular mechanisms while evaluating outcomes mainly through monocular acuity—constrains our ability to properly assess emerging interventions. In this review, we summarize multilevel dysfunctions in amblyopia, evaluate outcome measures used in binocular therapy trials, and outline modern testing methods for rapid and clinically feasible assessment of binocular and higher-level visual functions. We propose a tiered framework for outcome selection that balances mechanistic relevance with feasibility by retaining visual acuity alongside at least one quantitative measure of binocular balance or suppression and one sensitive stereopsis assessment, with additional measures included when relevant to the intervention. We also highlight the need for open-source tools, standardized protocols, and reproducible research practices to improve accessibility and cross-study comparability of different testing methods for evaluating multi-level impairments in amblyopia.

Conclusions: Advances in the understanding of amblyopia and the development of mechanism-targeted binocular therapies require a corresponding shift in how treatment outcomes are evaluated. Reliance on monocular acuity alone is insufficient to capture the broader functional deficits and recovery processes associated with amblyopia. A flexible, mechanism-driven, and clinically feasible testing strategy using a battery of tests is needed to align outcome measures with therapeutic targets and to better evaluate functional recovery across multiple domains of visual processing.

1. Introduction

Amblyopia affects 1%–5% of the population, making it one of the most common neurodevelopmental visual disorders.[1–3] It occurs when there is abnormal binocular visual experience during the early years in childhood, which is historically considered to be the first 7 years.[4] Causes of amblyopia include refractive errors (e.g., anisometropia and high bilateral refractive errors), strabismus, visual deprivation (e.g., congenital or early-onset cataract and ptosis), occlusion (i.e., a specific form of deprivation after amblyopic therapy of therapeutic patching or

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https://doi.org/10.1016/j.aopr.2026.06.003
Received 27 March 2026; Received in revised form 25 May 2026; Accepted 9 June 2026
Available online 12 June 2026
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pharmacologic cycloplegia),[5] with the first two being the most common pediatric eye conditions.[6] Amblyopia results in impaired vision—the most commonly detected and evident dysfunction is reduced visual acuity (VA)—occurring unilaterally, or rarely bilaterally. Amblyopia is diagnosed when VA impairment cannot be explained by ocular physical abnormalities, i.e., structural pathology including optic nerve or macular lesions, media opacities, and abnormalities of the central visual pathways, etc. A widely accepted diagnostic criterion of VA deficit in amblyopia is interocular best-corrected visual acuity (BCVA) difference of two or more Snellen or logMAR lines, with the better eye within the normal range (unilateral amblyopia), or BCVA in both eyes is worse by two or more Snellen or logMAR lines than the age-referenced normal VA (bilateral amblyopia).[7]

For over a century, diagnosis and treatment for amblyopia have relied on VA. However, in the past few decades, evidence from many studies indicates that the dysfunction of amblyopia is not limited to reduced VA. Emerging evidence suggests that impaired binocularity is the core deficit.[8–10] Abnormalities in interocular suppression, rather than in VA, significantly impact stereoacuity, limiting everyday visual experience in amblyopic observers.[11] For example, abnormal binocular interaction has been found in amblyopia. Amblyopia not only involves a reduction in visual input from the amblyopic eye, but the amblyopic eye also exhibits weaker suppression than the fellow eye. Furthermore, recent studies have demonstrated that amblyopia is a multifaceted visual disorder with deficits spanning low-to high-level visual processing, including neural, perceptual, oculomotor, and clinical dysfunctions, such as temporal processing, attention, eye movement, and reading.[6,12–14] These multi-level deficits do not have direct relationships with visual acuity differences or spatial deficits in the amblyopic eye.

Although the effectiveness and success rate of amblyopia treatment decline with increasing age,[15–18] treatments need to be offered in regard to children's age. The standard treatment for amblyopia includes surgical correction of visual axis occlusion causing deprivation amblyopia (e.g., cataract, ptosis, etc.), correction of refractive errors, and forced seeing by the amblyopic eye (e.g., patching, atropine, Bangerter filters, etc.).[7] An individualized treatment plan needs to be considered depending on the cause of amblyopia because a significant regression of amblyopia, occurring at a rate of 25%, has been observed following the discontinuation of patching treatment six months later.[19] On the other hand, binocular (dichoptic) therapy targeting the rebalancing of the two eyes is considered one of the most exciting and potentially powerful advancements in treatment for amblyopia in recent decades. In this type of therapy, the key point is presenting normal stimuli to the amblyopic eye and filtered stimuli, such as lower contrast, blur, low/high spatial frequency deprivation, etc., to the fellow eye. During the course of binocular therapies, if successful, the amblyopic eye learns to integrate information better and overcome the strong suppression imposed by the fellow eye over time. Although binocular therapies were considered as a promising treatment for amblyopia, and the associated software and hardware were developed to improve its efficiency,[20–23] some clinical studies have shown that binocular treatment for amblyopia is not necessarily superior to standard patching.[24] This reflects a misalignment: binocular therapies target binocular interaction mechanisms to alleviate amblyopia, yet clinical trials have primarily evaluated their efficacy with monocular outcomes.

In the past, researchers have developed many tests with psychophysics methods to accurately measure binocular functions, such as binocular balance point (e.g., binocular rivalry,[25,26] binocular combination,[27,28] etc.) and suppression (e.g., dichoptic masking,[29–31] continuous flash suppression (CFS),[32,33] etc.). Threshold can be precisely measured by different methods, such as the constant stimuli procedure and the adaptive staircase procedure. However, measuring even one single function by these methods might take 20 to 40 min, which limits their application in clinical settings. Thus, VA, which can be simply and quickly measured with a standard test, is mostly considered the primary outcome. Binocular measures are sometimes included in some clinical trials, but are assessed mainly with coarse measures. Consequently, the benefits of binocular therapies have not been properly evaluated by quantitative testing of relevant binocular visual functions but are somehow evaluated primarily by their ability to reduce interocular VA difference in clinical trials. Hence, we might be faced with a therapeutic paradox: "treating" amblyopia by chasing acuity while ignoring its root cause. Recently, new rapid, quantitative tools have been well developed, which might help to better capture the benefit in binocular visual processing during binocular therapy for amblyopia. In addition, given our advanced knowledge of amblyopia deficits throughout low-to high-level functions, if future therapies targeting these multi-level deficits are developed, we will also risk encountering this paradox where we evaluate them based on gains in monocular visual acuity in the poor eye measured rather than improvements in their targeted mechanisms. Instead, we should aim to examine amblyopia using a more holistic approach by developing and employing multiple tests.

In this review, we discuss some multilevel dysfunctions that are not limited to or explained by a large VA difference in amblyopia. We review visual function tests used in numerous clinical trials that evaluated binocular therapy and standard patching therapy in the last decade. Additionally, we provide an overview of modern visual tests that can quickly and reliably capture abnormalities. We also suggest practical solutions to make it easier for clinicians and researchers to overcome the therapeutic paradox with protocols that promote open science practices and methodological reproducibility.

2. Beyond visual acuity: multilevel deficits in amblyopia

Although amblyopia is classically characterized as a loss of spatial resolution (i.e., VA) in the amblyopic eye, numerous studies indicate that visual deficits exist that cannot be solely attributed to the VA impairment. Evidence has shown that deficits are not limited to the amblyopic eye but also exist in the fellow eye. Additionally, some deficits can be observed in treated amblyopes who have achieved normal VA after appropriate treatment. Here, we discuss key examples of these deficits in amblyopia across different levels of the visual cortex.

2.1. Contrast sensitivity function (CSF)

CSF describes visual sensitivity as a function of spatial frequency. It is similar with VA test as they both determine spatial vision, but also different as CSF is at threshold (low contrast) level while VA test is at suprathreshold (high contrast) level. It is believed that CSF, which can assess spatial resolution across a wide range of contrast and spatial frequency levels, characterizes spatial deficits better than letter acuity in amblyopia.[34,35] Contrary to the general idea, not only the amblyopic eye, but also the "normal" fellow eye showed abnormal CSF.[36] Reduced contrast sensitivity was observed in the fellow eye over low-to high--spatial frequencies.[36] In addition, remained deficient in CSF was found in the amblyopic eye in treated amblyopia while their VA already reached normal range after occlusion therapy.[37] More reduction was found in contrast sensitivity at higher spatial frequencies.[37] Although VA and CSF are both considered to describe monocular visual functions and VA tests are thought to exam the cutoff spatial frequency, the functional deficits of amblyopia at threshold level rather than suprathreshold level might induce the visual function difference assessed by VA and CSF tests.

2.2. Binocular balance and interocular suppression

Recent investigations demonstrate that amblyopic observers exhibit a severe degree of binocular imbalance[27,28,38–43] and that this cannot be corrected even if the contrast level of the stimulus shown to the amblyopic eye matches its poor contrast sensitivity.[28] This imbalance was also observed in treated amblyopes who responded robustly to standard patching therapy, achieving minimal VA difference between

the two eyes.[44,45] Studies have demonstrated that interocular suppression might play an important role in binocular interactions.[43,46] The disruption of the inhibitory interactions between the two eyes, which is the imbalance of the strength of interocular suppression, causes the balance point to be abnormally biased to the fellow eye. The suppression induced by the fellow eye (suppression of the amblyopic eye) was found to be within the normal range but much stronger than the suppression induced by the amblyopic eye (suppression of the fellow eye).[29–32,47] Binocular balance is critical for maintaining stereopsis,[48] which is important in everyday visual experience with both eyes open.[9] This deficit in binocular balance (interocular suppression) reinforces the notion that standard patching therapy, which mainly targets improving VA of the poor eye, does not resolve other associated deficits of amblyopia.

2.3. Delay and temporal synchrony in temporal processing

Amblyopia exhibits dysfunction in temporal processing, which refers to how the human cortex perceives and processes visual information over time and is critical for the perception of moving objects in daily life. Amblyopes experience interocular processing delays due to differences in visual processing speed between the two eyes. This delay has also been observed both in neuroimaging studies[49,50] and psychophysical studies.[14,51] Contrary to the conventional belief that the amblyopic eye with poorer spatial resolution[52] would be the slower eye compared with the fellow eye, studies show that not only the amblyopic eye but also the fellow eye can be the delayed eye with slower information processing speed.[14,51] Such interocular delay did not show any correlation with amblyopes' interocular velocity differences or other clinical characteristics. Additionally, amblyopes exhibit poor visual abilities in temporal asynchrony detection, which is the ability to group multiple elements together based on their common temporal characteristics,[53,54] and temporal asynchrony discrimination, which is to distinguish between multiple element groups.[55] Such reduced detection and discrimination ability was found when amblyopes viewed with their monocularly amblyopic eye and dichoptically. It is still observed that even with stimuli are shown at high contrast levels,[54,56] the dichoptic deficits still exist among treated amblyopes, even when the monocular deficit is resolved.[57]

2.4. Saccadic and fixation stability in eye movement

Eye movement abnormalities have been reported in amblyopia. Amblyopes show increased saccadic latency, which indicates slower or delayed saccades, when fixating with their poor eye relative to controls or their fellow eye.[58] Although interocular differences in VA and saccadic latency are correlated[59] Gambacorta et al.[60] observed that increased saccadic latency was found to be still significant in strabismic amblyopia even when the contrast levels of the stimuli were matched between eyes. The binocular advantage, which means a more accurate, precise, and faster response during binocular viewing than monocular viewing,[61] was barely significant in the saccade of amblyopia. Reduced fixation stability, which refers to less precise or less stable fixation, was observed under monocularly amblyopic eye viewing, monocularly fellow eye viewing, and binocular viewing conditions.[62–66] Even though VA/BCVA is within the normal range in the fellow eye in amblyopia, the fellow eye still shows fixational instability more so than normal adults.[64,65] Recently, a causal relationship from abnormal eye movement to impaired acuity was found by Levi and Chung.[67] Blurring the image in one eye of normal observers does not reproduce eye movement abnormalities that are typically observed in amblyopia,[68,69] while acuity is reduced when random jittering is introduced on a visual target to stimulate fixation instability.[70] In addition, amblyopic eye's fixation instability might misplace a visual target on parafoveal areas, thereby degrading acuity further.[71,72] Thus, as fixational stability affects perception but not vice versa, this relationship between fixational instability and acuity seems causal and unidirectional.

2.5. Attention

Amblyopia is associated with deficits in visual attention, particularly in tasks requiring high attentional load.[73] Eye movements are strongly associated with attention,[74] and the same cortical structures in frontal, parietal, and extrastriate cortex are involved in eye movement and attention control.[75–78] Thus, the abnormal eye movements in amblyopia are also considered to be attentional deficits.[79] Additionally, amblyopes show poor performance in visual attention tasks that require higher-order visual processing and executive functions even when the tasks are completed under binocular viewing conditions.[12] Attention was biased in favor of the fellow eye in strabismic and mixed amblyopes during a behavioral attention tracking task,[13] while it was equally distributed between two eyes in normal observers. This was not attributed to poor spatial resolution of the poor eye as interocular contrast balancing between eyes was conducted to eliminate effects of abnormal interocular suppression (reduced VA). Furthermore, even under the binocular viewing conditions, amblyopes still showed poorer tracking accuracy compared to controls.

2.6. Reading

Slow reading has been observed in amblyopic children and adults compared with their age-matched controls.[80–86] Although strabismic amblyopes read more slowly than anisometropic amblyopes, slow reading does not seem to be due to strabismus. Reading speed has been found to be slower in different types of amblyopia under monocular amblyopic eye, monocular fellow eye, and binocular viewing conditions. Amblyopia affects reading ability, which might be related to amblyopes' ocular motor impairments rather than monocular or binocular visual deficits. Amblyopes' reading performance is not related to the VA of the amblyopic eye. Eye movements might play a key role in reading. Saccade is needed for the eyes to move forward and regress backward between words and through lines of text,[87] and fixation is needed for understanding the context.[88] Slower reading speed in amblyopia is related to increased numbers of forward saccades and reduced fixation stability.[6,88,89] In addition, children who were successfully treated for amblyopia or strabismus remain with persistent impaired reading performance.[82,90] Slow reading can impact academic performance in school[91,92] and other daily activities throughout the lifetime.[6]

3. Monocular and binocular outcome measures in amblyopia treatment trials

Amblyopia is increasingly recognized as a disorder involving deficits that extend far beyond the traditional hallmark of reduced VA in the affected eye. As outlined in the preceding section, individuals with amblyopia exhibit a range of impairments across multiple levels of visual processing, including abnormalities in contrast sensitivity, binocular balance and interocular suppression, temporal processing, eye movement control, attention, and reading. These deficits are often present in both the amblyopic and fellow eyes, and can persist even after successful acuity-restoring treatments, indicating that they are not merely secondary consequences of poor spatial vision. In recent decades, binocular treatments—such as dichoptic therapies that aim to rebalance interocular suppression—have been developed to address these broader deficits. However, despite their theoretical rationale, clinical trials comparing binocular therapies with occlusion or spectacles have not consistently demonstrated superior outcomes. Notably, we observed that even in studies of binocular therapy, treatment efficacy continues to be evaluated primarily through monocular visual acuity, rather than through comprehensive assessment of binocular or higher-level visual functions. This disconnect between treatment goals and outcome measures prompted us to review the tests used in recent clinical trials comparing binocular and patching therapies.

Studies have questioned the primary acuity-based endpoint[8] based

on the growing understanding of amblyopes' suppression deficits. However, as listed in the table, we noticed that the evaluation of binocular therapy still primarily relies on improvements in monocular spatial vision. Monocular visual function was assessed by VA test, and three studies also examined CSF. Some studies only compared VA or BCVA for assessing visual function improvements produced by amblyopia treatments.[96,100,102,106,117]

Stereoacuity was considered to be one of the most important binocular functions. However, it should be noted that stereoacuity was mostly assessed by clinical tests, including the Randot Stereoacuity Test (14 out of 19 studies[93–95,97–99,104,105,107,108,110,112,113,115]), Stereo Butterfly Test (7 out of 19 studies[94,95,98,99,104,105,113]), Titmus Stereoacuity Test (3 out of 19 studies[101,109,116]), TNO Test (3 out of 19 studies[103,108,111]), Fly Stereoacuity Test (1 out of 19 studies[110]), Frisby stereo-test (1 out of 19 studies[114]) and Osterberg test (1 out of 19 studies[103]), rather than laboratory tests. These tests are commonly used for measuring stereoacuity in ophthalmic practice and have different levels of disparity ranging from 1.3 to 3.56 log arcseconds (corresponding to 20-3600 arcsec). On the other hand, the improvements in stereoacuity after treatment are only approximately 0.2-0.4 log arcseconds in the studies of Wygnanski-Jaffe et al.[115] and Yao et al.[101] When compared with the disparity levels of the stereoacuity test (e.g., 2.9, 2.6, 2.3, 2, 1.8 log arcseconds), this value would be rarely detectable when participants who exhibit poor stereopsis or are stereoblind. This might also be the reason that stereoacuity improvements were mostly observed in participants with measurable stereoacuity at baseline.[110]

Birch et al.,[118] also demonstrated that binocular outcomes following amblyopia binocular therapy are sparse, even though one of the most important rationales for this therapy is the promotion of binocular function recovery. The assessment of binocular function was mostly focused on stereoacuity. Among studies that we reviewed in Table 1, in addition to some studies that used in-training parameters (e.g., interocular contrast/luminance during dichoptic game) to investigate interocular suppression,[97] only six studies measured suppression before and after the treatment.[95,101,103,104,113,114] Although in recent years, many tests were developed for measuring interocular suppression[119] — for example, a binocular combination test, a binocular rivalry test, and a dichoptic masking test — such tests were barely used in studies based on clinical trials or with a large sample size. This might be because these tests are more difficult to complete due to longer testing duration or are harder to understand, especially in children, when compared with clinic tests. Results from the study by Dahlmann-Noor et al.[114] also suggested that only 38% (5 out of 13) of subjects whose stereoacuity could be measured by clinical stereoacuity test could complete a random-pixel stereo-test.

Moreover, as we mentioned above, amblyopes' disorders spread across multiple levels of the cortex, and high-level dysfunctions play a key role in daily life. Evidence has shown that higher-level function could also be improved after amblyopia treatment. Webber et al.[120] found that fine motor skills of amblyopic children could be improved after binocular treatment provided by home-based dichoptic iPod game play. Shah et al.[121] showed that both eye-hand coordination performance and visual functions, including monocular and binocular functions, could be improved by eye-hand coordination training based on perceptual learning theory. However, there is a lack of knowledge regarding higher-level function recovery by different amblyopia therapies. Study by Vedamurthy et al.,[93] was the only study that involved high-level abnormality when comparing treatment efficacy between binocular treatment and standard therapies (Table 1). Consequently, such benefits across different levels of behavioral functions could only be observed when the functions are properly examined.

In summary, this section highlights a persistent over-reliance on monocular VA as the primary outcome measure in amblyopia treatment studies, despite a shift toward addressing binocular deficits using novel treatment methods. The assessment of binocular function itself remains largely confined to clinical stereoacuity tests, which may lack the sensitivity to detect subtle but meaningful improvements. Furthermore, the field has yet to systematically incorporate evaluations of higher-level visual functions, such as eye-hand coordination, leaving a significant gap in our understanding of how different therapies impact real-world visual abilities beyond monocular acuity gain of the weak eye.

4. Modern testing methods for measuring visual disorders in amblyopia

With modern display technology, it has become possible to apply automated algorithms to reduce testing times (e.g., adaptive staircase procedures) and implement these tests on affordable and portable devices (Fig. 1). With modern software packages, it has now also become possible for users with no coding background to construct visual tests that were otherwise not possible without programming skills. For these reasons, we believe that it is both relevant and timely to provide a brief overview of visual tests that could effectively inform about the status of monocular or binocular dysfunctions in amblyopia, which we believe could also be implemented in clinical settings.

4.1. Contrast sensitivity function (CSF)

Measuring the full CSF is complicated as it requires multiple levels of contrast and spatial frequency. To make the measurement both precise and flexible, Lesmes et al.,[122] first applied Bayesian adaptive estimation in CSF and developed a quick CSF (qCSF) method. qCSF used a truncated log-parabola with four parameters, which are the peak gain, the peak spatial frequency, the bandwidth, and the truncation level at low spatial frequency, to estimate thresholds across the full spatial-frequency range. By estimating the CSF parameters via Bayesian rule, a full CSF curve can be efficiently measured with 50 trials (within 5 to 10 min), and its precision matched that achieved with 300 trials.[123] Hou et al.,[124] further developed the qCSF method with 10-alternative forced choice, rather than the original 2-interval forced choice, to improve measurement efficiency. Subjects were asked to indicate the letter they saw from 10 filtered letters. A 10-digit version of the qCSF test was also developed for non-English speaking populations.[125] These methods were shown to be sufficiently rapid, accurate, and precise in both normal and amblyopic observers,[123] and were very sensitive to the CSF changes.[126]

4.2. Stereoacuity

With the technique of dichoptic display combined with pixel disparity, it is possible to assess human stereoacuity using a fine, continuous index rather than a discrete index. Reynaud et al.[127] developed a quick Disparity Sensitivity Function (qDSF) task based on a Bayesian method to measure stereopsis across spatial frequency. Stimuli were 2-D fractal noise stereograms with disparity between eyes. The subjects were asked to indicate the orientation of the disparity corrugation. This task can measure the threshold for detecting disparity in the form of sinusoidal corrugations. It has been validated as reliable and robust, often requiring less than 10 min to obtain a complete measure of disparity sensitivity across a wide range of spatial frequencies (0.94–9.57 cycles per degree). Although the simplicity of the task makes it suitable for use with large samples, particularly in clinical settings, it still requires specific set of laboratory equipment including passive polarized glasses and 3D monitor.

Hess et al.[128] introduced a novel Random Dot Stereo Test using a handheld device (iPod) and a psychophysical testing procedure. The stimuli consisted of two closely positioned disks formed from random red and green dots on a dark background. The edges of the disks were blurred using a Gaussian window. The dots forming the disks were randomly positioned. To elicit depth perception from these disks, the dots had positional offsets, such that one of the two discs was perceived as in front of the plane while the other disc was seen as behind the plane. Disparity was measured by instructing the subject to indicate which disk

Table 1
Studies of evaluation of comparison between binocular treatment and standard therapy for amblyopia.

Study	Participants	Treatment	Assessments
Vedamurthy et al., 2015[93]	38 adults aged 19–66 years	*Game group* (n = 23): playing dichoptic action game for 40 h in total (1.5–2 h/session, 2–5 times/week) *Movie group* (n = 15): watching movie with monocular patching for 40 h in total (1.5–2 h/session, 2–5 times/week)	1. **VA:** Bailey–Lovie logMAR letter charts, or high-contrast ETDRS format chart with Sloan optotypes 2. **Stereoacuity:** Randot Stereotest 3. **Contrast sensitivity function:** quick Contrast Sensitivity Function (qCSF) with Bayesian adaptive procedure 4. **Reading speed:** standardized MN Read Acuity Chart 5. **Self-report of amblyopia state:** Amblyopia Strabismus Questionnaire Evaluation (ASQE)
Holmes et al., 2016[94]	385 children aged 5–13 years	*Binocular group* (n = 190): binocular iPad game 1 h/day *Patching group* (n = 195): patching of the fellow eye 2 h/day	1. **BCVA:** ATS-HOTV protocol (5–7 years), E-ETDRS (7–13 years) 2. **Stereoacuity:** Randot Butterfly, Randot Preschool stereoacuity test 4. **Ocular alignment:** simultaneous prism and cover test, prism and alternate cover test 4. **Adherence:** calendar report (both group), data from device (binocular group) 5. **Adverse events:** self-report
Kelly et al., 2016[95]	28 children aged 4–10 years	*Binocular group* (n = 14): binocular iPad game 1 h/day, 5 day/week *Patching group* (n = 14): patching of the fellow eye 2 h/day, 7 days/week	1. **BCVA:** ATS-HOTV protocol (5–7 years), E-ETDRS (7–13 years) 2. **Stereoacuity:** Randot Butterfly, Randot Preschool stereoacuity test 3. **Extend of suppression:** Worth 4-dot test at 7 different distances 4. **Depth of suppression:** dichoptic motion coherence test (<7 years), dichoptic contrast eye chart (≥7 years) 5. **Adherence:** calendar report
Rajavi et al., 2016[96]	50 children aged 3–10 years	*Case group* (n = 25): Interactive Binocular Treatment (I-BiT™) together with patching *Control group* (n = 25): patching alone	1. **BCVA:** the Snellen E-chart
Gambacorta et al., 2018[97]	21 children aged 3–8 years	*Dichoptic training group* (n = 10): playing game dichoptically with reduced contrast to FE for 1 h/time, 1–3 times/week (20 h in total) *Monocular training group* (n = 11): playing game with FE patched for 1 h/time, 1–3 times/week (20 h in total)	1. **BCVA (monocular and binocular):** Bailey-Lovie log-MAR letter charts, or high-contrast ETDRS format chart with Sloan optotypes 2. **Stereoacuity:** Randot Stereotest 3. **Reading speed (monocular and binocular):** standardized MNREAD Acuity Chart 5. **Interocular suppression:** in-game alignment of reducing the luminance and contrast level of the FE's image when sessions began 4. **Compliance:** drop-out rate
Manh et al., 2018[98]	100 teenagers aged 13–17 years	*Binocular group* (n = 40): dichoptic falling block games for 1 h/day for 16 weeks *Patching group* (n = 60): patching for 2 h/day for 16 weeks	1. **BCVA:** E-ETDRS protocol 2. **Stereoacuity:** Randot Butterfly test, Randot Preschool stereoacuity test 3. **Diplopia (presence and frequency):** standardized questionnaire (parent-reported) 4. **Adherence:** log calendars (both groups), objectively recorded data by the iPad (binocular group)
Holmes et al., 2019[99]	138 participants aged 7–13 years	*Binocular treatment group* (n = 69): Dig rush dichoptic game on iPad with spectacles wearing (if needed) for 1 h/day, 5 days/week for 8 weeks *Control treatment group* (n = 69): spectacles only (if needed)	1. **BCVA:** E-ETDRS protocol 2. **Stereoacuity:** Randot Butterfly test, Randot Preschool stereoacuity test 3. **Ocular alignment:** simultaneous prism and cover test, prism and alternate cover test 4. **Diplopia (presence and frequency):** parent-reported questionnaire 5. **Adherence:** the log calendars (both group), objectively recorded adherence data from the iPad device (binocular group only)
Birch et al., 2020[100]	15 children aged 4–13 years	*Current treatment group* (n = 8): optical correction, single vision glasses or bifocals, and occlusion therapy. *Binocular group* (n = 7): current treatment add contrast-rebalanced binocular iPad game (Dig Rush) play for 5 h/week for 4 weeks.	1. **BCVA:** E-ETDRS protocol (≥7 years), ATS-HOTV protocol (<7 years)
Yao et al., 2020[101]	103 children aged 3–13 years	*Binocular group* (n = 36): playing binocular game with improved push–pull model personalization training system and polarized anaglyphic glasses for 20 min/session, 2 sessions/day for 3 months *Patching group* (n = 38): 2–6 h/day of patching depending on the severity of amblyopia for 3 months *Combined group* (n = 29): both binocular game and patching of FE for 3 months	1. **BCVA:** Tumbling E ETDRS 2. **Stereoacuity:** Titmus stereoacuity test, fine stereoacuity and dynamic stereoacuity measured by the improved push-pull model personalization training system 3. **Interocular suppression:** contrast ratio, signal to noise ratio measured by the improved push– pull model personalization training system 4. **Ocular alignment:** prism and alternate cover test
Handa et al., 2022[102]	40 patients aged 3–12 years	*Occlu-tab group* (n = 20): playing eye-hand coordination training games using Occlu-tab with invisible tablet terminals only in AE and a binocular open view for 1 h/day, 3 days/week for 8 weeks	1. **BCVA:** Snellen chart

(*continued on next page*)

Table 1 (*continued*)

Study	Participants	Treatment	Assessments
		Eye patch group (n = 20): conventional eye patch for 1 h/day, 3 days/week for 8 weeks	
KalnicaDorosenko et al., 2021[103]	22 participants aged 7–18 years	*Dichoptic game group* (n = 11): playing specialized dichoptic computer game for 25 min/day *Occlusion group* (n = 11): occlusion of FE for 2–4 h/day	1. **BCVA (near and distance):** VA test with open lines of optotypes 2. **Suppression:** Bagolini striated glasses test 3. **Stereovision:** TNO test (near), Osterberg test (distance) 4. **Strabismus angle:** Hirschberg test, cover-uncover test, alternate cover test, prism alternate cover test
Jost et al., 2022[104]	65 children aged 3–7 years	*Binocular treatment group* (n = 32): contrast-rebalanced dichoptic movies for 3 movies/week for 2 weeks at least (optional to 6 weeks). *Patching group* (n = 33): patching for 2 h/day, 14 h/week, for 2 weeks.	1. **BCVA:** Allen Pictures (very young children), ATS-HOTV protocol (aged 3–6 years), E-ETDRS (aged 7 years) 2. **Stereoacuity:** Randot Preschool Stereoacuity Test, Stereo Butterfly Test 3. **Extemd of suppression:** Area of suppression scotoma converted from Worth-4-dot test at different distances 4. **Depth of suppression:** balance point calculated by contrast based on dichoptic eye chart
Manny et al., 2022[105]	182 children aged 4–7 years	*Binocular group* (n = 92): binocular iPAD game (Dig Rush) with spectacles (if wore) for 1 h/day, 5 days/week, for 8 weeks *Spectacles group* (n = 90): spectacle correction alone	1. **Distance VA:** ATS-HOTV protocol 2. **Stereoacuity:** Randot Butterfly test, Randot Preschool stereoacuity test 3. **Ocular alignment (distance and near):** simultaneous prism and cover test, prism and alternate cover test 4. **Diplopia:** parent-reported questionnaire 5. **Adherence:** parent-reported (both group), logged data by iPad (binocular group)
Iwata et al., 2022[106]	58 children aged 3–8 years	*Polarizing film group* (n = 24): dichoptically perform activities (watch TV, use tablet terminals and smartphones, and read books) with a polarizing film for 2 h/day for 2 months *Eye patch group* (n = 34): perform activities with eye patch for 2 h/day for 2 months	1. **BCVA** 2. **Compliance rate**
Wygnanski-Jaffe et al., 2023[107]	103 children aged 4–9 years	*CureSight group* (n = 51): dichoptic video watching with the CureSight that based on eye-tracking-based dichoptically real-time blur around fovea for 5 days/week for 16 weeks *Patching group* (n = 52): patching for 2 h/day, 7 days/week for 16 weeks	1. **Distance VA (monocular and binocular):** E-ETDRS protocol with Lea numbers optotype (>7 years), HOTV protocol with Lea symbols optotype (<7 years) 2. **Stereoacuity (near):** Randot Preschool Stereoacuity test 3. **Ocular alignment (distance and near):** simultaneous prism and cover test, prism and alternate cover test 4. **Diplopia, headaches, and eye strain:** a protocol-defined questionnaire (parent-reported) 5. **Adherence:** screen gaze data recorded by eye-tracker (CureSight group), the guardians' manual self-reported logs (patching group)
Roy et al., 2023[108]	55 children aged 5–15 years	*Video game group* (n = 27): playing dichoptic game with adjusted contrast for 2 h/day, 7 days/week, for 3 months *Patching group* (n = 28): occlusion of FE for 6 h/day, 7 days/week, for 3 months	1. **BCVA:** ETDRS (distance) 2. **Contrast sensitivity:** Pelli-Robson chart 3. **Stereoacuity:** near Randot stereo test and TNO test (near), distance Randot stereo test (distance) 4. **Compliance:** self-reported 5. **Transient side effects (headache, watering, blurring of vision, and eye pain):** self-reported
W. Zhu et al., 2023[109]	34 children aged 4–9 years	*Full treatment group* (n = 12): video watching via CureSight system that based on eye-tracking-based dichoptically real-time blur around fovea for 90 min/day, 5 days/week for 12 weeks *Part-time treatment group* (n = 8): video watching via CureSight system for 90 min/day, 3 days/week for 12 weeks *Patching treatment group* (n = 14): patching of FE for 2 h/day, 7 days/week for 12 weeks	1. **BCVA (distance and near):** E-ETDRS, Bailey-Lovie Word Reading Chart (near) 2. **Stereoacuity:** Titmus stereoacuity test
Q. Zhu et al., 2023[110]	32 children aged 5–12 years	*Combined group* (n = 21): watching 3D movie for 30 h in total (1–1.5 h/session, at least 3 session/week) with Bangerter filter on FE to reduced VA (0.2 logMAR worse than AE), together with patching for 2–6 h/day depending on amblyopia severity for 6 weeks *Patching group* (n = 14): patching alone for 2–6 h/day depending on amblyopia severity for 6 weeks	1. **BCVA:** Tumbling E ETDRS 2. **Binocular function score:** Results of Randot Preschool Stereoacuity Test and Worth-4-dot test were combined 3. **Stereoacuity:** Fly Stereoacuity Test with LEA Symbols (near), a method of evaluating stereoacuity with 3D shutter glasses technology (distance) 4. **Adherence:** time and content of binocular treatment recorded in electronic form, personalized calendar by legal guardians
Meqdad et al., 2024[111]	86 subjects (68 children and 18 adults) with median age of 13.31 years	*VR group* (n = 44): dichoptic anti-suppression amblyopia Virtual Reality training by the Diplopia Game included in Vivid Vision software for 2 h/week for 10 weeks *Patching group* (n = 42): daily patching for 2 continuous hours/day for 10weeks	**1. BCVA:** single crowded letter on an ETDRS chart via a computer display projector 2. **Near stereoacuity:** TNO test 3. **Adherence:** the percentage of the actual received therapy dose to the total prescribed dose
Kadhum et al., 2024[112]	33 children aged 4–12 years	*Gaming group* (n = 16): dichoptic action video game with contrast rebalancing using the Oculus Rift VR goggles for 1 h/week for 24 weeks *Occlusion group* (n = 17): electronically monitored	1. **BCVA:** crowded tumbling E chart 2. **Stereo acuity (near):** circles Randot Stereotest 3. **Contrast sensitivity:** Pelli-Robson chart (older subjects), CSV-1000 (younger children)

(*continued on next page*)

Table 1 (*continued*)

Study	Participants	Treatment	Assessments
		occlusion using the Occlusion Dose Monitor for 2 h/day, 1 week/6 weeks, for 24 weeks	4. **Ocular motility and alignment (near and distance):** cover-uncover and alternating cover test 5. **Treatment efficiency:** (VA gain (logMAR)×100h)/ cumulated measured treatment hours
Jost et al., 2024[113]	34 children aged 3–5 years	*Dichoptic cartoons group* (n = 17): watching contrast-rebalanced dichoptic cartoons for 4 h/week for 2 weeks *Patching group* (n = 17): patching FE with eye patches for 2 h/day, 7 days/week, for 2 weeks	1. **BCVA:** ATS-HOTV protocol 2. **Stereoacuity:** Randot Preschool Stereoacuity Test and Stereo Butterfly Test 3. **Extend of suppression:** Worth 4-dot test at 7 different distances 4. **Severity of suppression:** contrast balance index measured by dichoptic eye chart 5. **Manual dexterity:** Movement Assessment Battery for Children, 2nd Edition 6. **Adherence:** system streaming logs (dichoptic cartoons group) and parental report (both groups)
Dahlmann-Noor et al., 2024[114]	32 children aged 3–8 years	*BBV group*: dichoptic balanced binocular viewing of movies with customized to interocular acuity difference at baseline for 1 h/day *Control group*: standard occlusion for 2–6 h/day for or atropine 1% eyedrops for pharmacological blurring	1. **Interocular balance/suppression:** VacMan suppression test to measure interocular contrast ratio at balance point, Sbisa suppression 2. **BCVA:** HOTV judgements 3. **Stereoacuity:** Frisby stereotest, VacMan random-pixel stereoacuity test 4. **Adherence:** device 'usage' function (BBV group), occlusion dose monitor (occlusion), digital photographs of the child's eyes (atropine)
Wygnanski-Jaffe et al., 2025[115]	149 children aged 4–9 years	*Binocular treatment group* (n = 75): watching dichoptic video with the CureSight that based on eye-tracking-based dichoptically real-time blur around fovea for 90 min/day, 5 days/week, for 16 weeks (120 h in total) *Patching group* (n = 74): wearing an adhesive patch over FE for 2 h/day, 7 days/week, for 16 weeks (224 h in total)	1. **VA (distance and binocular):** E-ETDRS protocol (aged ≥7 years), HOTV protocol (aged 4-7 years) 2. **Stereoacuity (near):** Randot Preschool Stereoacuity test 3. **Adherence:** treatment logs of screen gaze (binocular treatment group), guardians' manual self-reported logs (patching group) 4. **Ocular alignment:** simultaneous prism and cover test, prism and alternate cover test 5. **Treatment satisfaction:** questionnaire 6. **Adverse Events Related to the Study Intervention:** questionnaire
Chen et al., 2025[116]	42 children aged 4–8 years	*Gamified binocular therapy group* (n = 20): playing dichoptic game via The Vision Planet Training System for 30 min/ session, 2 sessions/day, 7 days/week, for 6 months *Patching group* (n = 22): patching of FE for 90 min/session, 1 sessions/day, 7 days/week, for 6 months	1. **Distance BCVA:** Lea symbols chart 2. **Stereoacuity:** Titmus stereo test 3. **Adherence:** automatically recorded session duration, frequency, and completion status via backend system (binocular therapy group), self-reported caregiver logs (patching group), questionnaire
Huang et al., 2025[117]	60 children aged 4–8 years	*CAM training group* (n = 30): dichoptic Cambridge Visual Stimulator training based on the theory of perceptual learning for 15–30 min/session, 1 session/week for 24 weeks or BCVA ≥20/25 *VR training group* (n = 14): Virtual Reality-assisted dichoptic visual training based on a computer game Diplopia Game for 5–20 min/game, 2 games/session, 1 session/week for 24 weeks or BCVA ≥20/25 *Control group* (n = 26): glasses wearing only for 24 weeks or BCVA ≥20/25	1. **BCVA:** Landolt C chart

ATS-HOTV: Amblyopia Treatment Study; E-ETDRS: Electronic Early Treatment Diabetic Retinopathy Study; ETDRS: Early Treatment Diabetic Retinopathy Study; AE: amblyopic eye; FE: fellow eye.

they perceived as behind the screen plane. Equipped with a staircase adaptive procedure, each test took approximately 3 min (40 to 60 trials), with reliable results. Interestingly, the authors observed that when using a random-dot stimulus shown on a tablet, 30% of the supposedly normal population displayed abnormal stereovision. This observation was unexpected, as the traditional Randot test typically shows a very narrow distribution of stereo-sensitivity in normal populations. This discrepancy indicates that the fine resolution of a task designed for measuring its target visual function can uncover subtle but significant deficits in binocular vision even in visually intact populations.

Baldwin et al.[129] developed a Disparity Detection and Discrimination Task on handheld digital tablet devices. The stimuli consisted of isotropic log-Gabor dots in the background, where a quarter of the screen formed a wedge either in front of or behind the screen's plane. The unique feature of this task is that it uses the same stimulus parameters to test detection and discrimination, allowing investigation of the two processes using spatially matched stimuli. Essentially, subjects were required to report the location where they perceived a wedge-shaped floating in depth (detection) or to indicate which of two wedge shapes was floating in front of the screen (discrimination). This setting can eliminate monocular and binocular cues that might allow a stereo-blind subject to perform the tasks and also ensures the tasks are easily understood. The authors observed that although 98% of their subject pool (228 participants) were able to reliably detect depth cues, only 69% of them were able to discriminate different degrees of depth. This suggests that discrimination of depth involves a further downstream visual pathway than depth detection, highlighting the need for more sophisticated visual tests to be used for measuring depth perception in clinical settings.

4.3. Binocular balance/interocular suppression

Kwon et al.[40] developed a novel computer-based and binocular rivalry based method (Dichoptic Letter Chart) where each eye was shown

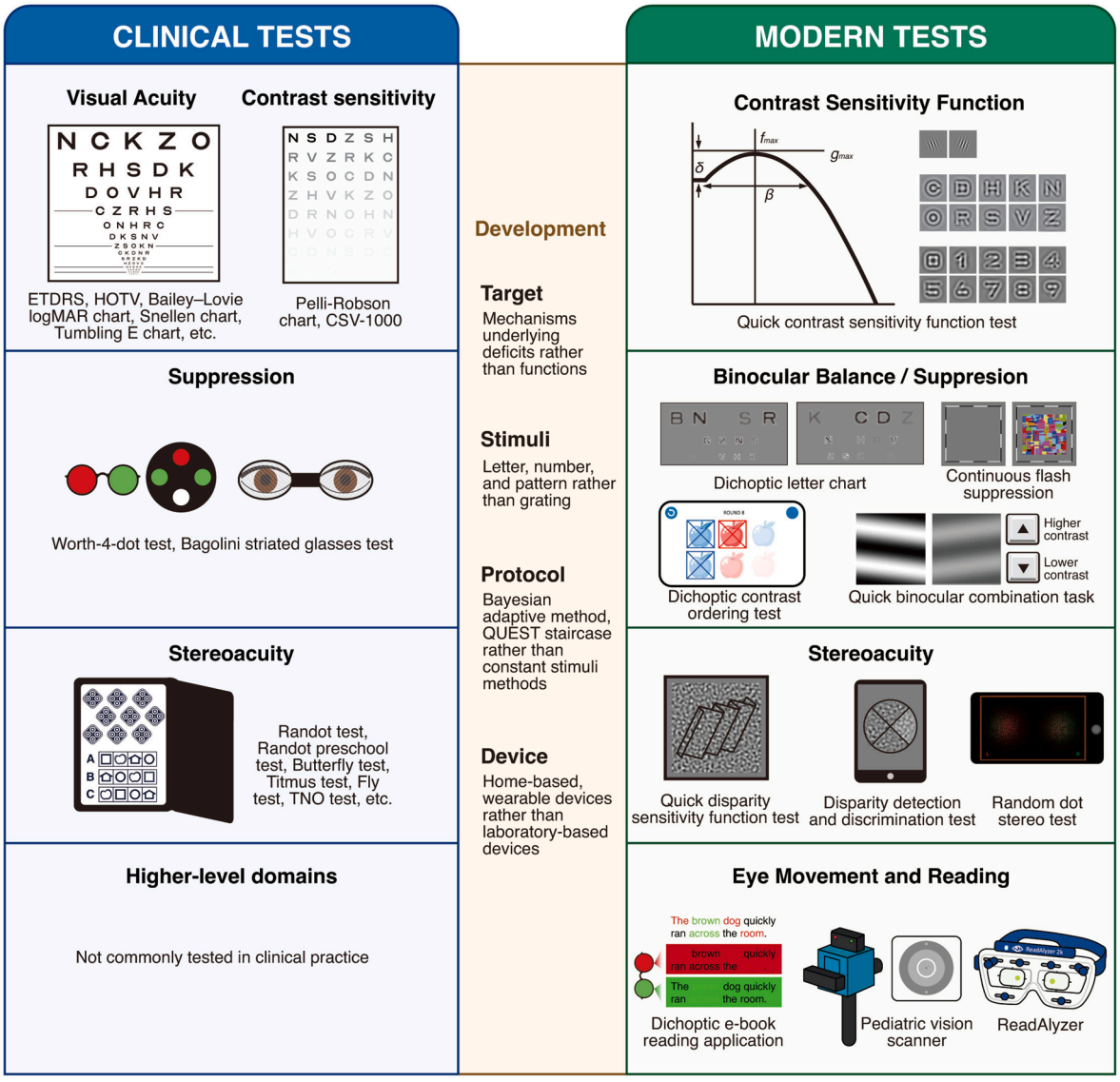


Fig. 1. Summary of some of widely used clinical and modern tests to measure different levels of visual functions in amblyopia.

with a unique letter chart of band-pass filtered Sloan letters arranged in a layout similar to that of the Early Treatment Diabetic Retinopathy Study (ETDRS) acuity chart on a grey background. Its similarity to the ETDRS acuity chart can make it accessible for both experimenters and tested individuals without the need for them to take additional time to learn the visual test. Dichoptic presentation of the two unique letter charts was made possible with stereo-shutter glasses. At each position of the chart, the letter's identity and contrast level differed, and participants were asked to read aloud the perceived letter. The aim of this test was to measure the point of contrast levels at which the stimulus visibility of both eyes was the same. Since the two eye's stimuli were different, at this point of equilibrium, observers were expected to perceive binocular rivalry, during which each eye's stimulus competed for perceptual dominance. This test yields reliable results of binocular balance across various levels of spatial frequency.[40] This is the most used test for interocular suppression in the studies we reviewed in Table 1 (3 out of 6 studies) although the authors did not specify the tested spatial frequency.[95,104,113]

Binocular fusion is a process by which the two eyes integrate visual information into a coherent, combined image. The differences in the two images are perceptually removed by suppression, whereas their similarities are preserved by fusion. To measure binocular balance through the process of perceptual combination between the two eyes and to ensure the task can be quickly finished, Min et al.,[130] developed a quick Binocular Orientation Task by applying the adjustment method. In their orientation task, observers were instructed to directly adjust the visibility of one eye's stimulus using the keyboard until both eyes' stimuli were fused into a flat grating. The task was found to be reliably repeatable from 0.5 to 4 cycles per degree in both normal and amblyopic observers. Each measurement at one spatial frequency would take about 3 min, which allows multiple spatial frequencies to be tested in clinical settings, as amblyopes showed various degrees of binocular imbalance across different spatial frequencies.[28,40] Despite the authors' success in developing a protocol that is quick and reliable, this method would still require elaborate equipment setup, including a computer, head-mount goggles, and possibly the purchase of proprietary programming software (Matlab) to run the experiment.

Baldwin et al.[131] introduced the Dichoptic Contrast Ordering Test as a clinically convenient tool to measure binocular balance in normal and visually impaired observers. Subjects were asked to wear red/green anaglyph glasses and view the screen so that different stimuli were shown dichoptically. Subjects were asked to rank images in order based on their visibility (from most to least visible). Based on the information from each trial, the test dynamically estimated a single scaling factor that minimized

differences in stimulus visibility between the two eyes. One measurement session would take about 2–3 min. Although there were some systematic differences in the results obtained from those of the dichoptic letter chart, this could be due to the fact these tests target different mechanisms of binocular imbalance. Nevertheless, the results were found to be strongly correlated between the two tests in both normal[131] and amblyopic observers.[132] Importantly, the imbalance obtained from the Dichoptic Contrast Ordering Test in amblyopes was found to be strongly related to their stereopsis and VA,[132] demonstrating that the tool could be used in clinical settings to monitor the state of amblyopia.

In continuous flash suppression, rapidly changing high-contrast Mondrian texture masks are presented to one eye while a target stimulus is presented to the other eye, rendering the target temporarily invisible through interocular suppression. CFS paradigms are commonly used to quantify interocular suppression by measuring elevations in the contrast detection thresholds of a probe target presented to one eye while dynamic masks are shown to the fellow eye. To facilitate the creation of CFS stimuli, Wang et al.[133] developed CFS-crafter, an open-source point-and-click platform that allows users to generate, modify, and analyze tightly controlled CFS stimuli without requiring expertise in image processing or programming. Using the same CFS framework, Zhao et al.[134] developed the Chameleon paradigm, which maintained color consistency between target and masking stimuli through alpha blending principles to enhance stimulus integration and masking effectiveness, and the authors made the code openly available to encourage broader adoption. Although these CFS-based methods have not yet been systematically tested in amblyopic populations, they show considerable promise because laboratory-based CFS tasks have been shown to effectively characterize the imbalanced interocular suppression associated with amblyopia.[32,47]

4.4. Eye movement and reading

The Pediatric Vision Scanner (PVS), which determines ocular alignment through binocular retinal birefringence scanning, provides an objective measure of simultaneous foveal fixation in both eyes. During a 2.5-second scan at 40 cm, the device generates a binocularity score (BIN; 0%–100%) based on the proportion of bilateral fixation events. In a clinical validation study,[135] using a pass/refer cutoff of 60% BIN, the PVS achieved 96% sensitivity and 96% specificity for detecting amblyopia and/or strabismus. Importantly, the device detected anisometropic amblyopia even in the absence of clinically measurable strabismus. Consistent with these findings, several investigations demonstrate that fixation stability can be reliably measured in children as young as three years old,[136] enabling objective assessment of binocular visual function in pediatric populations without requiring complex behavioral tasks. More recently, clinical trials have begun incorporating fixational stability as an outcome measure alongside VA, contrast sensitivity, and stereopsis,[67] reflecting growing recognition of fixation stability as a quantifiable biomarker of amblyopia severity and treatment response.

ReadAlyzer is an infrared eye movement recording system mounted in goggles worn over people's eyes, enabling participants to perform reading tasks in naturalistic settings throughout measurement sessions.[88] It analyzes key reading components such as the number of fixations, forward saccades, regressive saccades, fixation duration, reading speed, and eye teaming. Eye movements can reportedly be tracked at sampling rates of up to 2000 Hz; however, measurement reliability may decline when recordings contain substantial artifacts, excessive head movements, or blinking, or when eyeglass frames obstruct the infrared sensors.[137]

Dranitsaris et al.[138] developed a prototype of a dichoptic e-book reading application that can be installed on tablet devices. In this task, dichoptic reading is achieved through anaglyph red/green presentation using red/green glasses. The contrast of text seen by each eye can be adjusted independently. In cases of amblyopia, dichoptic reading speed increased when contrast was reduced in the fellow eye, although not all amblyopic participants experienced such improvement. This approach not only demonstrated that dichoptic reading is possible and can be tested in amblyopia but also provided a potential training protocol for amblyopia targeting both interocular suppression and reading deficits.

5. Practical implementation of modern testing methods in clinical trials and practice

A full battery of all available visual function tests is neither practical nor necessary in most clinical settings, particularly in pediatric populations where attention span, task comprehension, and fatigue impose clear constraints. Outcome selection should therefore follow a tiered approach that balances mechanistic relevance with feasibility (Fig. 2). At a minimum, clinical trials evaluating the efficacy of novel binocular therapies should retain VA to ensure comparability with existing literature, and should be complemented by one quantitative measure of binocular balance or interocular suppression and one sensitive assessment of stereopsis. When time and resources permit, extended outcomes such as contrast sensitivity function (e.g., qCSF) and fixation stability or eye movement measures can provide additional insight into spatial and oculomotor deficits beyond acuity. Higher-level functions such as temporal processing, attention, and reading performance may be included as exploratory endpoints, particularly in studies explicitly targeting these domains, but are generally less feasible for routine implementation in large-scale clinical trials.

Outcome measures should span distinct domains of visual function in amblyopia, including monocular spatial vision (e.g., VA, contrast sensitivity), binocular interaction (e.g., suppression or interocular balance), and binocular integration (e.g., stereopsis), with additional higher-level domains (e.g., temporal processing, attention and reading) included where relevant to the intervention. Improvements in one outcome do not necessarily generalize to others, as different tests probe related but dissociable components of binocular vision. One clear example of this dissociation is that normalization of interocular VA differences in treated amblyopes does not eliminate binocular imbalance.[44] Although there have been increasing efforts to characterize relationships among visual functions, current evidence suggests that these measures should not be assumed to reflect a single underlying latent construct.[139,140] At the same time, partial redundancy exists within domains: different implementations of binocular balance (e.g., binocular combination and dichoptic letter chart) often produce correlated estimates of interocular imbalance,[131] suggesting that a single well-validated and feasible measure is typically sufficient in many clinical contexts.

In practice, total testing duration per visit should ideally be limited to approximately 20–30 min to maintain compliance and data reliability, even much shorter for children. This constraint necessitates prioritizing rapid, adaptive procedures and minimizing task complexity while still capturing mechanistically distinct aspects of binocular vision. A practical testing schedule should include baseline, mid-treatment, and post-treatment assessments, with extended measures reserved for baseline and post-treatment visits to reduce fatigue and disengagement, especially for pediatric populations. This corresponds to a minimal core battery consisting of VA, one suppression or binocular balance measure, and one stereopsis assessment, with additional tests included only when they target the specific mechanism of the intervention. For binocular or dichoptic therapies, outcomes that directly quantify interocular suppression or balance are most appropriate as primary endpoints, with stereopsis serving as a secondary measure.

While many modern visual tests demonstrate good test–retest reliability, this evidence is frequently derived from studies conducted by the developers of the task within limited experimental settings. It remains challenging to directly compare their validity or determine whether they measure equivalent mechanisms across paradigms because a substantial number of modern psychophysical tests are not consistently accessible or standardized across research settings, as they rely on proprietary

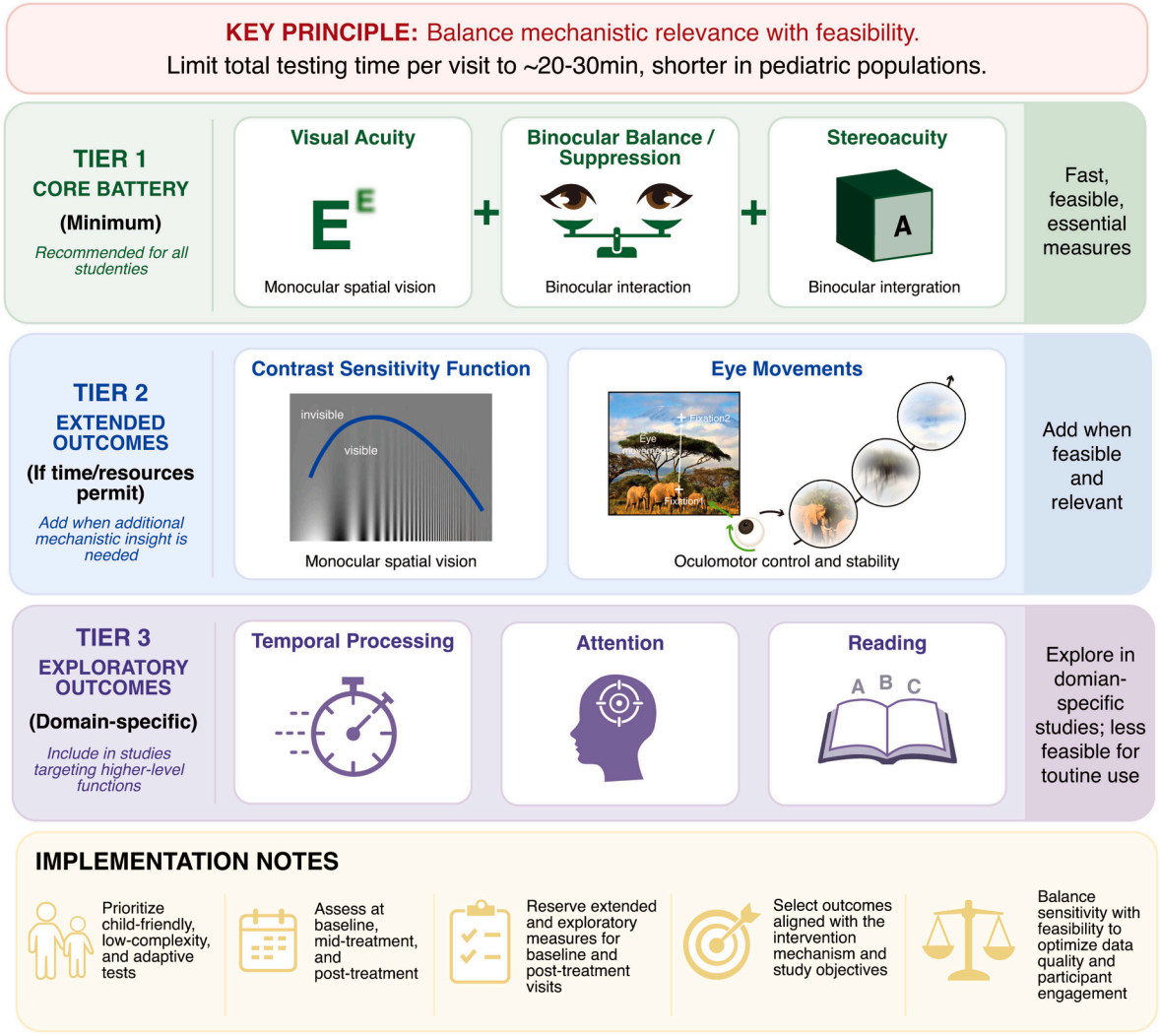


Fig. 2. A diagram showing how outcome selection in clinical trials could follow a tiered approach that balances scientific relevance with clinical feasibility.

implementations or laboratory-specific code. This lack of standardization and independent validation limits objective comparison of test performance across paradigms. Additionally, these issues extend to standard clinical tests for measuring visual functions. For example, TNO, Titmus, Frisby, and RDS tests are designed to measure stereopsis but show different results from the same populations.[141,142] Therefore, when comparing the results of different studies, it is crucial to pay attention to the research methods used and to be aware of the potential differences that may arise from different tests and laboratory groups.

The optimal test battery may also vary depending on the amblyopia subtype.[143] Individuals with strabismic amblyopia typically exhibit stronger suppression and poorer stereopsis, making suppression-focused measures particularly informative, whereas anisometropic amblyopia often retains some stereopsis and may be better characterized using sensitive disparity-based assessments. Mixed amblyopia may require a combination of both approaches. Thus, a single standardized battery may not be appropriate for all patients, and outcome selection should be guided by the dominant deficit profile as well as the mechanism targeted by the intervention. This further supports a flexible, mechanism-driven approach to outcome selection rather than a fixed test battery applied uniformly across all patients.

Beyond outcome selection, the clinical utility of these tests also depends on their implementation. Results can vary substantially depending on task design and stimulus conditions,[144–146] even within multiple versions of the same task,[147] and this difference can be amplified when testing clinical populations who can potentially exhibit larger standard deviations in performance.[130] Importantly, these considerations reflect an inherent trade-off between sensitivity and feasibility, as more sensitive psychophysical measures often require longer testing times or greater cognitive demands, whereas simpler and shorter tasks are more practical but may provide less precise estimates. Tests must be simple, intuitive, and robust to variability in attention, particularly in younger children. Forced-choice paradigms with a small number of response options (e.g., two-alternative forced choice) can improve reliability and reduce variability, whereas more complex response formats such as continuous adjustments or prolonged keypress responses may introduce additional noise. Stimulus design should also be adapted to the testing population; for example, non-alphabetic symbols, numbers,[125,148] or naturalistic images[131] may be more appropriate than letters or abstract gratings in young or non-English-speaking populations.

Efficiency can be further improved through the use of adaptive psychophysical algorithms. While traditional methods such as constant stimuli require large numbers of trials, adaptive approaches based on Bayesian estimation (e.g., qCSF,[122] qDSF,[127] QUEST[149]) can substantially reduce testing time while maintaining precision.[122–124] These methods are particularly well-suited for clinical environments where time constraints are critical. Most adaptive procedures have been developed for tasks with objective correct responses; extending these approaches to subjective binocular measures remains an important direction for future work.

Table 2
List of measurement tools for measuring binocular visual functions with different levels of availability to the public.

Test Name	Primary reference	Targeted mechanism	Availability/Implementation
CFS-crafter	Wang et al., 2022[133]	Interocular suppression	Open-source
Charmeleon paradigm	Zhao et al., 2026[134]	Interocular suppression	Open-source
Quick contrast sensitivity function test (qCSF)	Lesmes et al., 2010[122]	Contrast sensitivity	Commercial
Quick disparity sensitivity function task (qDSF)	Reynaud et al., 2015[127]	Stereoacuity	Not publicly available
iPod random dot stereo test	Hess et al., 2016[128]	Stereoacuity	Patented
Disparity detection and discrimination task	Baldwin et al., 2024[129]	Stereoacuity	Patented
Dichoptic contrast ordering test	Baldwin et al., 2024[131]	Sensory eye dominance	Patented
Dichoptic letter chart	Kwon et al., 2015[40]	Sensory eye dominance	Not publicly available
Quick orientation combination task	Min et al., 2022[130]	Sensory eye dominance	Not publicly available
Dichoptic e-book reading application	Dranitsaris et al., 2026[138]	Reading	Patented
Pediatric Vision Scanner	Loudon et al., 2011[135]	Eye Movement, fixation stability	Commercial
ReadAlyzer	Kelly et al., 2017[88]	Reading	Commercial

Finally, broader adoption of modern testing methods will depend on accessibility and reproducibility. Table 2 summarizes some of the currently available visual tests in both open-source and commercial formats, highlighting the relative scarcity of accessible tools. Increasing the availability of standardized, well-documented implementations will be critical for enabling cross-study comparisons and consistent evaluation of test performance. The use of open-source software platforms for stimulus presentation,[150] data collection,[151] and analysis[152] can lower cost barriers and facilitate standardization across sites. Sharing code, analysis pipelines, and (where appropriate) anonymized or synthetic datasets[153] can further enhance reproducibility and accelerate translation from laboratory research to clinical application. In addition, providing clear implementation guidelines for clinical use will be essential to ensure that these methods can be reliably adopted across diverse settings.

Study approval

Not Applicable.

Author contributions

The authors confirm contribution to the paper as follows: Conceptualization: LG, SHM, ZS, XT; Investigation: LG, SHM; Methodology: LG, SHM, XY, LL, YZ. All authors wrote and revised the manuscript, and approved the final version of the manuscript.

Declaration of generative AI use

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were used to generate, write, or edit any part of this manuscript. All authors contributed to the conception, data analysis, drafting, and revision of the article independently.

Funding

This work was supported by National Natural Science Foundation for Young Scientists Fund Program C (8250040184) to Ling Gong.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank all the peer reviewers for their opinions and suggestions.

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