DIAGNOSTIC ACCURACY OF VISUAL FIELD TESTS FOR CHILDREN: A SYSTEMATIC REVIEW

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Abstract

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New England College of Optometry, 2023

Purpose

Assessing visual field (VF) using standard perimetry in young and neurologically impaired children may be challenging. To address the challenges associated with standard conventional perimetry (SCP) in children, new pediatric VF tests have been reported while their accuracy has not yet been rigorously evaluated. This systematic review seeks to determine the diagnostic accuracy and feasibility of new VF tests for pediatric patients with disorders of the visual pathway, contributing to clinically relevant evidence and guiding future research.

Methods

A literature search was conducted in March 2021 with no restriction on publication date. The following databases and grey literature were searched for English language studies comparing a non-standard pediatric VF test (index test) to manual kinetic perimetry (MKP), standard automated perimetry (SAP), and/or confrontation testing (CT) (reference standards): EMBASE, PubMed (MEDLINE and PMC), Ovid MEDLINE, Web of Science, Scopus, VisionCite, Cochrane Library (CENTRAL and CDSR), ClinicalTrials.gov, African Index Medicus, LILACS, Trip, OpenGrey, and EBSCO OpenDissertations. Children ≤ 18 years ($n > 3$) with suspected or known VF defects were included. Case reports, case series, editorials, and letters were excluded. The review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for protocols and Diagnostic Test Accuracy (DTA) reviews. The risk of bias was assessed using a modified Quality Assessment of Diagnostic Accuracy Studies

(QUADAS-2) tool. Two reviewers (MR, DLM) independently performed study selection and assessed risk of bias. The data were extracted and recorded by one reviewer (MR) and verified by another (DLM). Any disagreements were resolved by a third reviewer (NCR) or through discussion with all reviewers.

Results

A total of 10,276 studies was assessed on title and abstract and 212 full texts were assessed for eligibility. Twenty-seven studies (of a total of 1,938 children) published between 1990 and 2021 were included. Children's ages ranged from 2 months to 18 years. The studies reported 17 index tests, which were sorted into broad categories: behavioral methods (6 in 7 studies), electrophysiological methods (2 in 5 studies), modifications of standard perimetry (8 in 9 studies), and eye tracking (1 in 6 studies). The risk of bias, based on the QUADAS-2 results, was unclear or high for most studies. Concerns regarding applicability were low. Eight studies utilizing behavioral (n=3), visual evoked potential (VEP) (n=2), and eye tracking (n=3) showed sensitivities of 60 to 100%, 75%, 70-100%, and specificities of 88.9-100%, 85.8-87.5%, and 50-100%, respectively.

Conclusions

Results of this review suggest that eye tracking and non-standard behavioral methods of VF testing may be reliable alternatives for children unable to perform SCP. However, the validity of new VF tests for children may be limited to certain conditions and ages. Findings have been only descriptively assessed and a meta-analysis was not performed due to heterogeneity, insufficient quantitative data, and small number of studies included. More detailed studies with better reporting are needed to determine the diagnostic accuracy and feasibility of new pediatric VF tests.

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List of Abbreviations

AAO	American Academy of Optometry
AED	Anti-epileptic Drugs
ARVO	Association for Research in Vision and Ophthalmology
BEFIE	Behavioral Visual Field
CI	Confidence Interval
CT	Confrontation Testing
CVI	Cerebral Visual Impairment
DTA	Diagnostic Test Accuracy
ERG	Electroretinogram
FDT	Frequency Doubling Technology
FN	False Negative
FP	False Positive
FT	Full Threshold
GKP	Goldmann Kinetic Perimetry
HCQ	Hydroxychloroquine
HFA	Humphrey Field Analyzer
HPR	High-Pass Resolution
IRB	Institutional Review Board
LED	Light Emitting Diode
LGN	Lateral Geniculate Nucleus
mfERG	Multifocal Electroretinogram
mfVEP	Multifocal Visual Evoked Potential

MKP	Manual Kinetic Perimetry
OKP	Oculokinetic Perimetry
PLP	Preferential Looking Perimeter
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVL	Periventricular Leukomalacia
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies 2 [revised tool]
RCT	Randomized Controlled Trial
SAP	Standard Automated Perimetry
SCP	Standard Conventional Perimetry
SITA	Swedish Interactive Thresholding Algorithm
SKP	Semiautomated Kinetic Perimetry
SNR	Signal-to-Noise Ratio
STARD	Standards for Reporting of Diagnostic Accuracy Studies
SVOP	Saccadic Vector Optokinetic Perimetry
SWAP	Short Wavelength Automated Perimetry
TBI	Traumatic Brain Injury
TN	True Negative
TP	True Positive
VEP	Visual Evoked Potential
VF	Visual Field
VR	Virtual Reality
WSKP	White Sphere Kinetic Perimetry

Chapter 1: Introduction

Assessing visual field (VF) defects in children is important for the diagnosis and management of ophthalmic diseases and neurological disorders. Cerebral/cortical visual impairment (CVI), visual impairment due to brain damage, is among the leading causes of vision loss in children. VF defects, such as hemianopia and inferior VF defects, are among the visual impairments found with CVI (Fazzi et al., 2007; Dutton, 2013). These VF defects can result in impaired spatial orientation and mobility (Bakke et al., 2019). VF constriction caused by an antiepileptic medication (vigabatrin) may provide rationale for change in treatment (Sergott, 2014). VF changes may be the only evidence of progression in pediatric brain tumors (Huang and Lee, 1997). VF testing has been shown useful for monitoring the progression and determining the severity of vision loss, such as in pediatric glaucoma or vigabatrin associated VF loss (de Souza et al., 2000; Spencer & Harding, 2003). Visual impairment in young children can negatively affect many areas of development, including cognitive, social, psychological, motor, and language, and may negatively impact education, which can lead to reduced quality of life and lasting consequences (Yekta et al., 2022). Accurate VF tests may aid in diagnosis and management of visually impaired children, and help with providing appropriate rehabilitation, thus improving quality of life.

Children with neurological impairment have a high incidence of visual impairment (Hegde et al., 2021). Conditions such as low birth weight, cerebral palsy, premature birth, and genetic conditions are common causes of developmental delay (Hegde et al., 2021). Visual impairment, including VF defects, may go undetected in this population due to other ongoing health issues and the child's or parent's inability to recognize problems with their vision (Hegde

et al., 2021). The challenges of VF testing in young and neurologically delayed children are well known, which include difficulty with understanding instructions, maintaining central fixation and sustaining attention, and inhibiting innate saccadic responses (Bowl et al., 2018). The vigilance and sustained attention required with standard perimetry is possible in neurotypical children only by age 5 to 8 years (Patel et al., 2015, Tschopp et al., 1998, 1999). Manual kinetic perimetry (MKP), primarily Goldmann kinetic perimetry (GKP), and static automated perimetry (SAP) are appropriate reference standards for normal children aged 5 years and older. However, not all children can be reliably tested; in a large normative study Patel et al. (2015) found that about 80% of children can be tested reliably with GKP and 64% with SAP. Tschopp et al. (1998, 1999) showed that SAP can be successful in normal (or neurotypical) children as young as age 5 with appropriate familiarization procedures, however, test duration may need to be shorter in younger children. Sensitivity may also be reduced due to attentional factors. Confrontation testing (CT) is a nonquantitative technique that is commonly used to assess children who are unable to perform SCP, particularly children younger than 5 years and those with disability, yet this method is relatively insensitive to VF defects that are not moderate to dense (Shahinfar, Johnson & Madsen, 1995; Bowl et al., 2018*).* Thus, CT is more sensitive to posterior pathway VF defects than to anterior pathway VF defects (Johnson & Baloh, 1991). A limitation of CT is that it is susceptible to examiner variability due to the test not being standardized (Bass et al., 2007). Testing young or neurologically impaired children for VF defects using SCP is not always feasible or accurate and has poor reliability in children under the age of 7 years (Bowl et al., 2018). Thus, VF defects in young children may go undetected because of the lack of appropriate and accurate VF tests. Also, accurate VF testing in pediatric populations requires clinical

experience for assessing their responses as well as knowledge of effects on VFs of diseases and disorders affecting these populations.

Over time, the field of VF testing has evolved to introduce non-conventional methods in addition to standard methods to address the challenges of VF testing in children. Such methods include behavioral [e.g. white sphere kinetic perimetry (WSKP; Agrawal et al., 2009), behavioral visual field screening test (BEFIE; Koenraads et al., 2015), light emitting diode perimetry (LED; Satgunam et al., 2017), game-based perimetry (Aslam et al., 2018), preferential looking perimeter (PLP; Allen et al., 2012)], electrophysiological [e.g. visual evoked potential (VEP; Spencer & Harding, 2003), electroretinography (ERG; Moskowitz et al., 2012)], modifications of standard perimetry [e.g. Rarebit (Martin & Nilsson, 2007), frequency doubling technology (FDT; Han et al., 2017)], and eye tracking [e.g. Saccadic Vector Optokinetic Perimetry (SVOP); Murray et al., 2016)].

1.1 Standard Methods

Standard methods of VF testing have been adopted into routine clinical practice, such as SAP, MKP, and CT. SAP is not commonly used in young children and continues to be the gold standard in adults. MKP such as GKP, may be a more appropriate gold standard for children due to its distinct advantages over SAP. Because of the challenges associated with standard conventional perimetry (SCP), which includes SAP, MKP, and Peritest (Greve, Dannheim & Bakker, 1982), CT remains the most commonly used method of VF testing in young or neurologically impaired children.

1.1.1 Confrontation Testing

Qualitative evaluation of the VF is most frequently carried out using CT (Johnson et al., 2011). The patient is asked to close one eye and while looking into the examiner's open eye either count or report when they can visualize the examiner's fingers in each VF quadrant; this is kinetic confrontation done by gaze eversion. Finger puppets or colorful objects can be used to evaluate VFs in children who cannot understand the examiner's instructions: an object is presented to the child's central vision for fixation while another object is moved centrally from the peripheral field as the examiner monitors the child's orienting to the peripheral object (Johnson et al., 2011). The validity of CT depends upon the specific set of methods used and the type of field defect (Shahinfar, Johnson & Madsen, 1995). VFs in children under 5 years are assessed using CT (Schiefer et al., 2005). CT only allows the assessment of major neurological field defects (e.g. hemianopia), unlike other standard methods of VF testing. CT using quadrant finger counting in adults was shown to have a sensitivity of 35% and a specificity of 100%, unless a red target was used, which resulted in a higher sensitivity value of 73% (Pandit, Gales & Griffiths, 2001).

1.1.2 Kinetic Perimetry

Kinetic perimetry maps the boundary of the seeing field by having the patient indicate when a stimulus of a certain size and intensity is seen as it moves from a non-seeing area toward the center of the perimeter (Racette et al., 2018). The Goldmann perimeter, used with a standard method of manual kinetic perimetry (MKP), is no longer commercially available but is still used in many clinical settings. However, MKP is currently available with other commercial perimeters. Patel et al. (2015) conducted a study to compare the feasibility and reliability of

Octopus 900 semi-automated kinetic perimetry and GKP. They found that GKP was more reliable than Octopus 900 for children under 9 years.

Kinetic perimetry has unique advantages over static perimetry, including improved spatial resolution (Racette et al., 2018). GKP allows measurement of the whole VF, peripheral and central areas, meaning areas where sensitivity to a stimulus is lost can be more clearly defined. In testing with Goldmann hemispheric perimeters, the far peripheral field can be tested while in standard static perimeters, only the central field of 30 degrees is tested (Racette et al., 2018). MKP is also relatively faster at assessing the periphery as a result of a moving target (Racette et al., 2018). One major advantage of kinetic perimetry is that it allows for greater flexibility and can be adapted to the patient's abilities. As a result, kinetic perimetry is suitable for patients who find it difficult to perform perimetry, such as young children or neurologically impaired patients, the elderly, and for those with low vision. It is commonly used for detecting peripheral field changes due to peripheral retinal diseases (Racette et al., 2018). One limitation of kinetic perimetry is that it is highly dependent on the examiner's level of experience and skill (Pineles et al., 2006). There is variability in efficiency and quality of kinetic perimetry among examiners. It is more difficult to compare the results of kinetic perimetry from one clinic to another, since there is are no agreed standards for conducting the test (Pineles et al., 2006). Moreover, kinetic perimetry is difficult to perform routinely, as it is not completely automated. However, Octopus 900 perimeter has a semi-automated kinetic module (Bhaskaran et al., 2021).

1.1.3 Static Perimetry

SAP has been the biggest advancement for perimetry and currently is considered the gold standard for testing VFs in adults (Alencar & Medeiros, 2011; Spry, 2005; Khizer et al., 2022; Nam et al., 2009). SAP uses a computerized system to position the peripheral stimuli and control

stimulus size and intensity. Typically, thresholds for detection of light intensity at fixed positions in the central VF are measured (Racette et al., 2018; Montelongo et al., 2021). This form of perimetry involves a white stimulus that is presented against a white background. Examples of currently available automated perimeters include the HFA (Humphrey Field Analyzer), the Humphrey Matrix, and the Octopus perimeter (Alencar & Medeiros, 2011). The Peritest is an automatic perimeter that predates HFA and has an established history of VF testing for identification of VF defects (Greve, Dannheim & Bakker, 1982). This VF test includes one or more stimuli in static perimetry and determines the sensitivity threshold by using a measured point in the fovea. According to Greve, Dannheim & Bakker (1982), the Peritest has been shown to identify defects that are less likely to be detected by kinetic perimetry.

Software algorithms have been one of the major developments in automated perimetry in recent decades. There are differences between algorithms in terms of test-retest reliability and test duration. Examples of commercially available algorithms using HFA include full-threshold (FT), Fastpac (Young et al., 1995), and variants of the Swedish interactive thresholding algorithm (SITA) (McKendrick, 2005; Bengtsson et al., 1998). The FT algorithm is a standard method in static threshold perimetry and uses a staircase strategy (Turpin et al., 2003). Fastpac was shown to screen for VF defects in two-thirds the testing time of the FT algorithm (Young et al., 1995). SITA, the most commonly used HFA algorithm, has a considerably shorter test duration without sacrificing accuracy by means of adapting to the patient's response to stimuli during the test (McKendrick, 2005). SITA-Standard dates back to 1997, and SITA Fast has been used since 1998 (McKendrick, 2005; Bengtsson et al., 1998; Le et al., 2022). Donahue & Porter, (2001) assessed VFs in children by comparing HFA SITA with FT via a retrospective review. They performed SITA in children as young as 6 years. They found that SITA decreased testing

time by at least 50% in comparison with FT. The mean testing time for SITA was reported to be 6.5 minutes, whereas FT took 13 minutes (Donahue & Porter, 2001). Stiebel-Kalish et al. (2004) performed HFA SITA Fast in children with prepubertal idiopathic intracranial hypertension as young as 4 years. Akar et al. (2008) compared HFA Fastpac with SITA Fast, and found that SITA Fast was a more reliable method for assessing VFs in normal children older than 8 years of age. Thus, developments in SAP, such as faster thresholding algorithms, have allowed VF testing in younger children.

However, numerous studies have recognized the difficulties of performing SAP on children, including lack of concentration, poor cooperation and understanding of using a buzzer, problems with maintaining fixation, variability, and poor reliability of results (Mutlukan & Damato, 1993; Johnston et al., 1989; Lakowski & Aspinall, 1969; Tschopp et al 1998; Blumenthal et al., 2004; Morales & Brown, 2001). SAP is particularly challenging in children younger than 5 years due to their innate saccadic response caused by the presentation of light stimuli in the peripheral field (Ross et al., 1994; Munoz et al., 1998; Mutlukan & Damato., 1993). The series of studies by Tschopp et al. (1998; 1999) showed that vigilance rather than age is a better predictor of visual sensitivity in children between 5 and 8 years (Tschopp et al., 1999). The requirement of being positioned on the chin and forehead test to restrict head movements is also difficult for some children. As a result, SAP is usually suitable for older children. Akar et al. (2008) determined that SAP may provide reliable results in healthy children ages 8 years and above. Several studies have attempted using test strategies, such as familiarization, to improve testing using SAP in children (Tschopp et al., 1995). Tschopp et al. (1995) used a familiarization strategy for children ranging from 5-8 years prior to performing a screening test. They found that

with the familiarization procedure, they were able to obtain reliable results in children as young as 5 years.

SAP provides several advantages over MKP. Some advantages of SAP include avoiding examiner bias and standardized target presentation (Schiefer et al., 2005). SAP is easy to use as a result of it being fully automated, sensitivity of the field can be tested rapidly, and it has relatively high accuracy (Alencar & Medeiros, 2011). Static perimetry is suitable for diseases with slow progression and for this reason, is used most often in clinical practice for patients with macular diseases and glaucoma (Pineles et al. 2006). SAP is standardized and can be reliably reproduced, as a result there is less reliance on the examiner's skill and less variability as with kinetic perimetry. One major limitation of static perimetry is that the boundaries of small scotomas cannot be well defined. Another limitation is that static perimetry is usually restricted to the central 30 degrees of the VF (Keltner & Johnson, 1984). However, the central VF is essential to assess in glaucoma and other diseases. Static perimetry also requires sustained attention by the patient and ability to indicate detection of a peripheral target by a button press, similar to kinetic perimetry.

1.2 Non-Standard Methods

A number of new VF tests have been developed in recent decades for young or neurologically impaired children who are unable to be tested with standard perimetry in an attempt to improve testing and diagnostic accuracy (Heidary, 2016). Although these new VF tests have distinct advantages over SAP, they have not yet been adopted into routine clinical practice.

1.2.1 Behavioral Methods

Studies from the 1980s and 1990s explored the development of VF in infants using behavioral methods and either kinetic or static peripheral stimulus presentation. In kinetic methods, the peripheral target moved from non-seeing to seeing field, while in static methods, a non-moving peripheral target was presented at fixed locations (Mayer & Fulton, 1993). A hybrid of these two methods was also employed (Futenma, 1977). All these methods rely upon observation of infant's visual behaviors, crucially the infant's fixation of a central stimulus followed by an orienting eye-head movement toward the visual periphery (Mayer & Fulton, 1993). The observer judges the peripheral location of the stimulus based upon the direction of the infant's eye-head movement amongst a possible set of coordinates (e.g. right or left, up or down). A match between the observer's judgment and the location of the peripheral target indicates the infant detected it (Mayer & Fulton, 1993). Generally, these visual field test methods can be considered variations of the "preferential looking technique" developed initially to measure infant visual acuity (Teller, 1981) and later many other visual functions.

WSKP was first developed by Mohn & van Hof-van Duin (1986). Satgunam et al. (2017) describe WSKP as having successfully mapped the VF in young children by recording the child's eye or head movement, especially in the key VF meridians. WSKP moved along one of the 4 arcs towards fixation and the child's eye-head movement to the target is monitored by a hidden examiner. WSKP was used to obtain normative data on monocular and binocular VF extent and to test young patients, including infants at risk of neurological disorders due to perinatal events (hypoxia, periventricular white matter damage or intraventricular hemorrhage) (Van Hof-van Duin et al., 1986, 1987, 1989; Groenendaal et al., 1989; Harvey et al., 1997; Scher

et al., 1989), and prematurely born infants with retinopathy of prematurity (ROP) (Luna et al., 1989; Quinn et al., 1996).

Static perimetry was used to obtain monocular VF extent in normal infants between birth and 6 months (Maurer & Lewis, 1991; Lewis & Maurer, 1992). Hybrid static-kinetic perimetry involves stimuli that appear in one location for a period of time and then moved centrally until the stimulus is judged as detected. Futenma (1977) used this method to assess VFs in handicapped children, Cummings et al. (1988) in normal young children, and Mayer et al., (1988) in normal infants tested monocularly and binocularly. A static perimetry method using the same hemispheric perimeter was adapted for clinical testing (Mayer & Fulton, 1989).

Clinical perimetry using similar behavioral methods to those described above have been more recently reported. These include kinetic methods to assess VF extent: WSKP in children treated with vigabatrin for epilepsy (Agrawal et al., 2009) and in children with ROP (Quinn et al., 1996), and BEFIE, a different kinetic perimetry method also using a white sphere peripheral target (Koenraads et al., 2015; Portengen et al., 2020). Static perimetry has been employed using a game-based method (Casper's Castle) that involves a large plasma display and a visuo-motor response using a keypad (Aslam et al., 2018; Allen et al., 2012). Hybrid static-kinetic perimetry with LED stimuli was used to assess VF extent in normal infants and those at risk of VF defect (Satgunam et al., 2017).

1.2.2 Electrophysiological Methods

The electroretinogram (ERG) is a type of electrophysiological diagnostic test that measures both electrical and retinal activity in response to a light stimulus. Retinal neurons combined with retinal glial cells generate signals for the ERG (Fishman, 2001). Thus, the ERG is an objective test of retinal function. An electrode is placed on or near the cornea, allowing

electrical activity generated by the retina to be captured at the surface of the cornea. The ERG provides diagnostic information on inherited and acquired retinal disease and monitors its progression (Fishman, 2001). Comaish et al. (2002) used ERG (and EOG) to compare the VFs of epilepsy patients who received vigabatrin to those receiving other anti-epileptic drugs (AEDs). They demonstrated that VF loss associated with vigabatrin was strongly correlated with loss of the b-wave and reduced oscillatory potentials of the ERG.

Similarly, objective visually evoked potential (VEP) electrophysiological testing can also be useful when results from subjective tests, such as behavioral VF tests, are unreliable, inconclusive, or not feasible (Alshowaeir et al., 2015). VEP is also useful for excluding non-organic VF loss and following the progression of diseases. However, there are many types of VEP and testing requires specialized equipment and experienced examiners (Simon et al., 2004). VEP is used to generate electrophysiological responses to stimulation of the VF. The VEP evaluates signals from the patient's visual cortex recorded from electrodes attached to the scalp (Alshowaeir et al., 2015). Kelly & Weiss (2006) compared pattern VEP to GKP and found VEP to be a reliable alternative for detecting VF loss in children with optic pathway gliomas. Maitland et al. (1982) used pattern VEP, full and half field for VF defects due to chiasmal or retro-chiasmal lesions. They concluded that VEP was not reliable for the detection of subtle VF defects and has limited value for homonymous or bitemporal hemianopsias. They also reported significant variability between patients with similar VF defects, making interpretation difficult.

Multifocal VEP (mfVEP) allows recording from several areas of the VF simultaneously to create an objective VF map (Simon et al., 2004). mfVEP has a short testing time and does not depend on subjective responses. For example, the use of mfVEP in children was reported for detecting VF loss associated with vigabatrin, a medication used to treat epilepsy (Hammoudi et

al., 2005). Similarly, other studies have also reported the utility of mfVEP in epileptic children (Kim et al., 2006). Harding et al. (2002) concluded that the method called field specific VEP was reliable for detecting VF loss associated with vigabatrin and high feasibility in children of at least 3 years of age. Fortune et al. (2007) found the diagnostic performance of mfVEP to be similar to that of SAP in individuals with high-risk ocular hypertension or early glaucoma.

1.2.3 Modifications of Standard Perimetry

Rarebit perimetry involves detecting minute stimuli displayed on a screen and creates a detailed map of different areas of the VF (Johnson et al., 2011). Rarebit perimetry is useful for detection of early VF defects as a result of glaucoma and neuro-ophthalmologic disorders. Moreover, it is inexpensive, fast, and simple to conduct (Salvetat et al., 2007). Martin & Nilsson (2007) found that rarebit perimetry was able to detect glaucomatous changes in children with pediatric glaucoma as young as 6 years old.

Frequency doubling technology (FDT) perimetry involves observing rapidly counterphase flickered sinusoidal gratings of low spatial frequency (less than 1 cycle per degree) (McKendrick, 2005). This leads to a perceptual effect, known as frequency doubling, where twice as many light and dark bars appear to the observer than are physically present. This effect takes place in response to the stimulation of the magnocellular ganglion cell pathway (McKendrick, 2005). The advantages of FDT include portability, reduced testing time, low cost, and high test-retest reliability. This technique does not require the patient to use a chinrest and has larger targets than used in standard perimetry, allowing for more successful testing in children (Blumenthal et al., 2004). Becker et al (2003) determined that FDT perimetry could reliably be performed in children older than 10 years. Similarly, Blumenthal et al. (2004) found that children 8 years and older could reliably perform FDT. Quinn et al. (2006) improved

compliance with a familiarization procedure on children 5-15 years of age, although there remained difficulties testing the youngest children with FDT. Moreover, FDT increased sensitivity and specificity for detecting early VF loss due to glaucoma, and decreased individual variability, making it useful for detecting progressive VF loss (McKendrick, 2005). FDT is suitable for detecting VF defects in optic neuropathy patients, but is less useful for defining hemianopic defects. It is minimally influenced by cataracts and refractive error (Johnson et al., 2011; McKendrick, 2005)

High-pass resolution perimetry (HPR), also referred to as ring perimetry, is presumed to assess the density of retinal ganglion cells (parvocellular system) (McKendrick, 2005). This form of perimetry uses light and dark ring-shaped stimuli that are high-pass filtered. The targets exhibit a vanishing effect when the detection and identification thresholds match (Johnson, 2011). Advantages of high-pass resolution perimetry include short testing time and being able to detect early glaucomatous VF loss. VF progression due to glaucoma can be detected earlier using HPR compared to HFA (Marraffa et al., 1995). In their study, Marraffa et al. (1995) found that HPR perimetry was most appropriate for children with congenital glaucoma due to easier and shorter testing, and its game-like resemblance.

1.2.4 Eye Tracking Methods

SVOP uses eye tracking technology to assess behavioral responses to VF stimuli in the central 30 degrees of the VF (Murray et al., 2016; Tailor et al., 2016). By assessing detection of peripheral targets using eye tracking, young children, and those with neuro-disability can perform VF tests better than with conventional methods (Murray et al., 2016). In comparison to confrontation testing, which fails to identify smaller central scotomas, SVOP has shown to identify more VF defects, allowing for enhanced monitoring (Murray et al., 2016). Moreover,

unlike standard perimetry, the individual can perform the test in free space either seated on their parent's lap, by themselves, or in a wheelchair (Heidary, 2017).

Eye tracking provides a solution to assess VFs quickly and objectively in non-verbal children and eliminates examiner bias (Mooney et al., 2021). This method also works almost as well as the gold standard HFA in young neurotypical children (Jones, 2020). Leitner et al. (2021) refers to this formally as the eye-tracking-based-visual-field-analysis, an assessment based on SAP that considers eye movements of patients in real time. These authors found that by identifying patients who compensate for deficits/defects through eye movements, "saccade-compensating" inaccuracies can be ruled out diagnostically for young and non-verbal patients (Leitner et al., 2021).

Several groups have evaluated the feasibility and accuracy of SVOP testing in normal children and those with neurological disability. Murray et al. (2018) found SVOP to be useful for the assessment of VFs in pediatric patients (2.9-15 years) with brain tumors. Most of the children were able to reliably perform SVOP. They also found that SVOP could offer an additional measure for glaucoma assessment due to glaucoma patients having higher saccadic reaction times (Murray et al., 2016). Tailor et al. (2016) found accuracy of SVOP to be relatively poor when compared to GKP in children of 1-16 years. More recently, Perperidis et al. (2021) successfully assessed VFs in healthy infants ranging from 3.5-12 months using a modified SVOP test strategy. The limitations of SVOP include certain dysfunctions that can interfere with SVOP testing and prevent accurate assessment of gaze position. This includes nystagmus, pupillary dilation, significant refractive error, limitation of head movement, and requirement of calibration (Heidary, 2017; Perperidis et al., 2021). For instance, in a study by Mooney et al. (2021),

children with severe strabismus were excluded from analysis because of their incompatibility with the eye tracker.

In summary, both standard and non-standard methods of VF testing have benefits and drawbacks. Standard perimetry like SAP and MKP have earned their gold standard status, but lack the leniency in sustained attention that many children require to successfully complete a VF test. Consequently, young and developmentally delayed children cannot reliably be tested with standard perimetry methods. New, non-standard methods of perimetry have been developed to test children, such as behavioral tests, electrophysiological methods, modifications of standard perimetry, and eye tracking. These methods share unique features, such as objectively testing retinal function, and kinetic or static peripheral stimulus presentation. However, these tests have unknown accuracy (e.g. sensitivity and specificity) in detecting VF defects in children.

1.3 Diagnostic Test Accuracy Reviews

Systematic reviews summarize evidence that fits pre-determined criteria to answer a valid research question (Galada, 2022). A systematic review uses systematic methods that reduce bias and provide more trustworthy findings from which to draw clinically-relevant conclusions. Starting with a good research question, reviewers search for studies to include by utilizing a search strategy. Studies are screened to see if they meet inclusion and exclusion criteria. Next, reviewers extract the data of interest, and assess the quality of included studies. Lastly, reviewers summarize the extracted data, and if methodologically valid, results are pooled via meta-analysis (statistical summary), but if not, results are captured via narrative synthesis (descriptive summary).

A diagnostic test accuracy (DTA) review is a type of systematic review conducted to evaluate the accuracy of diagnostic tests (Campbell et al., 2015). DTA reviews identify whether

a new test of interest is as or more accurate than an existing test, or whether it is more effective, implying it is more convenient, cost-effective and/or efficient to use on certain populations and/or for testing certain conditions. Answering these clinically-relevant questions informs decisions on which diagnostic test to use for which patient populations. The primary DTA studies included in systematic reviews compare a relevant diagnostic test (an "index test") to an existing, gold standard diagnostic test (a 'reference standard' or 'reference test') to accurately determine whether a target condition is present or absent in a patient (Campbell et al., 2015). The diagnostic accuracy of a test is measured by its sensitivity and its specificity.

A test is highly sensitive when the chance for a false negative is low. A false negative test result is when a patient has the target condition but the test misses detecting it. Sensitivity is represented by the proportion of patients with the target condition who are correctly detected by the diagnostic test. On the other hand, a test is highly specific when the chance for a false positive is low. A false positive test result occurs when a patient does not have the condition but the test identifies the patient to have the condition. Specificity implies the proportion of patients without the condition of interest who are correctly identified by the diagnostic test. Lastly, if a diagnostic test is both highly sensitive and highly specific, then that test has a good chance at accurately diagnosing patients with the condition (sensitivity) and without the condition (specificity).

1.4 Research Questions

There is a need for early and accurate assessment of VF defects in young and neurologically impaired children. Several new pediatric VF tests have been reported in recent decades as described earlier, however their diagnostic accuracy has not yet been rigorously evaluated. Therefore, this systematic review aims to determine the diagnostic accuracy and

feasibility of new non-standard pediatric VF tests (index tests) compared to conventional methods of VF testing (reference standards) in children with suspected or known VF defects due to disease or disorder of the visual pathway. This systematic review involves a broad inclusion of index tests, including those designed to detect VF defects associated with specific disease/disorders (e.g. optic gliomas), and index tests that can detect more general or common VF defects associated with pediatric disorders (e.g. anoxic perinatal brain damage). Reference standards included were standard perimetry including SAP (e.g. HFA, Octopus static perimetry, strategies using HFA), Peritest, and MKP (e.g. GKP). CT was used as a reference standard for children who were unable to perform standard perimetry. Although there are limitations in using CT as a reference standard as discussed above, there is no other standard perimetric method for children under age 5 years, or for children with developmental disabilities. The outcome of this systematic review will generate data to help more accurately assess VF defects in young and neurologically impaired children, and, as needed, provide guidelines for improved methods of perimetry in children. The results of this systematic review will aid in interpretation of VF testing in children, both specifically in clinical settings and for use in evidence-based screening guidelines as well as identify knowledge gaps and outline areas for future investigation.

Chapter 2: Methods

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for protocols (Moher et al., 2015) and DTA reviews (McInnes et al., 2018). The protocol for this review has been registered in PROSPERO [CRD42021220402].

2.1 Search Methods

2.1.1 Information Sources

A literature search was conducted in March 2021. The following electronic databases were searched: EMBASE, PubMed (MEDLINE and PMC), Ovid MEDLINE, Web of Science, Scopus, VisionCite, Cochrane Library (CENTRAL and CDSR), ClinicalTrials.gov, African Index Medicus, LILACS, Trip, OpenGrey, and EBSCO OpenDissertations. The following grey literature was searched: The Association for Research in Vision and Ophthalmology (ARVO), American Academy of Optometry (AAO) Meeting, Vision Sciences Society Annual Meeting, and Vision Science Society.

2.1.2 Search Strategy

The electronic search strategy was formulated in collaboration with the New England College of Optometry (NECO) librarian, Heather Edmonds. The following terms were used in the search strategy: VF tests, perimetry, standard automated perimetry, SAP, Humphrey, HFA, manual kinetic perimetry, MKP, Goldmann, Octopus, confrontation testing, children, infants, pediatric, and adolescent. The electronic search strategy is outlined in Appendix 1.

2.2 Inclusion Criteria

2.2.1 Participants

Studies included evaluated children with suspected or known VF defects and, if possible, normally developing control subjects without risk of VF defects. Studies that included any participants that received both an index test and a reference standard and up to 18 years of age were eligible for inclusion. Studies that included children with disabilities were also included.

2.2.2 Index Tests

All studies that proposed new formal VF tests to assess children with suspected or known VF defects were included. Index tests include, but were not limited to, BEFIE screening test, LED perimetry, SVOP, video game-based perimetry, PLP, WSKP, rarebit perimetry, FDT, and VEP.

2.2.3 Reference Standards

Three different well validated reference standards were accepted, including MKP (e.g. GKP), SAP (e.g. HFA, all HFA algorithms, Octopus 900 static), Peritest, and CT for children who were unable to be tested with MKP or SAP. In the case of SAP HFA, multiple testing algorithms have been explored and used as a reference standard over time. For example, Donahue & Porter (2001) sought to validate the SITA standard algorithm, which was adopted as a reference standard in later studies (Han et al., 2017; Moya et al., 2003; Mendieta et al., 2021).

2.2.4 Target Conditions

Studies included proposed new VF tests to assess children (age 18 years and under) with suspected or known VF defects due to disorders of the visual pathway (ocular structures, including retina, optic nerve, optic chiasm and retrochiasmal structures, including optic tract, lateral geniculate nucleus (LGN), optic radiation, visual cortex). Examples of target conditions potentially resulting in VF loss in pediatric patients include the following: optic glioma and other brain tumors, neonatal hypoxic ischemic brain injury, traumatic brain injury (TBI), hemorrhagic infarction, stroke, cerebral visual impairment (CVI), periventricular leukomalacia (PVL), congenital brain malformations (e.g. schizencephaly), hydrocephalus, congenital ocular malformations (e.g. coloboma; optic nerve hypoplasia), ROP, retinal degeneration and other

retinal diseases, glaucoma, seizure disorder, and treatment with the anti-epileptic drug, vigabatrin.

2.2.5 Study Design

Studies that reported diagnostic accuracy values that could be used to calculate sensitivity and specificity were included. To help increase the sample size of this review, studies were included that did not report sensitivity and specificity, but had a primary objective of comparing a non-standard VF test (index test) to a pre-stated reference standard. Only studies that analyzed data from children separately from adults were included. The following types of studies were included: prospective, retrospective, randomized controlled trials (RCT), cross-sectional, cohort studies, and case-control studies. Case reports, editorials, and letters were excluded. Abstracts were included if sufficient information was presented. The searches were restricted to English language studies. There were no restrictions on publication date.

2.3 Data Collection, Quality Assessment, and Analysis

2.3.1 Data Management

The web-based software, DistillerSR, was used to facilitate the systematic review process (screening, data extraction, and quality assessment). References were managed in EndNote. Given the nature of a systematic review, there was no direct involvement with human subjects and all data were already de-identified. This systematic review was determined to be exempt from human subject approval requirements by the Institutional Review Board.

2.3.2 Selection Process

Two reviewers (MR, DLM) independently screened the titles/abstracts followed by the full-texts using the inclusion criteria. Any disagreements were resolved by a third reviewer (NCR) or through discussion with all reviewers.

2.3.3 Data Collection Process

The data were extracted and recorded by one reviewer (MR) and verified by another (DLM). Any discrepancies were resolved by a third reviewer (NCR) and through discussion amongst reviewers.

2.3.4 Data Items

Standardized data extraction forms were used to extract information on the following: study characteristics (author, publication date, study design, time interval between the VF test and reference standard, total number of participants and ages), index test, reference standard, and study outcomes (sensitivity, specificity, feasibility). Where possible the following values were recorded: true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN).

2.3.5 Outcomes

The primary outcomes include index test sensitivity and specificity with the 95% confidence intervals (CI) for each study in which these data were recorded. The secondary outcomes include feasibility of index tests in children categorized by age range and developmental status. Feasibility was defined as the proportion of children who were successfully able to complete the VF test.

2.3.6 Data Synthesis

Findings from this systematic review have been descriptively assessed in a narrative synthesis due to the heterogeneity of the included studies, insufficient data, and a low number of studies. Review Manager, version 5.4 (Review Manager, 2020) was used to create forest plots from the sensitivity and specificity data of those studies reporting and was also used to summarize the risk of bias and applicability concerns for the included studies.

2.3.7 Risk of Bias in Individual Studies

The risk of bias of each study was independently assessed by two reviewers (MR, DLM) using the modified Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) checklist (Whiting et al., 2011). Any discrepancies were resolved by a third reviewer (NCR) and through discussion amongst reviewers. The QUADAS-2 checklist is comprised of 11 signaling questions (Table 1), which are divided into four domains: patient selection, index test, reference standard, and flow and timing. The risk of bias and applicability scores were evaluated based on QUADAS-2 guidance shown in Table 1. The definitions for “Yes”, “No”, and “Unclear” were agreed by consensus.

Table 1. Signaling questions for QUADAS-2

DOMAIN	Yes	No	Unclear
PATIENT SELECTION	Describe methods of patient selection: Describe included patients (prior testing, presentation, intended use of index test and setting):		
1. Was a consecutive or random sample of patients enrolled?	If the study clearly states that the participants were recruited consecutively or randomly (either retrospectively or prospectively)	If there is concern that the participants have been entered based on their known risk of VF loss	Insufficient information to assess this item
2. Was a case-control design avoided?	If the study design is a prospective cohort	If a group of participants with known VF are compared to a group of participants without the VF loss (controls)	Insufficient information to assess this item
3. Did the study avoid inappropriate exclusions?	If the study provides reasons for excluding participants	Exclusion of patients with a diagnostic profile that would normally be included in clinical practice or if the study excludes participants without specifying reasons	Insufficient information to assess this item
Risk of bias: Could the selection of patients have introduced bias?	Overall judgement at reviewer's discretion, with reasons		
Concerns regarding applicability: Are there concerns that the included patients do not match the review question?			
INDEX TEST	Describe the index test and how it was conducted and interpreted:		
4. Were the index test results interpreted without knowledge of the reference standard?	If the index test was performed prior to the reference standard, the study must directly state that blinding of the observer was performed	The observer was not blinded to the results of the reference standard	Insufficient information to assess this item
5. If a threshold was used, was it pre-specified?	If the criteria for an abnormal VF was pre-specified	If the criteria for an abnormal VF was not pre-specified	Insufficient information to assess this item

Risk of bias: Could the conduct or interpretation of the index test have introduced bias?	Overall judgement at reviewer's discretion, with reasons		
Concerns regarding applicability: Are there concerns that the index test, its conduct, or interpretation differ from the review question?			
REFERENCE STANDARD	Describe the reference standard and how it was conducted and interpreted:		
6. Is the reference standard likely to correctly classify the target condition?	All reference standards used meet the pre-stated criteria. For those capable of being tested, MKP (e.g. GKP), SAP (e.g. HFA, Octopus 900 static), and Peritest will be used. CT will be used as the reference standard for children who are unable to be tested with MKP or SAP).	One or more reference standards used do not meet the pre-stated criteria.	Insufficient information to assess this item
7. Were the reference standard results interpreted without knowledge of the results of the index test?	The observer scores the reference standard without knowledge of the index test. If the index test is performed prior to the reference test, this signaling question should only receive a "Yes" score if there is an explicit statement made about the appropriate blinding of the observers to the index test.	If the observer was not blinded to the index test	Insufficient information to assess this item
Risk of bias: Could the reference standard, its conduct, or its interpretation have introduced bias?	Overall judgement at reviewer's discretion, with reasons		
Concerns regarding applicability: Are there concerns that the target condition as defined by the reference standard does not match the review question?			

FLOW AND TIMING	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2 x 2 table (refer to flow diagram): Describe the time interval and any interventions between index test(s) and reference standard		
8. Was there an appropriate interval between index test and reference standard?	If there were less than 3 months between the performance of the two tests. If there was longer than 3 months between tests, the authors should specifically state that they checked there was no progression in VF defects of patients between the tests.	If there were greater than 3 months between index and reference standard and there was no indication that progression of VF defects was monitored.	Insufficient information to assess this item
9. Did all patients receive a reference standard?	All children who received the index test received a reference standard. Children who could not cooperate with perimetry were tested using CT.	If some of the children who received the index test did not receive verification of their VF defect using a reference standard.	Insufficient information to assess this item
10. Did all patients receive the same reference standard?	If the patients who received a reference standard received the same reference standard that meets the pre-stated criteria	If the patients who received a reference standard did not receive the same reference standard	Insufficient information to assess this item
11. Were all patients included in the analysis?	If the total number of children enrolled in the study were included in the descriptive or quantitative analysis	If the total number of children enrolled in the study were not included in the descriptive or quantitative analysis or if there are children who did not receive the reference standard	Insufficient information to assess this item
Risk of bias: Could the patient flow have introduced bias?	Overall judgement at reviewer's discretion, with reasons		

VF, visual field; SAP, standard automated perimetry; HFA, Humphrey Field Analyzer; MKP, manual kinetic perimetry; GKP, Goldmann kinetic perimetry; CT, confrontation testing.

Chapter 3: Results

3.1 Search Results

A total of 20,449 records were identified from the initial search. The remaining 10,276 records after duplicate removal were assessed on title and abstract and 212 full texts were assessed for eligibility. Of these, 185 studies were excluded and 27 studies were included in the systematic review. The search results were reported according to the PRISMA guidelines (Figure 1).

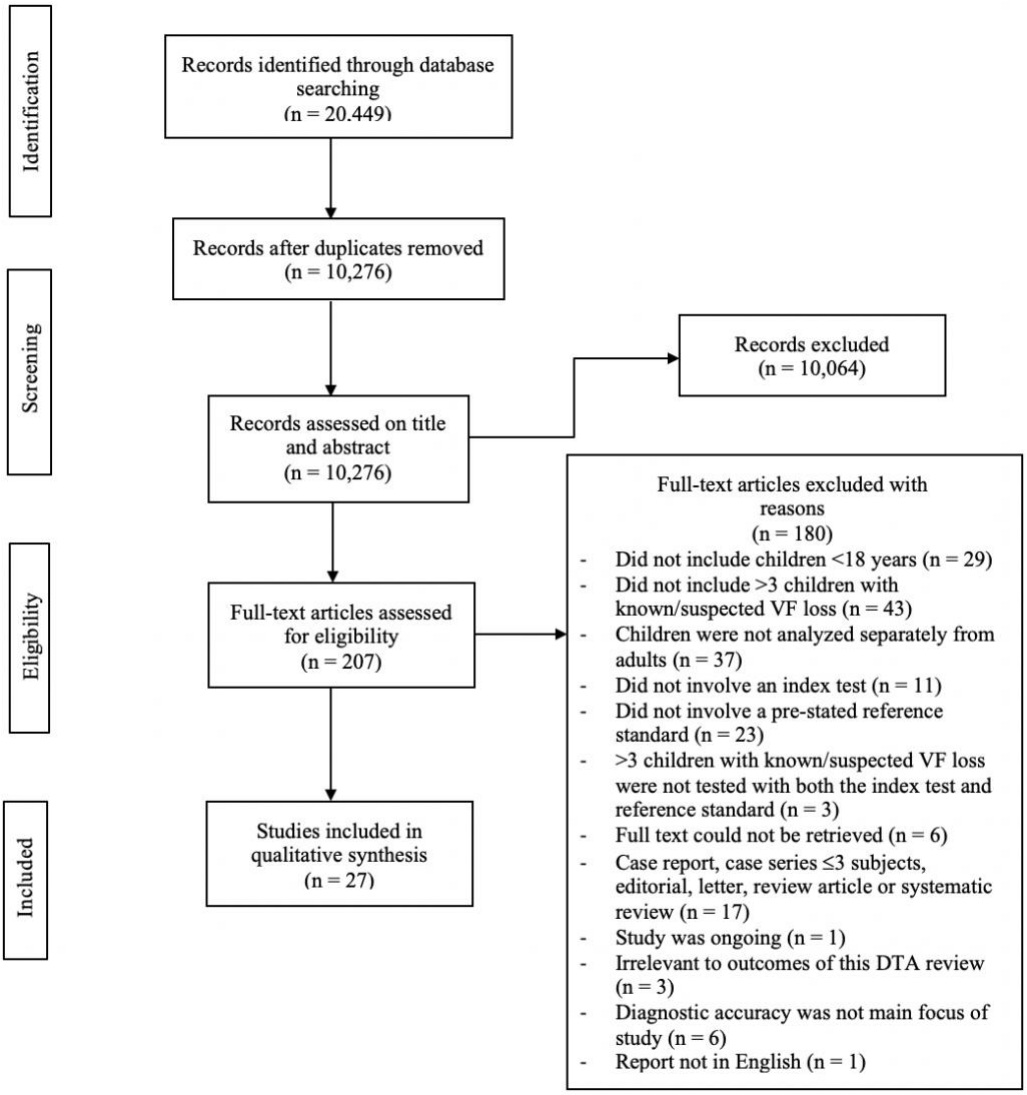

Figure 1. PRISMA Flowchart

3.2 Characteristics of Included Studies

Characteristics of the included studies are presented in Table 2. This narrative synthesis includes 27 studies (of 1,938 children), published between 1990 and 2021. Children included in this study ranged from 2 months to 18 years. There were 6 case-control, 12 prospective, 5 retrospective, and 4 cross-sectional studies. The studies investigated 17 different index tests, which are sorted into broad categories: behavioral methods (6 in 7 studies; PLP, WSKP, BEFIE screening test, game-based perimetry, Starlight test, and light emitting diode (LED)), electrophysiological methods (2 in 5 studies; VEP, ERG), modifications of standard perimetry (8 in 9 studies; SITA, Rarebit, oculokinetic perimetry (OKP), semiautomated kinetic perimetry (SKP), blue-on-yellow, frequency doubling technology (FDT), microperimetry, Octopus kinetic perimetry), and eye tracking (1 in 6 studies; SVOP). Common reference standards were GKP (13 studies) and HFA (13 studies) followed by CT (6 studies). Eight of 27 (29.6%) studies used more than one reference standard. Eight studies utilizing behavioral (3), VEP (2), and eye tracking (3) tests showed sensitivities of 60-100%, 75%, 70-100%, and specificities of 88.9-100%, 85.8-87.5%, and 50-100%, respectively. Paired forest plots are shown in Figure 4 for the seven studies that reported sensitivity and specificity data. The AlWattar et al (2019) and Tailor et al. (2015) studies were not included in the forest plot because the missing TP, FP, FN and TN values were needed to generate the forest plot in RevMan.

Table 2. Characteristics of included studies

Study	Participants		Study design	Target conditions; VF defects	Index test; Field parameters/stimulus	Reference standard
	n <18 years	Age range (years) (mean or median)				
Behavioral methods						
Agrawal et al., 2009	28	1-11 (6)	Prospective cohort	Vigabatrin-associated; Dense hemianopia/quadrantanopia/ general constriction	WSKP; 4 quadrants/suprathresh old object	GKP
Allen et al., 2012	74	3-10 (6.6)	Prospective cohort	Dense hemianopia/ quadrantanopia/general constriction	PLP; Suprathreshold lights	CT
Aslam et al., 2018	126	4-16 (12)	Prospective cohort	Glaucoma; Variable/relative defects	Game-based; SAP points - suprathreshold lights (potential for dimmer lights screen for defects)	HFA
Hirai et al., 1998	16	8-12	Case controlled study	Functional field defect	Starlight test	HFA, GKP
Koenraads et al., 2015	697	0.3-27.1 (3.4)	Prospective cohort	Dense hemianopia/ quadrantanopia/general constriction	BEFIE; 4 quadrants/supra-threshold object	GKP, HFA, Peritest
Portengen et al., 2020	115	BEFIE: 0.7-11.8 (4.5) SCP: 4.5-17.4 98.3)	Retrospective cohort	Dense hemianopia/ quadrantanopia/general constriction	BEFIE	GKP, HFA, Peritest
Satgunam et al., 2017	Total 29; 19 infants (normal: 5, developmenta l delay: 14) developmenta l delay: 5; cognitive impairment: 5	Developmental delay: 1.16-6; Cognitive impairment: 9 - 18	Prospective cohort	Dense hemianopia/ quadrantanopia /general constriction	LED; suprathreshold	HFA, CT

Electrophysiological methods						
Harding et al., 2002	39	3-15	Prospective cohort	VGB-associated; hemianopsia/ quadrantanopia	Field-specific VEP	Not specified
Kelly & Weiss, 2006	15	N/A (12.7)	Retrospective cohort	Optic pathway tumors; hemianopia/quadrantanopia	VEP	GKP
Marmoy, Handley & Thompson, 2021	9	2-14 (9)	Retrospective cohort /Observational case-series	Hemianopia	Pattern-onset and OFFset VEP	Octopus 900 static, CT
Moskowitz et al., 2012	114	2.4-266.1 months (22.9 months)	Retrospective cohort	VGB-associated; general field loss	ERG	HFA, GKP
Spencer & Harding, 2003	39	3-15 (9.5)	Prospective cohort	VGB-associated; peripheral field defect	Field-specific VEP	HFA
Modifications of standard perimetry						
Barnes et al., 2019	10	7-17 (20)	Prospective cohort	Retinal dystrophies; hemianopia/quadrantanopia/ general constriction	SKP	GKP
Clark, Timms & Franks, 1990	13	7-16 (mean 10.7)	Prospective cohort	Neuro-ophthalmic disease	OKP	GKP
Donahue & Porter, 2001	5	6-17	Retrospective cohort	Optic neuropathies (pediatric IIH, brain tumors)	SITA standard**	FT
Han et al., 2017	274 eyes	6-12	Cross-sectional	Glaucoma; variable field loss	FDT	HFA
Lobefalo et al.,1998	100	10.1-16.3 (13.3)	Prospective cohort	IDDM due to Diabetes, microalbuminuria	Blue on yellow	HFA
Martin & Nilsson, 2007	30	6-15	Prospective cohort	Pediatric glaucoma; neuro-ophthalmic/hemianopia/ quadrantanopia/general constriction	Rarebit	GKP
Moya et al., 2003	46	6-15 (10.29)	Prospective cross-sectional	Glaucoma; variable field loss	FDT	HFA
Patel et al., 2019	30	5-15 (11.1)	Cross-sectional	Neuro-ophthalmic disease	Octopus 900 kinetic	GKP
Youssef et al., 2017	40	N/A (14.37)	Case-control cross-sectional	HCQ associated retinal toxicity	Microperimetry	HFA

Eye tracking methods						
AlWattar et al., 2019*	18	10-18 (16)	Prospective cohort	Hemianopia/quadrantanopia	SVOP	HFA
Fleck et al., 2012*	7	N/A (47 months)	Prospective cohort	Hemianopia/quadrantanopia	SVOP	Not specified
Kooiker et al., 2016	126	1-14 (7.6)	Prospective cohort	Dense hemianopia/ quadrantanopia	Eye tracking; suprathreshold - quadrants	GKP, CT
Murray et al., 2016	Total: 22; Child patient: 10; Healthy children: 12	Child patients: 5-15 (11.5); Healthy children: 6-14 (10.4)	Prospective cohort	Hemianopia/quadrantanopia	SVOP	HFA
Murray et al., 2018	16	2.9-15 (7.2)	Prospective cohort	Brain tumors	SVOP	GKP, CT
Tailor et al., 2015	Total: 37; Neuro-disability: 16 Confirmed /suspected VF defect: 21	1–16; Neuro-disability: 1-16 Confirmed or suspected VF defect: 10– 16	Prospective cohort	Neuro-ophthalmic disease/neuro-disability; Dense hemianopia/ quadrantanopia	SVOP	GKP, CT

WSKP, white sphere kinetic perimetry; GKP, Goldmann kinetic perimetry; PLP, preferential looking perimeter; CT, confrontation testing; SAP, standard automated perimetry; HFA, Humphrey Field Analyzer; BEFIE, behavioral visual field screening test; LED, frequency doubling technology; VGB, vigabatrin; VEP, visual evoked potential; ERG, electroretinography; SKP, semiautomated kinetic perimetry; OKP, oculokinetic perimetry; IIH, idiopathic intracranial hypertension; SITA, Swedish interactive thresholding algorithm; FDT, frequency doubling technology; IDDM, insulin dependent diabetes mellitus; HCQ, hydroxychloroquine; SVOP, Saccadic Vector Optokinetic Perimetry; *abstract; **see section 2.3.3 on reference standards.

3.3 Assessment of Methodological Quality

The methodological quality is summarized in Figure 2 and detailed in Figure 3 and Table 3 for all studies. The risk of bias for each domain was determined using the 11 signaling questions from QUADAS-2 (Table 1). Patient enrollment was unclear for majority of the studies (74%) since many did not clearly state whether patients were consecutively or randomly enrolled. A majority of the studies (62%) avoided inappropriate exclusions. Most studies (62%) did not clearly state whether the index test results were interpreted without knowledge of the reference standard and vice versa. The criteria for an abnormal VF were not specified in 62% of studies. The reference standard(s) used in 30% of studies was inappropriate and not likely to correctly detect VF defects. The time interval between the index test and reference standard was not clearly stated in 67% of studies. Not all children were capable of testing with a reference standard in 62% of studies and not all children received the same reference standard in 67% of studies. Lastly, not all children were included in the analysis in 67% of studies in this review due to their inability to be tested with a reference standard or due to uninterpretable results. Based on the QUADAS-2 results (Figure 2), the overall risk of bias was high/unclear, while concern regarding applicability was low.

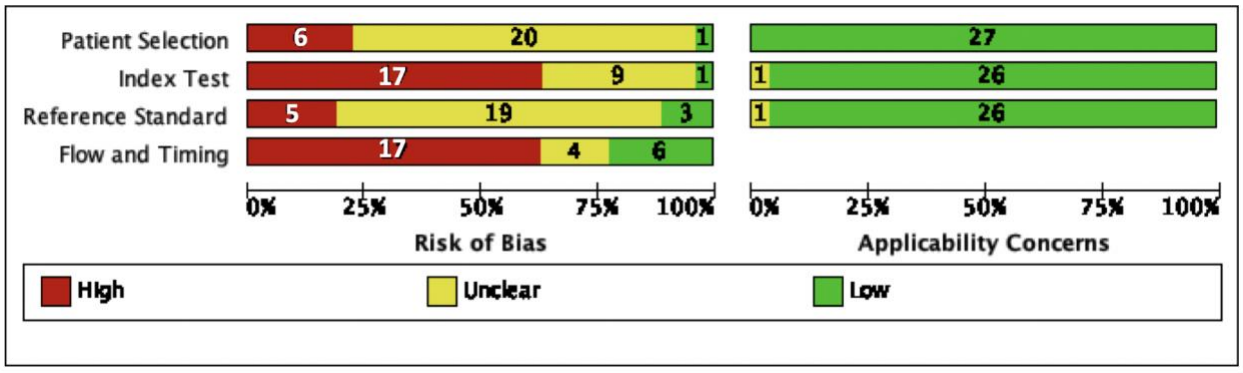

Figure 2. QUADAS-2 risk of bias assessment shows an overall high/unclear risk of bias and low applicability concerns.

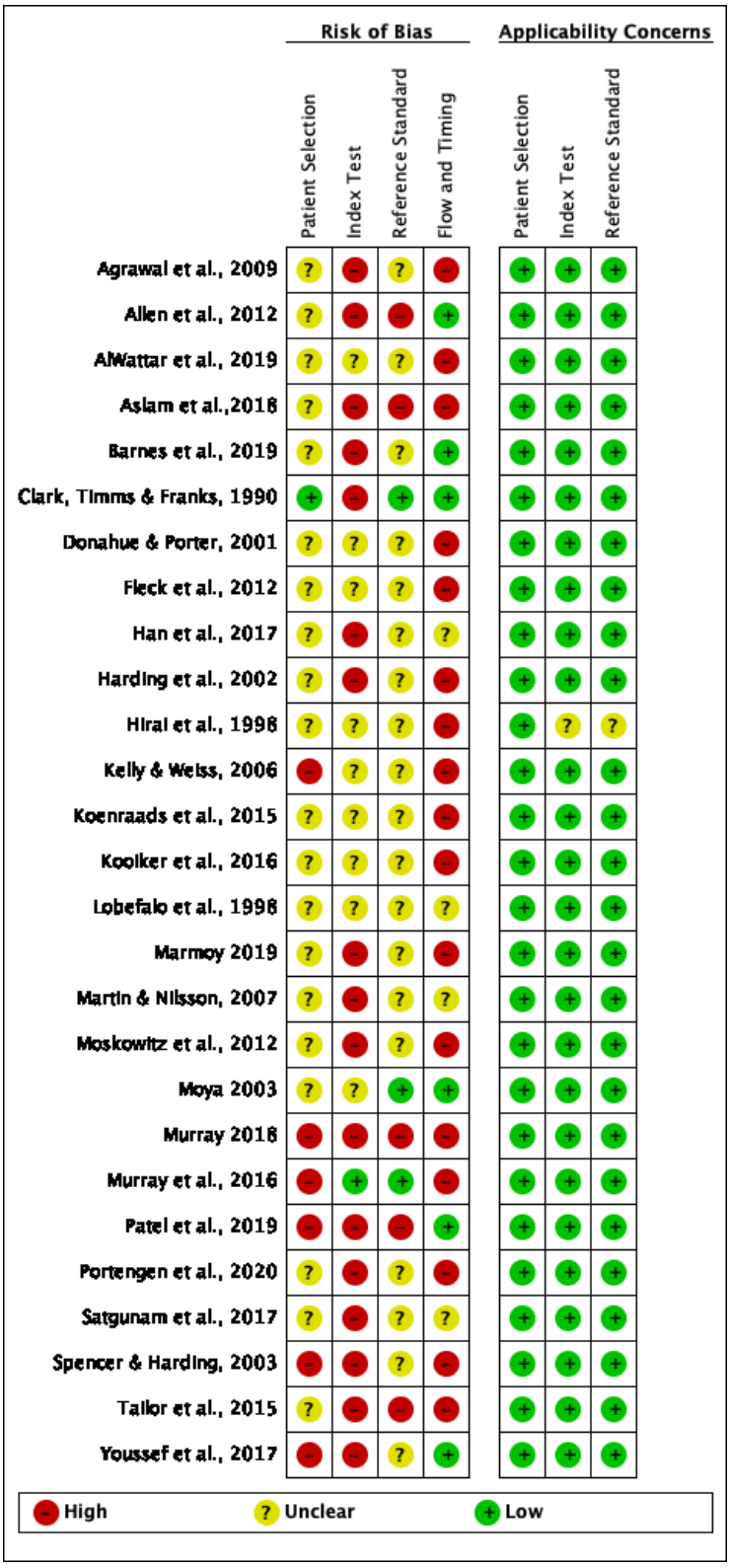

Figure 3. Risk of bias and applicability concerns summary for each included study.

Table 3. QUADAS-2 risk of bias signaling questions for each included study

	QUADAS-2 Signaling Questions										
	Domain 1			Domain 2		Domain 3		Domain 4			
Study	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**
Behavioral methods											
Agrawal et al., 2009	U	U	Y	Y	N	Y	U	U	N	Y	N
Allen et al., 2012	U	U	Y	U	N	U	N	Y	Y	Y	Y
Aslam et al., 2018	U	U	Y	N	N	Y	N	U	N	Y	N
Hirai et al., 1998	U	U	U	U	U	U	U	U	N	Y	U
Koenraads et al., 2015	U	U	Y	U	Y	Y	U	U	N	N	N
Portengen et al., 2020	Y	U	Y	U	N	Y	U	U	Y	N	U
Satgunam et al., 2017	U	Y	U	U	N	Y	U	U	N	N	N
Electrophysiological methods											
Harding et al., 2002	U	Y	U	U	N	Y	U	U	N	N	N
Kelly & Weiss., 2006	U	N	Y	U	Y	Y	U	Y	N	N	N
Marmoy, Handley & Thompson, 2021	U	Y	Y	N	N	U	U	U	Y	N	Y
Moskowitz et al., 2012	U	U	Y	U	N	Y	U	U	N	N	N
Spencer & Harding, 2003	U	U	N	U	N	Y	U	Y	N	N	N
Modifications of standard perimetry											
Barnes et al., 2019	U	Y	Y	U	N	Y	U	Y	Y	Y	Y
Clark, Timms & Franks., 1990	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Donahue and Porter 2001	U	U	U	U	Y	Y	U	U	N	Y	N
Han et al., 2017	U	U	U	U	N	U	U	U	U	U	U
Lobefalo et al., 1998	U	U	Y	U	N	U	U	U	Y	Y	Y
Martin & Nilsson, 2007	U	U	U	U	N	U	U	U	Y	Y	Y
Moya et al., 2003	U	Y	Y	Y	U	Y	Y	Y	Y	Y	Y
Patel et al., 2019	U	Y	N	N	N	Y	N	Y	Y	Y	Y
Youssef et al., 2017	U	N	Y	U	N	Y	U	Y	Y	Y	Y
Eye tracking studies											
AlWattar et al., 2019*	U	Y	Y	U	U	Y	U	U	N	Y	N
Fleck et al., 2012*	U	Y	U	U	U	U	U	U	N	U	U
Kooiker et al., 2016	U	U	Y	U	Y	Y	U	U	N	N	N
Murray et al., 2016	N	U	Y	Y	Y	Y	Y	Y	N	Y	N
Murray et al., 2018	U	Y	N	N	Y	U	N	U	N	Y	N
Tailor et al., 2015	U	U	Y	N	N	Y	N	U	N	Y	N

Yes , Unclear No; *abstract

3.4 Diagnostic Accuracy

Eight of 27 studies reported sensitivity and specificity data (Table 4). The range of sensitivity in these studies was 60 to 100% and the range of specificity 50 to 100%. Allen et al (2012) compared the diagnostic accuracy of PLP, a behavioral method, with CT in healthy children and children who had neurological or ocular pathology ages 3-10 years. PLP was found to have a sensitivity and specificity of 100%. Of the 21 children who had uninterpretable results from CT, PLP provided interpretable results in 15 children (71%). Game based perimetry (Casper's Castle) reported by Aslam et al. (2018) had a comparable sensitivity (81.4%) and specificity (88.9%) when compared with HFA in healthy children and children with simulated glaucomatous defects (4-10 years). Koenraads et al. (2015) compared the diagnostic accuracy of the BEFIE test with SCP (GKP, HFA, Peritest) in young healthy or neurologically impaired children. The BEFIE test had a lower sensitivity (60%) due to absolute scotomas and relative VF defects being undetected, but had relatively high specificity (98%).

Spencer & Harding (2003) reported a sensitivity of 75% and a specificity of 85.7% for field-specific VEP, an electrophysiological method, compared to HFA in vigabatrin-treated children (3-15 years) with epilepsy. Harding et al. (2002) found a similar sensitivity (75%) and specificity (87.5%) as Spencer & Harding (2003) for field-specific VEP in an earlier study with a similar sample of patients. Murray et al. (2016) also found sensitivity and specificity of 100% for SVOP, an eye tracking method, when compared with HFA in children ages 5-15 years. However, high false-positive rates and number of fixation losses resulted in the exclusion of many HFA tests, as they were considered unreliable. Another study by Murray et al. (2018) compared the diagnostic accuracy of SVOP with GKP in children with brain tumor, ages 2.9-15 years, in which 6 patients performed both tests. SVOP in this study also yielded a sensitivity of 100%, but

lower specificity (50%). In contrast, Tailor et al (2016) found SVOP to be of poor accuracy (50%) when compared with CT in younger children (1-16 years) with neuro-disability and a relatively higher accuracy (64.7%) in older children (10-16 years) when compared with GKP.

The confidence intervals (CIs) in Figure 4 and Table 4 describe with 95% certainty that the true sensitivity and specificity values for that index test lie within the listed interval. Behavioral methods had wider CIs for sensitivity (50-100%) and narrower CIs (hence greater accuracy) for specificity (81.2-100%) than SVOP and VEP studies. CIs were not reported in VEP and SVOP studies and were estimated in RevMan for the forest plots (Figure 4). Overall, eight studies utilizing behavioral (3), VEP (2), and eye tracking (3) tests showed sensitivities of 60-100%, 75%, 70-100%, and specificities of 89-100%, 85.7-87.5%, and 50-100%, respectively.

Table 4. Included studies that reported sensitivity and specificity

Study	Index Test	Reference Standard	Sensitivity % (CI)	Specificity % (CI)
Behavioral methods				
Allen et al., 2012	PLP	CT	100 (95 CI, 82-100)	100 (95, 90-100)
Aslam et al., 2018	Game-based	HFA	81.4 (95, 81.2-95)	88.9 (95, 81.2-95)
Koenraads et al., 2015	BEFIE	GKP, HFA, Peritest	60 (95% CI, 50-71)	98 (95% CI, 95-100)
Electrophysiological methods				
Spencer & Harding, 2003	VEP	HFA	75*	85.78*
Harding et al., 2002	VEP	Unspecified	75*	87.5*
Eye tracking methods				
AlWattar et al., 2019**	SVOP	HFA	70*	91.5*
Murray et al., 2016	SVOP	HFA	100*	100*
Murray et al., 2018	SVOP	GKP, CT	100*	50*

Eight studies categorized by type of index test showing varying sensitivity and specificity. CI, confidence interval; PLP, preferential looking perimeter; CT, confrontation testing; HFA, Humphrey Field Analyzer; BEFIE, behavioral visual field screening test; GKP, Goldmann kinetic perimetry; VEP, visual evoked potential; SVOP, Saccadic Vector Optokinetic Perimetry; *95% confidence interval missing; **abstract.

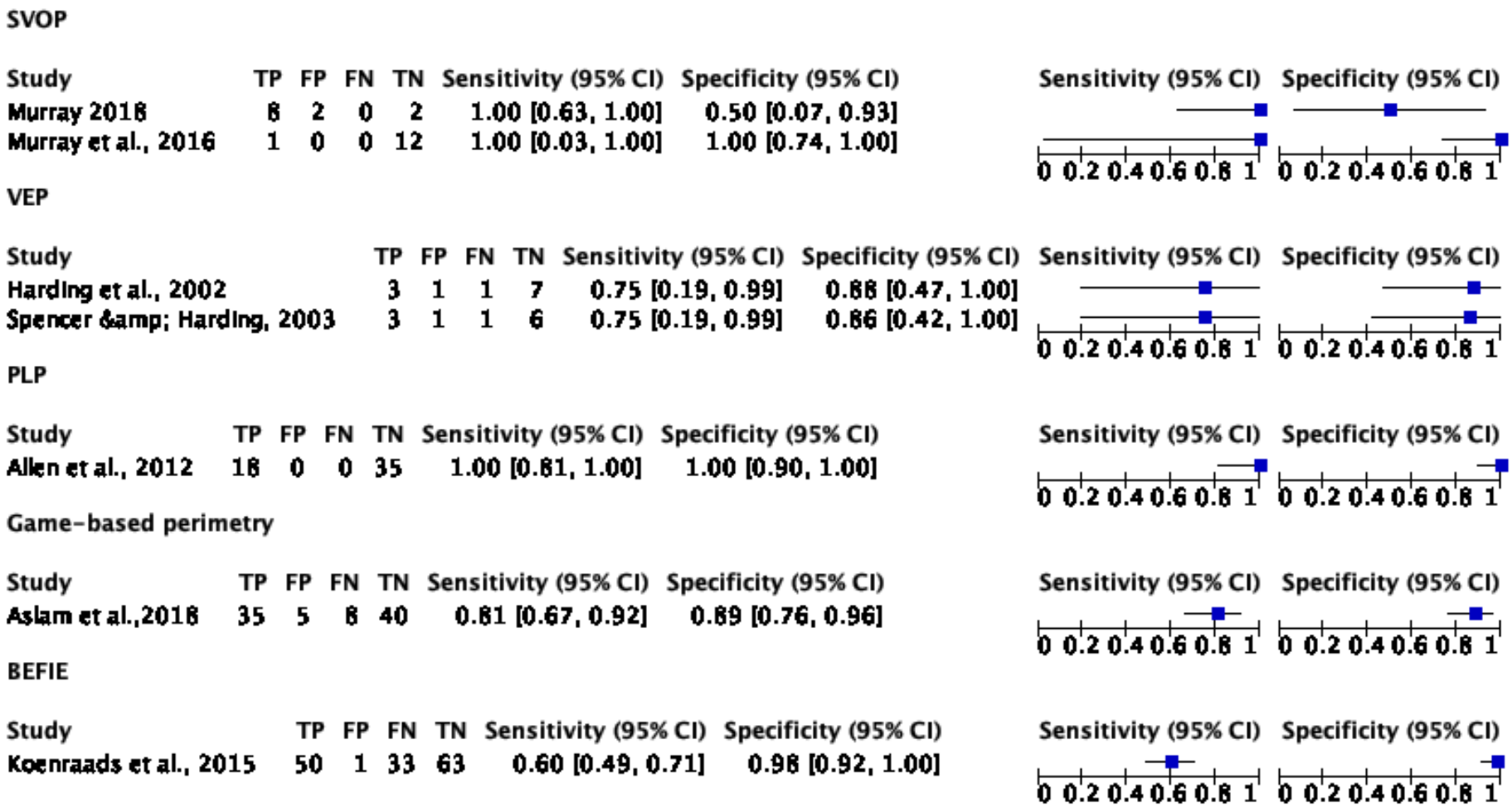

Figure 4. Paired forest plots showing sensitivity and specificity. Eight studies utilizing behavioral (3), VEP (2), and eye tracking (3) tests showed sensitivities of 60-100%, 75%, 70-100%, and specificities of 88.9-100%, 85.8-87.5%, and 50-100%, respectively. TP, true positive; FP, false positive; FN, false negative; TN, true negative; CI, confidence interval; BEFIE, behavioral visual field (BEFIE) screening test; VEP, visual evoked potential; SVOP, Saccadic Vector Optokinetic Perimetry; PLP, preferential looking perimeter.

3.5 Feasibility

Nine of 27 (33.3%) studies reported feasibility data (Table 5). PLP was successfully performed in 32/32 (100%) healthy children and 36/42 (85.7%) children with ocular or neurological pathology (3-10 years) (Allen et al., 2012). Moreover, PLP could be performed in 15/21 (71%) of children who had uninterpretable results from CT. For example, a 10-year-old patient with unilateral blindness resulting from an optic nerve glioma could not perform CT because of an inability to maintain central fixation, but was able to be tested with PLP. WSKP demonstrated a high feasibility of 90.3%, where 28/31 Vigabatrin-treated children (1-19 years) were able to be tested. The remaining 3 children who could not be tested had severe developmental delay. In the game-based perimetry study (Casper's Castle) conducted by Aslam et al., (2018), 109/126 (86.5%) from the simulated glaucoma group successfully completed the VF test (4-16 years). Spencer & Harding, (2003) found that field-specific VEP could be performed in 35/39 (89.7%) of the children (3-15 years) with epilepsy taking vigabatrin. Patel et al. (2019) reported that 22/29 (75.9%) children (5-15 years) completed Octopus perimetry and the remaining 7 were unable to as a result of poor cooperation and not being able to plot the blind spot.

In different studies, SVOP demonstrated feasibility that varied from 63.6% to 94.5%. AlWattar et al. (2019) reported successful completion of SVOP testing (33 points) in 17/18 (94.4%) pediatric patients (10-18 years) with known or suspected VF loss. In a study by Tailor et al. (2016), 19/21 (90.5%) of the children (10-16 years) with known or suspected VF defects successfully performed the SVOP test with reduced protocols (14 points) while 13/21 (62%) were able to complete the full protocol (40 points). The remaining two children who could not complete reduced protocol SVOP had childhood glaucoma which interfered with testing due to

corneal changes. In the neuro-disability group (1-16 years), 16/16 (100%) of children (1-16 years) could be tested with reduced protocols, while only 2/16 (12.5%) were able to complete the full protocol (Tailor et al., 2016). Murray et al (2018) found that 12/16 (75%) children (2.9-15 years) with known or suspected brain tumors successfully performed SVOP testing. SVOP could not be performed in the remaining four children in the study because of poor quality eye tracking (Murray et al., 2018). In an earlier study by the same group, 14/22 (63.6%) of children completed the full protocol (41 test points, 2 sessions) of SVOP testing (Murray et al., 2016). All twelve (100%) healthy children were able to complete the full protocol, while only 2/10 (20%) child patients with suspected VF defects were testable. Half the protocol (1 session or 1 eye) was able to be completed by 8/10 (80%) child patients. Reasons for incomplete SVOP testing included long testing times and poor eye tracking. Overall, nine studies utilizing behavioral (n=3), electrophysiological (n=1), modifications of standard perimetry (n=1), and eye tracking (n=4) tests showed feasibility of 85.7-100%, 89.7%, 75.9%, and 20-100%, respectively.

Table 5. Included studies that reported feasibility

Study	Age range in years (mean or median)	Index Test	Feasibility (%)
Behavioral methods			
Agrawal et al., 2009	1-19 (6)	WSKP	VGB patients: 28/31 (90.3);
Allen et al., 2012	3-10 (6.6)	PLP	Healthy children: 32/32 (100) Ocular or neurological pathology: 36/42 (85.7)
Aslam et al., 2018	4-16 (12)	Game-based	Simulated glaucoma group: 109/126 (86.5)
Electrophysiological methods			
Spencer & Harding., 2003	3-15 (9.5)	Field specific VEP	35/39 (89.7)
Modifications of standard perimetry			
Patel et al., 2019	5-15 (11.1)	Octopus 900 kinetic	22/29 (75.9)
Eye tracking methods			
AlWattar et al., 2019*	10-18 (16)	SVOP	17/18 (94.4)
Murray et al., 2016	Child patients: 5-15 (11.5) Healthy children: 6-14 (10.4)	SVOP	Child patients: 2/10 (20) Healthy children: 12/12 (100)
Murray et al., 2018	2.9-15 (7.2)	SVOP	12/16 (75)
Tailor et al., 2015	Group 1 (neuro-disability): 1-16 Group 2 (confirmed or suspected VF defects): 10-16	SVOP	Group 1: 16/16 (100) Group 2: 19/21 (90.5)

Nine studies categorized by index test showing varying feasibility. WSKP, white sphere kinetic perimetry; VGB, vigabatrin; PLP, preferential looking perimeter; VEP, visual evoked potential; SVOP, Saccadic Vector Optokinetic Perimetry; *abstract.

Chapter 4: Discussion

This systematic review aimed to evaluate the diagnostic accuracy and feasibility of non-standard VF tests in children with diverse disorders of the visual pathway. In effect, this review addresses the challenges associated with standard perimetry in children. A diagnostic test accuracy (DTA) review has a primary objective of comparing a non-standard VF test (index test) to a pre-determined reference standard. This DTA review used broad inclusion criteria to increase the number of eligible studies. However, despite the broad inclusion criteria, only 27 studies were included, and only 8 studies reported sensitivity and specificity data (Figure 4; Table 4). Studies of all types of non-standard VF tests were included, with different visual pathway disorders (target conditions), as well as studies that used more than one reference standard. The different index tests were categorized as follows: behavioral methods, electrophysiological methods, modifications of standard perimetry, and eye tracking (Table 2). Since several studies did not report quantitative data, studies in which the results were qualitatively described were included and contributed to identifying the strengths and limitations of pediatric VF tests. A meta-analysis could not be performed due to sample heterogeneity, insufficient quantitative data, and a small sample of studies included. Consequently, findings from this systematic review have been descriptively assessed in a narrative synthesis. Some advantages of a narrative synthesis include comparison between study findings and identification of patterns in the results (Ryan 2013).

4.1 Interpretation of QUADAS-2 Results

The risk of bias, based on the QUADAS-2 results, was unclear or high for most studies, while concerns regarding applicability were low (Figure 2; Figure 3; Table 3). QUADAS-2 highlighted the need for improvement of the quality of the studies. There were several limitations

found in the studies included in this review that could account for the high/unclear risk of bias. Some reasons for the high or unclear risk of bias include inadequate reporting of methods, and missing important information, such as how the patients were selected, the time interval between the index and reference test, and if the index test results were interpreted without the knowledge of the reference standard and vice versa. Examples of bias in our review to be discussed in this section include verification bias, patient selection bias, and information bias.

Due to the challenging nature of VF testing in children, 63% of the studies found that not all children were tested using a reference standard, indicating partial verification bias. For example, in a BEFIE study by Koenraads et al. (2015), patients whose VFs could not be tested with SCP (GKP, Peritest, and HFA) were not tested with CT. Of the 697 children who were reliably tested with the BEFIE test, only 79 (11.3%) children (5.2-17.5 years) also received a reference standard (SCP). This means that healthy controls and older children without neurological impairment could be over-represented, as these children are more capable of being tested with a reference standard. Similarly, in the VEP study by Kelly & Weiss (2006), only 15 of 40 (37.5%) patients (8-20 years) were able to perform GKP. No explanation was provided for not attempting CT in the remaining patients who were unable to perform perimetry. In the VEP study by Harding et al. (2002), only 12 of 39 (30.8%) patients (3-15 years) completed perimetry and CT was not attempted in the remaining 27 (69.2%) patients. Such studies may have shown higher concordance of index test with reference standard because of a partial, internal verification bias. Moreover, differential verification bias exists across studies (67%), where more than one reference standard was used.

Furthermore, patient selection bias was evident in 74% of the studies because in most cases there was no consecutive or random enrollment. In these studies, patients with known or

suspected VF loss due to disorders of the visual pathway were recruited and a retrospective analysis of patient cases for evaluating diagnostic accuracy of pediatric VF tests was conducted. Thus, a case-control study design was evident in most studies, which could result in the overestimation of diagnostic accuracy because patients with known VF defects may possibly be easier for a VF test to detect.

In 30% of the studies, the reference standard was found to not be as sensitive as the index test. The reference standard did not correctly classify the target condition, and thus, the index test could not be correctly classified. For example, a study by Hirai et al. (1998) suggested that GKP was not appropriate for the detection and diagnosis of functional visual loss. In this study, the index test, called the Starlight test, performed by an 8-year old child determined that the patient's VF was normal as opposed to the substantial VF constriction mistakenly identified by GKP. Another example is the study by Martin & Nilsson (2007) which found that 60% of eyes (9/15) in their study demonstrated a normal VF using GKP while abnormal results were found with Rarebit perimetry.

Furthermore, the time interval between the index test and reference standard was not clearly stated in 67% of studies, indicating the possibility of bias due to differences in disease status. Information bias could also result in misestimation of index test accuracy. Most studies (67-70%) were unclear about whether the interpretation of the index test was done without knowledge of the reference standard results, and vice versa. There may be no way to guarantee lack of information bias unless both index test examiners and reference standard examiners are unaware of relevant test results. This is one of the drawbacks of case-control and retrospective study designs.

4.2 Diagnostic Accuracy and Feasibility

Based on the eight (30%) studies that reported sensitivity and specificity data, PLP, a behavioral method, yielded the highest sensitivity (100%) and specificity (100%) in children ages 3-10 years (Allen et al., 2012). However, it is possible that the examiner's interpretation of PLP results following CT may have been biased based on previous knowledge of the patients and their standard VF test results. SVOP, a method of eye tracking, had varying estimates of diagnostic accuracy (Table 4). Specificity of SVOP was reported to be low as 50% (3-15 years) and as high as 100% (5-15 years) in other studies (Murray et al. 2018; Murray et al. 2016). The study by Murray et al. (2016) did report sensitivity and specificity of 100% for SVOP, but also found high false-positive rates and fixation losses. Of the behavioral methods, the BEFIE test had the lowest sensitivity (60%) but high specificity (98%) (Koenraads et al., 2015). In general, non-standard behavioral methods demonstrated higher specificity and eye tracking methods showed higher sensitivities (Table 4). The two VEP studies each reported the same sensitivity (75%) and comparatively high specificities (86%-87.5%) (Spencer & Harding, 2003; Harding et al., 2002). VF tests that were modifications of standard perimetry, did not report any sensitivity and specificity values to measure their accuracy. The large range of CIs in some studies reporting sensitivity and specificity suggested low accuracy.

Multiple considerations go into deciding which VF test to conduct on a child. A clinician who wants to rule in a diagnosis will choose a highly specific test and one who wants to rule out a diagnosis will choose a highly sensitive test (Saunders et al., 2015). Although high values of sensitivity and specificity outcome measures are ideal, both measures represent a tradeoff with respect to the other. A highly sensitive test will be less specific and vice versa, and this impacts the value selected to diagnose a patient with a positive or negative test result, leading to

fluctuations in what we call “false positives” and “false negatives” (Saunders et al., 2015). Ultimately, even in a highly sensitive test, such as with sensitivity measures ranging from 70% to 100%, a positive test result will need to be independently confirmed when a condition has low prevalence (Saunders et al., 2015). Thus, test results are not interpreted as true positives and true negatives based on the sensitivity and specificity values and are impacted by factors like prevalence of a condition in the population and goals of the clinician when choosing a test and making a diagnosis and/or treatment decision (Saunders et al., 2015).

Only nine (33.3%) studies reported feasibility considered as the success rate of a VF test (Table 5). Feasibility was consistently higher for non-standard behavioral methods, ranging from 85.7% for children with ocular pathologies up to 100% for healthy children (Agrawal et al., 2009; Allen et al., 2012; Aslam et al., 2018). Only one study reported feasibility for both electrophysiological (Spencer & Harding et al., 2003) and modifications of perimetry (Patel et al., 2019) methods, reporting 89.7% (3-15 years) and 75.9% (5-15 years), respectively. For eye tracking studies, feasibility ranged from 20% to 100% (AlWattar et al., 2019; Murray et al., 2016; Murray et al., 2018; Tailor et al., 2015). That feasibility was much higher for behavioral methods suggests that these highly specific behavioral VF tests can be a good alternative for younger children who are unsuccessful in completing eye tracking tests. Overall, eye tracking methods such as SVOP and behavioral methods, such as PLP, show potential for diagnostic accuracy and feasibility. However, the small sample size of primary studies makes it difficult to conclude if these types of VF tests can be completed successfully by children in actual clinical settings.

4.3 Summary of Pediatric Visual Field Tests

Below is a discussion of an overview of non-standard pediatric VF tests included in this systematic review. See Table 2 for outcome measures described in this section as well as the strengths and weaknesses of each category of pediatric VF test.

4.3.1 Behavioral Methods

Behavioral tests depend upon the child's attention and ability to respond overtly to test stimuli. The child's age and developmental status covary with the type of field test that can be done, and with the types of field defects and conditions that can be tested. Thus, the types of behavioral tests that young children under age 5 years are able to perform - necessarily involving suprathreshold stimuli - can provide information about major field defects (e.g. hemianopia, quadrantanopia). Threshold testing as with SAP can be done with children age 5 and older, although the youngest require familiarization procedures, and extensive testing may not be successful. Many non-standard behavioral methods of VF testing have been reported in the past several years. WSKP can potentially identify vigabatrin associated VF loss (Agrawal et al., 2009). WSKP is shown to have similar VF extents as Goldman perimetry and is feasible in children and those with developmental delay (Agrawal et al., 2009). Thus, WSKP has been used successfully to test VFs in diverse pediatric disorders, including in infants with ROP (Luna et al., 1989; Quinn et al., 1996).

Casper’s Castle is a computer-based game that is appealing to children and does not require expert supervision (Aslam et al., 2018). This game-based perimetry is shown to be effective for the detection of scotomas and relative VF defects in children and has potential to be used as a screening tool for children of 5-7 years (Aslam et al., 2018). In general, gamification of perimetry is more engaging for the pediatric population. However, this particular method of VF

testing may not be suitable for children 9 years and older due to loss of fixation as the patient scans for the peripheral target (Aslam et al., 2018). Modification to increase complexity of the test might allow testing older children. Game-based perimetry may also not be suitable for children younger than 5 years and developmentally delayed children as it requires attention and cooperation. Eye tracking technology might improve diagnostic accuracy for children of all ages.

PLP may be useful for assessing VFs in children who otherwise can only be tested with CT. An advantage of PLP is that the child can perform the test without restriction while sitting on the parent's lap (Allen et al., 2012). While PLP is potentially able to identify dense VF loss, the test as constituted may be unable to detect reduced sensitivity or scotoma losses. Another limitation of PLP is that interpretation of the results requires experience in forced-choice preferential looking methods. The BEFIE test is another potential alternative to standard perimetry and was shown useful for identifying peripheral VF defects in young or neurologically impaired children with suspected pre- or post-chiasmal lesions (Koenraads et al., 2015). Its utility has been described in the early detection of conditions such as optic pathway glioma and craniopharyngioma as well as visual field defects of hemianopia and quadrantanopia (Koenraads et al., 2015). However, this method is not appropriate for detecting relative defects or absolute scotomas, and requires both an experienced examiner and observer (Koenraads et al., 2015).

4.3.2 Electrophysiological Methods

Electrophysiological tests (ERG & VEP) which do not rely on overt behavior represent a solution to the behavioral attention problems in testing young children. However, the substrates for responses to these tests, retinal function in ERG, and cortical function in VEP, constrain the types of VF defects/conditions that can be effectively tested. This is not an age or developmental

status issue, but rather what aspect or level or function of the visual system is tested by these methods. The role of VEP is well established in the literature for detecting vigabatrin-associated peripheral field loss in epileptic children (Harding et al., 2002; Moskowitz et al., 2012; Spencer & Harding, 2003). Studies have shown that field-specific VEP can be performed in children as young as 3 years of age (Harding et al., 2002). Some studies have even considered field-specific VEP combined with 30 Hz flicker ERG to be the most suitable technique for detecting VF loss associated with vigabatrin in children less than 10 years of age (Harding et al., 2002). Moreover, VEP is well tolerated in children, including those with developmental delay, and is reported to have high compliance (90%) (Harding et al., 2002). Spencer & Harding (2003) found that field-specific VEP is a robust test for detecting vigabatrin-associated peripheral VF loss in children (3-15 years). VEP has also been shown to be a sensitive, objective, reliable method for identifying VF loss secondary to optic pathway gliomas in children who are unable to cooperate with SCP (Kelly & Weiss, 2006). VF loss was reliably indicated by reduced amplitude and signal-to-noise ratio (SNR), whereas hemianopic VF loss could not reliably be identified using interhemispheric VEP asymmetry (Kelly & Weiss, 2006).

A limitation of VEP is that progressive VF loss cannot be measured when there is a severe reduction in VEP amplitudes and SNRs (Kelly & Weiss, 2006). Pattern-OFFset VEP has been shown to be effective for assessing the macular pathway, and may be useful for hemianopic patients who are not able to perform half-field testing such as children (2-14 years) or patients with nystagmus (Marmoy, Handley & Thompson, 2021). Pattern-OFFset VEP is also an objective method for identifying chiasmal and hemispheric defects. However, pattern-OFFset VEP may not be useful for evaluating peripheral field loss or VF loss with macular sparing, or post-chiasmal lesions (Marmoy, Handley & Thompson, 2021). Thus, some studies found VEP to

be more sensitive than BEFIE tests in children, but both with high measure of specificity (Spencer & Harding et al., 2002; Harding et al., 2002). VEP and other methods including game-based perimetry could be completed by children with various types of vision loss.

4.3.3 Modifications of Standard Perimetry

Several perimetric methods have been developed that do not depend on white-on-white stimulation (in HFA, for example), such as Rarebit perimetry and frequency doubling technology (FDT). Rarebit perimetry is a computerized technique that is shown to be suitable for detecting various glaucomatous VF defects in children of 6-15 years with pediatric glaucoma (Martin & Nilsson, 2007). Short testing time makes it advantageous for testing children. Oculokinetic perimetry (OKP) is a technique that involves the movement of eyes around a stationary target and tests the VF using a chart at reading distance (Clark, Timms & Franks, 1990). OKP was shown to be reliable in children of 7-16 years with ophthalmic and neurological disorders compared to GKP. Unlike GKP, OKP is not dependent on the perimetrist's skill or costly equipment and does not require prolonged fixation. The psychological response of the child, including reliability and cooperation, can also be better assessed using OKP due to the proximity of the examiner (Clark, Timms & Franks, 1990). Macular sparing in hemianopic defects were better shown by OKP (Clark, Timms & Franks, 1990). However, a disadvantage of OKP is that it tests only the central 25 degrees of the VF (Clark, Timms & Franks, 1990). Potential modifications to OKP may include using fewer than 100 points to reduce fatigue and using numbers instead of symbols to increase attention (Clark, Timms & Franks, 1990).

Compared to achromatic perimetry or white-on-white stimuli, blue-on-yellow perimetry (aka SWAP) has been shown to be more useful for detecting subtle VF defects in diabetic children (10-16 years) with microalbuminuria (Lobefalo et al., 1998). Blue-yellow color vision

deficits commonly precede diabetic retinopathy, due to the increased susceptibility of short wavelength cones to damage caused by hyperglycemia, and are also characteristic of dominant optic atrophy (Lobefalo et al., 1998; Lenaers et al., 2012). Microperimetry is another technique that could be useful for assessing retinal sensitivity in children who are taking hydroxychloroquine (HCQ), or have inherited retinal conditions affecting the macular area. Microperimetry tests the VF while also visualizing the fundus, allowing for the correlation between functional and retinal deficits (Youssef et al., 2017). One limitation of microperimetry is that it is very specific to macular testing, and in HFA perimetry, tests the central 10 degrees. Microperimetry in mid-peripheral retina is not yet possible, nor is binocular testing.

Octopus automated kinetic perimetry has the potential to replace GKP as the gold standard kinetic perimetry, importantly as GKP is no longer commercially available (Patel et al., 2019). Octopus automated kinetic perimetry was shown to be useful for children of 8 years or older with neuro-ophthalmic disease (Patel et al., 2019). However, there were more occurrences of inaccurately plotted blind spots, highlighting the importance of maintaining fixation; test accuracy in Octopus kinetic perimetry could be improved by halting the stimuli presentation until the patient reestablishes fixation. Additionally, Octopus perimetry underestimated severe VF loss shown by GKP (Patel et al., 2019). Due to the differences between GKP and Octopus kinetic perimetry, it is not advised to use the perimeters interchangeably and implications for switching from GKP to Octopus should be kept in mind.

The HFA SITA strategy, a modification of FT strategy, has shown potential for testing in children (6-17 years) in addition to adults. In comparison to FT, SITA was demonstrated to reduce testing time by 50% with no loss in accuracy (Donahue and Porter, 2001), leading to less variability due to a reduction in fatigue.

4.3.4 Eye Tracking Methods

A major advantage of eye tracking technology for VF testing includes that a fine motor response to indicate detection of a peripheral stimulus is not required. Eye tracking methods depend upon naturally occurring eye movements (saccades) in response to peripheral stimuli. Tobii Technology (Version 2 and later), used in all the eye tracking VF studies in this DTA review, allows for free head movement during testing, correcting for peripheral stimulus location by head-eye position. SVOP has shown greater potential for testing thresholds and sensitivity than non-standard behavioral testing. This potential is shown by studies of glaucoma using SVOP in adults (Grillini et al., 2021; Murray et al., 2017; Tatham et al., 2021; McTrusty et al., 2017).

However, in general there are limitations in SVOP and eye tracking. For instance, calibration is required, test times may be long especially in young children, and full field protocols may not be attained in young and neurologically impaired children (Murray et al., 2016; Murray et al., 2018; Tailor et al., 2016). Additionally, older children may become bored with the SVOP procedure (Murray 2011).

Additionally, there are factors that can contribute to poor eye tracking, resulting in an impaired corneal reflex and inaccurate pupil detection. These include "(1) dry eye and reduced ocular surface integrity, (2) spectacles, (3) irregular pupil shape, (4) strabismus, (5) nystagmus, and (6) eye makeup" (Murray et al., 2016; Murray et al., 2018). Poor eye tracking has been demonstrated in patients with unstable fixation due to marked optic atrophy and a cloudy cornea due to congenital glaucoma with buphthalmos (Murray et al., 2018). These problems are not unique to SVOP but are seen with eye tracking generally.

SVOP has not been shown to be successful in testing children under age 4 years, although Murray (2011) has described SVOP's potential for testing infants as young as 8 months old. Animations can be used in SVOP to help maintain attention in younger children during VF testing (Murray et al., 2018). More efficient eye tracking protocols and animations may enable successful testing of children younger than age 4 years. Game-based procedures may engage older children.

4.4 Strengths and Limitations

This review is likely the first DTA study of diagnostic accuracy and feasibility of pediatric VF tests. The results of this DTA review will add to the limited evidence base on pediatric VF test accuracy. Broad inclusion criteria increased the number of included studies, enabling identification of clinically relevant trends and patterns for future diagnostic and prognostic utility. Despite this, a relatively small number of studies met the eligibility criteria. Thus, the results of this DTA review may not be generalizable to the pediatric population. Also, studies of poor quality may have been included as a consequence of using broad inclusion criteria. Other limitations of this review include small sample sizes of the studies, and restriction to English language only. The results from this systematic review could not be quantitatively synthesized. Despite broad inclusion criteria including all non-standard pediatric VF tests, all visual pathway disorders, and multiple reference standards in studies reported over 31 years, no combinations could be evaluated in a comparable manner. As a result, a meta-analysis was not appropriate for these studies due to their heterogeneity and the small sample sizes included per comparison combination. As shown in Table 4, only 8 of 27 studies reported diagnostic accuracy values (sensitivity and specificity) and data that could be used to calculate those measures (TP, TN, FP, and FN).

Moreover, this DTA review identified several gaps in the field of VF testing in children. This review found that there is no consistent literature on the diagnostic accuracy of pediatric VF tests. Without sufficient studies and reliable and complete evidence, clinical practice is not well informed. Thus, more studies of these pediatric and other VF tests as they are developed are needed to determine diagnostic accuracy in children. Many studies in this DTA review had a high/unclear risk of bias. High/unclear risk of bias could be due to poor study design, inadequate reporting, and missing information. Moreover, the diagnostic accuracy values are based on small sample sizes due to the inability of most children to perform SCP. Accepting multiple reference standards, including CT, is another limitation of the review. However, not including CT as a reference standard would have excluded studies of younger and neurologically impaired children. Overall, the challenging nature of VF testing in children due to the attentional demands of the procedures may explain some of the limitations of these DTA studies.

4.5 Future Directions

To address the gaps in knowledge of pediatric VF testing identified by this DTA review, more detailed studies of pediatric VF tests with better reporting are needed to determine the diagnostic accuracy and feasibility of these tests. Moreover, studies with larger samples need to be conducted, and all participants should be tested with a reference standard. These studies must be designed so that appropriate quantitative data (e.g. sensitivity and specificity) can be analyzed. Murray et al. (2016) suggested giving children additional time to practice performing standard perimetry (e.g. HFA) to increase their testability and reliability of the results. Although clinically relevant outcomes of the VF tests that were studied and included in the systematic review were reported, future DTA studies should more closely follow reporting guidelines (e.g. STARD, PRISMA) and endeavor to reduce bias. Further research on eye tracking methods,

should consider conducting studies involving a larger number of participants, particularly children younger than 5 years, in order to determine more reliable estimates of sensitivity and specificity.

Lastly, an exciting new field in VF testing includes virtual reality (VR) testing currently being investigated in adults. These include both VR conventional VF exams for routine and ocular pathology patients, novel head-mounted VF screening devices, and supplementation of at-home glaucoma patient monitoring with the use of VR-enabled VF testing devices (Stapelfeldt et al., 2021, Mees et al., 2020, Hu et al., 2023). No published studies using VR perimetry met the eligibility criteria of this DTA review, and thus could not be included. However, the use of VR VF screening devices in children looks to be promising given the success of game-based perimetry and is an area of future research with clinical significance.

4.6 Conclusions

Findings from this DTA review suggest that validity of new tests of the VF for children may be limited to certain conditions and VF defects and ages. Neurological VF defects, such as hemianopia and quadrantanopia were more easily detected by most successful pediatric VF tests. Children ages 5 years and older are testable by most procedures with the use of familiarization and game-like methods. New innovations in VF testing in children have potential for superior VF accuracy with sensitivities and specificities of up to 100% for behavioural and eye tracking VF tests. Studies show that eye tracking perimetry is applicable to variety of conditions, although limited to children 5 years or older, and has the potential for being a reference standard for future VF testing in children. However, the results from this review should be interpreted with caution due to the small number of studies included, small sample size, heterogeneity, lack of well-designed studies comparing new index tests with reference standards, and limited sensitivity and

specificity data. Conclusions with regard to diagnostic accuracy may not be generalizable to the whole pediatric population. Overall, our review identified important gaps in studies on VF testing and highlighted areas for improvement for future research on test accuracy.

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Appendix 1: Search Strategy

Ovid EMBASE

(Perimetry/ OR Ophthalmic Perimeter/ OR (perimetr* OR perimetry OR campimetr* OR MKP OR MP1 OR MP-1 OR Accumap OR Easyfield OR Easy-field OR M700 OR MonCVOne OR Heidelb?rg-Edge OR Octopus-101 OR Octopus-500 OR Octopus-900 OR (HFA NOT height-for-age NOT hydrofluo* NOT human-flora NOT human-gut NOT home-field-advantage NOT MDI NOT cardi* NOT hydrox* NOT high-frequency-activit* NOT herbal-feed-additive NOT asthma NOT Hageman-factor NOT hexafluo* NOT Hypogloss* NOT health-facility-assessment NOT anemia NOT anaemia NOT PEFF NOT heart-failure NOT adipo* NOT ferulic-acid* NOT folic-acid* NOT healthy-families-america NOT resin NOT BDP NOT tetraflu* NOT primatene* NOT human-fetuin-A NOT inhaler NOT Ventolin NOT high-frequency-antigen NOT hind-foot NOT high-food-addiction NOT high-flight-activity NOT health-for-all NOT fulvic-acid* NOT fluoridate* NOT Hartree-Fock NOT hypofraction* NOT high-fat NOT hydrocarbon NOT phenylformamide NOT fluticasone NOT aerosol* NOT adenocarcinoma* NOT hemifacial-atrophy NOT atorvastatin NOT hologic NOT ethanol) OR (SAP NOT tree* NOT sensor-augmented-pump NOT secreted-aspartyl-proteases NOT saponin NOT XLP* NOT systolic NOT ascorbyl-palmitate NOT pancreatitis NOT pacemaker* NOT polymer* NOT saporin NOT surgical-antibiotic-prophylaxis) OR ((visual-field* OR confrontation OR tangent-screen*) ADJ2 (test* OR exam* OR screening OR assess*)) OR ((standard OR static OR automat* OR diurnal OR flash OR manual OR kinetic OR ophthalmic OR Humphrey OR Friedman* OR Goldman* OR Octopus OR Heidelb?rg) ADJ3 (perimetr* OR perimeter OR field-analy?er))).ab,ti.) AND (Juvenile/ OR (juvenile* OR youth* OR adolescen* OR child* OR preschool OR pre-school OR school-age* OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric* OR paediatric*).ab,ti.)

Ovid MEDLINE

(Visual Field Tests/ OR (perimetr* OR perimetry OR campimetr* OR MKP OR MP1 OR MP-1 OR Accumap OR Easyfield OR Easy-field OR M700 OR MonCVOne OR Heidelb?rg-Edge OR Octopus-101 OR Octopus-500 OR Octopus-900 OR (HFA NOT height-for-age NOT hydrofluo* NOT human-flora NOT human-gut NOT home-field-advantage NOT MDI NOT cardi* NOT hydrox* NOT high-frequency-activit* NOT herbal-feed-additive NOT asthma NOT Hageman-factor NOT hexafluo* NOT Hypogloss* NOT health-facility-assessment NOT anemia NOT anaemia NOT PEFF NOT heart-failure NOT adipo* NOT ferulic-acid* NOT folic-acid* NOT healthy-families-america NOT resin NOT BDP NOT tetraflu* NOT primatene* NOT human-fetuin-A NOT inhaler NOT Ventolin NOT high-frequency-antigen NOT hind-foot NOT high-food-addiction NOT high-flight-activity NOT health-for-all NOT fulvic-acid* NOT fluoridate* NOT Hartree-Fock NOT hypofraction* NOT high-fat NOT hydrocarbon NOT phenylformamide NOT fluticasone NOT aerosol* NOT adenocarcinoma* NOT hemifacial-atrophy NOT atorvastatin NOT hologic NOT ethanol) OR (SAP NOT tree* NOT sensor-augmented-pump NOT secreted-aspartyl-proteases NOT saponin NOT XLP* NOT systolic NOT ascorbyl-palmitate NOT pancreatitis NOT pacemaker* NOT polymer* NOT saporin NOT surgical-antibiotic-prophylaxis) OR ((visual-field* OR confrontation OR tangent-screen*) ADJ2 (test* OR exam* OR screening OR assess*)) OR ((standard OR static OR automat* OR diurnal OR

flash OR manual OR kinetic OR ophthalmic OR Humphrey OR Friedman* OR Goldman* OR Octopus OR Heidelb?rg) ADJ3 (perimetr* OR perimeter OR field-analy?er))).ab,ti.) AND (Child/ OR Infant, Newborn/ OR (juvenile* OR youth* OR adolescen* OR child* OR preschool OR pre-school OR school-age* OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric* OR paediatric*).ab,ti.)

PubMed

(Visual Field Tests[mh] OR (perimetr*[tiab] OR perimetry[tiab] OR campimetr*[tiab] OR MKP[tiab] OR MP1[tiab] OR MP-1[tiab] OR Accumap[tiab] OR Easyfield[tiab] OR OR M700[tiab] OR MonCVOne[tiab] OR Heidelberg-Edge[tiab] OR Octopus-101[tiab] OR Octopus-500[tiab] OR Octopus-900[tiab] OR (HFA[tiab] NOT height-for-age[tiab] NOT hydrofluo*[tiab] NOT human-flora[tiab] NOT human-gut[tiab] NOT home-field-advantage[tiab] NOT MDI[tiab] NOT cardi*[tiab] NOT hydrox*[tiab] NOT high-frequency-activit*[tiab] NOT asthma[tiab] NOT Hageman-factor[tiab] NOT hexafluo*[tiab] NOT Hypogloss*[tiab] NOT health-facility-assessment[tiab] NOT anemia[tiab] NOT anaemia[tiab] NOT PEFF[tiab] NOT heart-failure[tiab] NOT adipo*[tiab] NOT ferulic-acid*[tiab] NOT folic-acid*[tiab] NOT healthy-families-america[tiab] NOT resin[tiab] NOT BDP[tiab] NOT tetraflu*[tiab] NOT primatene*[tiab] NOT human-fetuin-A[tiab] NOT inhaler[tiab] NOT Ventolin[tiab] NOT high-frequency-antigen[tiab] NOT hind-foot[tiab] NOT high-food-addiction[tiab] NOT health-for-all[tiab] NOT fulvic-acid*[tiab] NOT fluoridate*[tiab] NOT Hartree-Fock[tiab] NOT hypofraction*[tiab] NOT high-fat[tiab] NOT hydrocarbon[tiab] NOT phenylformamide[tiab] NOT fluticasone[tiab] NOT aerosol*[tiab] NOT adenocarcinoma*[tiab] NOT hemifacial-atrophy[tiab] NOT atorvastatin[tiab] NOT hologic[tiab] NOT ethanol[tiab]) OR (SAP[tiab] NOT tree*[tiab] NOT sensor-augmented-pump[tiab] NOT secreted-aspartyl-proteases[tiab] NOT saponin[tiab] NOT XLP[tiab] NOT systolic[tiab] NOT ascorbyl-palmitate[tiab] NOT pancreatitis[tiab] NOT pacemaker*[tiab] NOT polymer*[tiab] NOT saporin[tiab] NOT surgical-antibiotic-prophylaxis[tiab]) OR ((visual-field*[tiab] OR confrontation[tiab] OR tangent-screen*[tiab]) AND (test*[tiab] OR exam*[tiab] OR screening[tiab] OR assess*[tiab])) OR ((standard[tiab] OR static[tiab] OR automat*[tiab] OR diurnal[tiab] OR flash[tiab] OR manual[tiab] OR kinetic[tiab] OR ophthalmic[tiab] OR Humphrey[tiab] OR Friedman*[tiab] OR Goldman*[tiab] OR Octopus[tiab] OR Heidelb?rg[tiab]) AND (perimetr*[tiab] OR perimeter[tiab] OR field-analyzer[tiab])))) AND (Child[mh] OR Infant, Newborn[mh] OR (juvenile*[tiab] OR youth*[tiab] OR adolescen*[tiab] OR child*[tiab] OR preschool[tiab] OR pre-school[tiab] OR school-age*[tiab] OR schoolchild*[tiab] OR teen*[tiab] OR toddler*[tiab] OR infant*[tiab] OR newborn*[tiab] OR baby[tiab] OR babies[tiab] OR neonate[tiab] OR pediatric*[tiab] OR paediatric*[tiab]))

Cochrane Library

Line 1: Choose MeSH, type Visual Field Tests, and click Look Up. Select “explode all trees”, and click Add/Edit search line.
Line 2: Cut and paste the following:
(perimetr* OR perimetry OR campimetr* OR MKP OR MP1 OR MP-1 OR Accumap OR Easyfield OR "Easy field" OR M700 OR MonCVOne OR Heidelb?rg-Edge OR “Octopus 101” OR “Octopus 500” OR “Octopus 900” OR (HFA NOT “height for age” NOT hydrofluo* NOT

"human flora" NOT "human gut" NOT "home field advantage" NOT MDI NOT cardi* NOT hydrox* NOT "high frequency activity" NOT "herbal feed additive" NOT asthma NOT "Hageman factor" NOT hexafluo* NOT Hypogloss* NOT "health facility assessment" NOT anemia NOT anaemia NOT PEFF NOT "heart failure" NOT adipo* NOT "ferulic acid" NOT "folic acid" NOT "healthy families America" NOT resin NOT BDP NOT tetraflu* NOT primatene* NOT "human fetuin A" NOT inhaler NOT Ventolin NOT "high frequency antigen" NOT "hind foot" NOT "high food addiction" NOT "high flight activity" NOT "health for all" NOT "fulvic acid" NOT fluoridate* NOT "Hartree Fock" NOT hypofraction* NOT "high fat" NOT hydrocarbon NOT phenylformamide NOT fluticasone NOT aerosol* NOT adenocarcinoma* NOT "hemifacial atrophy" NOT atorvastatin NOT hologic NOT ethanol) OR (SAP NOT tree* NOT "sensor augmented pump" NOT "secreted aspartyl proteases" NOT saponin NOT XLP* NOT systolic NOT "ascorbyl palmitate" NOT pancreatitis NOT pacemaker* NOT polymer* NOT saporin NOT "surgical antibiotic prophylaxis") OR ((visual NEXT field* OR confrontation OR tangent NEXT screen*) NEAR/2 (test* OR exam* OR screening OR assess*)) OR ((standard OR static OR automat* OR diurnal OR flash OR manual OR kinetic OR ophthalmic OR Humphrey OR Friedman* OR Goldman* OR Octopus OR Heidelb?rg) NEAR/3 (perimetr* OR perimeter OR field NEXT analy?er)))
Line 3: Choose MeSH, type Child, and click Look Up. Make sure "explode all trees" is selected, and click Add/Edit search line.
Line 4: Choose MeSH, type Infant, Newborn, and click Look Up. Make sure "explode all trees" is selected, and click Add/Edit search line.
Line 5: Cut and paste the following:
(juvenile* OR youth* OR adolescen* OR child* OR preschool OR "pre school" OR school NEXT age* OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric* OR paediatric*)
Line 6: Cut and paste the following:
(#1 OR #2) AND (#3 OR #4 OR #5)
Click the number at the end of Line 7 to get the results. Look at each of the tabs.

Scopus

(TITLE-ABS-KEY (perimetr* OR perimetry OR campimetr* OR mkp OR mp1 OR mp-1 OR accumap OR easyfield OR "Easy field" OR m700 OR moncvone OR heidelb?rg-edge OR "Octopus 101" OR "Octopus 500" OR "Octopus 900" OR (hfa AND NOT "height for age" AND NOT hydrofluo* AND NOT "human flora" AND NOT "human gut" AND NOT "home field advantage" AND NOT mdi AND NOT cardi* AND NOT hydrox* AND NOT "high frequency activity" AND NOT "herbal feed additive" AND NOT asthma AND NOT "Hageman factor" AND NOT hexafluo* AND NOT hypogloss* AND NOT health-facility-assessment AND NOT anemia AND NOT anaemia AND NOT peff AND NOT "heart failure" AND NOT adipo* AND NOT "ferulic acid" AND NOT "folic acid" AND NOT "healthy families america" AND NOT resin AND NOT bdp AND NOT tetraflu* AND NOT primatene* AND NOT "human fetuin A" AND NOT inhaler AND NOT ventolin AND NOT "high frequency antigen" AND NOT "hind foot" AND NOT "high food addiction" AND NOT high-flight-activity AND NOT "health for all" AND NOT "fulvic acid" AND NOT fluoridate* AND NOT "Hartree Fock" AND NOT hypofraction* AND NOT "high fat" AND NOT hydrocarbon AND NOT phenylformamide AND NOT fluticasone AND NOT aerosol* AND NOT adenocarcinoma*

AND NOT "hemifacial atrophy" AND NOT atorvastatin AND NOT hologic AND NOT ethanol) OR (sap AND NOT tree* AND NOT "sensor augmented pump" AND NOT "secreted aspartyl proteases" AND NOT saponin AND NOT xlp* AND NOT systolic AND NOT "ascorbyl palmitate" AND NOT pancreatitis AND NOT pacemaker* AND NOT polymer* AND NOT saporin AND NOT "surgical antibiotic prophylaxis") OR (("visual field*" OR confrontation OR "tangent screen*") PRE/2 (test* OR exam* OR screening OR assess*)) OR ((standard OR static OR automat* OR diurnal OR flash OR manual OR kinetic OR ophthalmic OR humphrey OR friedman* OR goldman* OR octopus OR heidelb?rg) W/3 (perimetr* OR perimeter OR field-analy?er)))) AND (TITLE-ABS-KEY (juvenile* OR youth* OR adolescen* OR child* OR preschool OR pre-school OR "school age*" OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric*)) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "HEAL")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Child") OR LIMIT-TO (EXACTKEYWORD , "Visual Field Tests") OR LIMIT-TO (EXACTKEYWORD , "School Child") OR LIMIT-TO (EXACTKEYWORD , "Infant"))

ClinicalTrials.gov
Other terms: “visual field test” OR perimetry

EBSCO Open Dissertations
Search: “visual field test” OR perimetry

Trip Database
Search: ("visual field test" OR perimetry) AND (child OR juvenile OR infant OR newborn OR pediatric OR paediatric)

OpenGrey
Search: "visual field test" OR perimetry lang:"en"

VisionCite
Advanced Search, select “VisionCite” radio button.
[First line]
Any field contains: perimetr* OR perimetry OR campimetr* OR MKP OR MP1 OR MP-1 OR Accumap OR Easyfield OR M700 OR MonCVOne OR Heidelberg-Edge OR Octopus OR HFA OR SAP OR visual-field-test* OR visual-field-exam* OR visual-exam-screening OR visual-field-assess* OR visual-field-analyzer OR visual-field-analyser OR tangent-screen OR Goldmann OR Humphrey OR Friedmann OR kinetic
[Second line]
AND Any field contains: juvenile* OR youth* OR adolescen* OR child* OR preschool OR pre-school OR school-age* OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric* OR paediatric*

African Index Medicus
Search: “perimetry”

AAO Abstracts
Search*: perimetry* or *"visual field test"*.

ARVO Annual Meeting/Vision Sciences Society Annual Meeting/OSA Fall Vision Meeting/ARVO Imaging in the Eye Conference
Search: *perimetry* and *visual field test* as Exact Phrase. Select "Meeting Abstract"

LILACS
Search #1
Line 1: *Visual Field Tests* in field Subject descriptor
Line 2: AND *Child* in field Subject descriptor
Look for articles that have "Language: en."
Search #2
Line 1: *Visual field test* in field Title words
Line 2: OR *perimetry* in field Title words
Look for articles that have "Language: en."
(Note: adding *child* in field Title words in combination with the above brings up zero results, so you're better off leaving it out)

Web of Science

((TS=(peripheral-vision OR Perimetr* OR Campimetr* OR MKP OR MP1 OR MP-1 OR Accumap OR Easyfield OR Easy-field OR M700 OR MonCVOne OR Heidelb*rg-Edge OR Octopus-101 OR Octopus-500 OR Octopus-900 OR (HFA NOT height-for-age NOT hydrofluo* NOT human-flora NOT human-gut NOT home-field-advantage NOT MDI NOT cardi* NOT hydrox* NOT high-frequency-activit* NOT herbal-feed-additive NOT asthma NOT Hageman-factor NOT hexafluo* NOT Hypogloss* NOT health-facility-assessment NOT anemia NOT anaemia NOT PEFF NOT heart-failure NOT adipo* NOT ferulic-acid* NOT folic-acid* NOT healthy-families-america NOT resin NOT BDP NOT tetraflu* NOT primatene* NOT human-fetuin-A NOT inhaler NOT Ventolin NOT high-frequency-antigen NOT hind-foot NOT high-food-addiction NOT high-flight-activity NOT health-for-all NOT fulvic-acid* NOT fluoridate* NOT Hartree-Fock NOT hypofraction* NOT high-fat NOT hydrocarbon NOT phenylformamide NOT fluticasone NOT aerosol* NOT adenocarcinoma* NOT hemifacial-atrophy NOT atorvastatin NOT hologic NOT ethanol) OR (SAP NOT tree* NOT sensor-augmented-pump NOT secreted-aspartyl-proteases NOT saponin NOT XLP* NOT systolic NOT ascorbyl-palmitate NOT pancreatitis NOT pacemaker* NOT polymer* NOT saporin NOT surgical-antibiotic-prophylaxis) OR ((Visual-field* OR confrontation OR tangent-screen*) AND (Test* OR exam* OR screening OR assess*)) OR ((standard OR static OR automat* OR diurnal OR flash OR manual OR kinetic OR ophthalmic OR Humphrey OR Friedman* OR Goldman* OR Octopus OR Heidelb*rg) AND (perimetr* OR perimeter OR field-analy*er)))) AND (TS=(juvenile* OR youth* OR adolescen* OR child* OR preschool OR pre-school OR school-age* OR schoolchild* OR teen* OR toddler* OR infant* OR newborn* OR baby OR babies OR neonate* OR pediatric* OR paediatric*)))