DEVELOPMENT OF A DIAGNOSTIC TEST BATTERY FOR THE VISUAL ASSESSMENT OF STROKE SURVIVORS

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Thesis Abstract

Advances in medical care and risk factor management have reduced the incidence of stroke, yet prevalence is expected to rise due to an ageing population and improved survival rates. Stroke survivors frequently experience a range of visual dysfunctions, including issues with central and peripheral vision, eye movements, vergence, accommodation, and perceptual anomalies (eg. light sensitivity, pattern glare, inattention). Primary eye care providers are increasingly required to provide visual care to these patients.

However, a literature review revealed limited evidence on diagnostic methods for post-stroke ophthalmic assessment, with findings favouring kinetic over automated perimetry and automated over confrontation techniques. No evidence was found supporting the accuracy of standard ophthalmic clinical tests in this group.

This thesis aimed to develop a diagnostic test battery for primary eye care through a three-round Delphi process with 11 expert practitioners (7 of whom completed). The final battery encompassed key aspects of a comprehensive eye examination, including visual, binocular, refractive, and ocular health assessments.

The battery was evaluated in an observational case-controlled diagnostic study involving 48 participants (22 stroke survivors, 26 controls). Subjects underwent both a typical sight test and the trial battery, including binocular vision, pattern glare, reading assessments, perimetry, pupil dilation, and retinal imaging. The trial battery identified more ocular surface, adnexal, and binocular anomalies than the sight test, but lacked sensitivity to field loss. Stroke survivors, particularly those with visual field loss, reported significantly increased pattern glare symptoms and slower reading speeds, with limited improvement from coloured overlays. Significant retinal thinning was observed in stroke survivors, especially in their left eye.

Sight testing in community optometry practice can fall short of the thorough care that stroke survivors deserve, further research is required to assess the scale and impact of this, to examine binocular vision in older adults, and investigate retinal biomarkers linked to stroke.

Dedicated to the memory of my sister

Catriona Ann Maciver

Gus am bris an là, agus an teich na sgàilean

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Chapter 1 Introduction

1.1 Stroke

While the prevalence of stroke is decreasing, it is estimated that around 100,000 people in the United Kingdom experience a stroke every year (Public Health Scotland 2023; Scottish Stroke Care Audit Report 2024; Sentinel Stroke National Audit Programme 2024) and over 1.3 million people live with the effects of acquired brain injury (Rowe 2011; Johnson et al. 2019; NHS England 2019; Department of Health 2022; Public Health Scotland 2023; StatsWales 2024). The diagnosis of stroke describes a syndrome of conditions characterised by a neurological deficit secondary to an acute focal injury of vascular origin on the central nervous system (Sacco et al. 2013). Historically, the definition of stroke had centred on the clinical signs common to the disease's onset, with the World Health Organisation defining stroke as a *"rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin"* (Aho et al. 1980). This definition separates stroke from the more temporary transient ischaemic attack (TIA) characterised by *"brief episode(s) of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction"* (Easton et al. 2009; Sacco et al. 2013).

1.2 Transient Ischaemic attack

TIA's have been identified as an important pre-cursor of stroke by a number of studies (Johnston et al. 2000; Coull et al. 2004; Daffertshoter et al. 2004; Hill et al. 2004), with a systematic review and meta-analysis (Wu et al. 2007) identifying that around 2-5% of patients who experience TIA will go on to suffer a stroke within 2 days and around 15-20% suffering a stroke within 90 days of the TIA. Due to this increase in risk, patients presenting with the symptoms of TIA should be investigated using blood vessel imaging, cardiac evaluation and laboratory testing (Easton et al. 2009), and where necessary management initiated to minimise the risk of progression to stroke.

1.3 Stroke Type

Strokes are responsible for around 10% of all deaths in the western world and are the second most common cause of death globally (Donnan et al. 2008). Stroke can be broadly classified into two major sub-types, ischaemic and haemorrhagic. Ischaemic strokes result from cerebral vascular occlusion and represent around 80% of presentations, with the more serious haemorrhagic strokes being encountered less frequently (**Table 1-1**). The resulting cerebral damage from stroke can lead to a number of difficulties, affecting an individual's social, functional and cognitive performance (Hafsteinsdóttir and Grypdonck 1997).

1.3.1 Ischaemic stroke

Ischemic stroke represents the most frequently encountered subtype of stroke, consisting of around 80% of all cases (Gubitz and Sandercock 2000). This condition typically results in a mortality rate of around 5% at one month, 16% after one year and 41-50% five years following the episode (Xian et al. 2011; Rohweder et al. 2017). Ischaemic stroke arises due to a focal deprivation of blood flow to a region of cerebral vasculature, which may be due to a number of causes. The most prevalent cause of cerebral ischaemia is arterial obstruction secondary to arteriosclerosis. The formation of arteriosclerotic plaques leads to progressive narrowing of the blood vessels, impairing cerebral perfusion. Alternatively, arterial plaques may break away from their initial site, forming mobile emboli that may impair or obstruct blood flow. These commonly arise due to vascular disease away from the cerebral vasculature (Arboix and Alió 2010; Pongmoragot et al. 2013; Hart et al. 2017) and may occur secondary to atrial fibrillation, though the mechanism of this is debated (Kamel et al. 2016). Emboli may also consist of non-thrombotic tissue, or may consist of a mix of thrombotic and non-thrombotic tissue possibly arising from valvular calcification or other pathologies (Hart et al. 2017).

Type of stroke	Definition
Central Nervous System (CNS) infarction	Brain, spinal cord, or retinal cell death attributable to ischemia. Diagnosis is based upon: (i) objective evidence of cerebral, spinal cord or retinal ischemia identified pathologically or by imaging, or; (ii) subjective symptoms indicative of cerebral, spinal or retinal focal ischaemic injury lasting >24 hours or leading to death, and; (iii) excluding other causes.
Silent CNS infarction	Presence of neuropathological / imaging signs of CNS infarction in the absence of clinical history of the lesion.
Ischemic stroke	Episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.
Stroke by Intracerebral haemorrhage	Rapid development of clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system, not caused by trauma.
Silent cerebral haemorrhage	Objective signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system not caused by trauma, in the absence of clinical history of the lesion.
Stroke by Subarachnoid haemorrhage	Rapid development of clinical signs of neurological dysfunction attributable to bleeding into the subarachnoid space, not caused by trauma.
Stroke by cerebral venous thrombosis	Infarction or haemorrhage in the brain, spinal cord, or retina because of thrombosis of a cerebral venous structure.
Stroke, other	An episode of acute neurological dysfunction persisting >24 hours or until death, without evidence to be classified otherwise, but presumed to be due to ischemia or haemorrhage.

Table 1-1. Definitions of stroke, of note signs or symptoms caused by reversible oedema without infarction or hemorrhage are not considered as a stroke. Adapted from Sacco et al, 2013.

1.3.2 Haemorrhagic stroke

While of lower prevalence, haemorrhagic stroke represents a more aggressive subtype of the syndrome, with higher mortality and associated morbidity (Sacco et al. 2013). The causative mechanism of haemorrhagic stroke is rupture of a cerebral blood vessel, resulting in structural disruption and damage due to the mass effect of lacunar infarct. However, a literature review (Gebel et al. 2000), reduction in cerebral blood flow (Francoeur and Mayer 2016), apoptosis and necrosis of cellular structures (Qureshi et al. 2003) and secondary oedema (Xi et al. 2002; Zheng et al. 2016) which result in atrophic damage (Kim et al. 2017). Haemorrhagic strokes may result in arterial bleeding into the cerebral parenchyma or may result in bleeding into cerebrospinal fluid in the subarachnoid space, permanently affecting the function of the central nervous system.

1.4 Signs and symptoms

The clinical signs and symptoms encountered may vary depending upon the region of vascular deprivation (**Table 1-2**), with areas receiving vascular perfusion from the affected vessel being most readily affected. This may be confused by variation in clinical signs and symptoms as some of these may be progressive, arising from lesions affecting the watershed zones of two non-anastomosing arterial systems (Momjian-Mayor and Baron 2005).

1.5 Visual effects of stroke

A number of visual sequelae have been reported following stroke. While widely recognised, the prevalence of visual field deficit following stroke is unknown, having been reported to vary from 6.9% (Tao et al. 2012) to as high as 63% (Gray et al. 1989). While many studies report on the presence of homonymous field defects, the most frequently encountered class of defect (Rowe et al. 2017) focusing only upon this subtype may overlook around ⅓ of the cases of peripheral vision defects that occur post stroke (Rowe et al. 2009). Reduction in peripheral vision has been found to inhibit daily activities from basic navigation to more complex tasks such as driving (Rubin et al. 2001). This can occur despite the presence of good visual acuity and can result in reduced quality of life (Rowe et al. 2013a; Qiu et al. 2014). Reliance on visual feedback increases with age, with particular feedback gained from peripheral vision (Khan et al. 2004). It is unsurprising then that visual field loss can result in reduced mobility and can lead to an increased risk of falls (Freeman et al. 2007; Dhital et al. 2010; Patino et al. 2010; Mehta et al. 2022) and have a major impact on the quality of life of stroke survivors (Vu et al. 2005; Journal et al. 2016). As the incidence of stroke increases with increasing age (Johnson et al., 2019; Rajati et al., 2023), falls resulting from visual loss can represent a risk factor for increased morbidity following stroke. While frequently observed, many stroke survivors with field defects are minimally affected by symptoms of the loss (Rathore et al. 2002; Jerath et al. 2011; Searls et al. 2012; Rowe 2013; Rowe et al. 2017), unless the central 10^0 is affected (Quigley et al. 2011; Hepworth et al. 2021). As such, it may be conservative to consider that the prevalence of visual field loss following stroke may err towards the higher end than reported in the literature.

Area of brain affected	Stroke outcome
Frontal Lobe	Change in behaviour/personality Loss of fine movement Loss of strength in upper limbs Difficulties of expression
Parietal Lobe	Difficulty in spatial processing Difficulty in hand eye coordination Inability to identify objects by touch Difficulty in discerning laterality and directionality Hemineglect Visual agnosia
Temporal Lobe	Difficulties with spoken language Hearing loss Difficulty in discerning complex sounds (music, tones, etc) Memory loss Aggression Disturbance of smell/taste
Occipital Lobe	Visual field loss Agnosia Acuity loss
Cerebellum	Balance issues Dizziness Nausea Ataxia
Brainstem	Decreased vital sign function Perception difficulties Balance issues Paralysis / hemiplegia / dysphagia

Table 1-2: Clinical signs and symptoms associated with brain areas affected following stroke (adapted from Chellappan et al. 2012)

Visual acuity is one of the most frequently employed methods of assessment of visual function in ophthalmic practice. Visual acuity is a useful measure of visual function, sensitive to changes due to refractive errors, pathology of the ocular media and posterior pole of the inner eye. In a study of 323 participants, Rowe et al (2009) found reduced acuity of <6/12 in 25% of patients when viewing distance targets and 26.5% of patients viewing near targets, with around half of those having acuity worse than 6/18. Within the group with acuity of <6/12 it was noted that 31% had comorbid ocular pathology suggesting that the reduction of acuity may not have been resultant from the stroke.

While no large studies on the effect of stroke on contrast sensitivity have been undertaken, reduction in contrast sensitivity has been suggested as an important feature of visual function loss following stroke. Contrast sensitivity has been observed to be lower following stroke and may have an impact upon the functional independence of individuals to undertake day to day tasks (Wolter and Preda 2006; Dos Santos and Andrade 2012). A pilot study found that contrast sensitivity measurements may vary across the visual field in hemianopic patients and may demonstrate anomalies in areas found to have normal responses to automated perimetry (Clatworthy et al. 2013).

Assessment of the integrity of ocular structures in the post stroke group is often under reported with pathology often recorded from a patient’s subjective history (Rowe et al. 2009; Rowe et al. 2017) identifying key pathology in 27-34% of this group, with several ocular sequelae have been documented following stroke. Rutner et al. (2006), in a retrospective review of patient records, reported an increased prevalence of ocular disorders in individuals with acquired brain injury compared to those without. Among stroke survivors, anterior eye disorders were observed to be particularly common. Eyelid ptosis has been observed in 6.7–9.6% of cases (Rutner et al. 2006; Rowe et al. 2017), and other eyelid anomalies such as eye lid retraction may also occur, leading to incomplete lid closure and subsequent corneal exposure. This exposure can disrupt the tear film, risking tear film hyperosmolarity, inflammation, and dry eye disease (Bron et al. 2017). Corneal epithelial lesions following exposure occur in around 5% of subjects following stroke (Rutner et al. 2006), increasing the risk of infection and decreasing optical clarity. Interestingly, despite these risk factors, symptoms of dry eye disease were found to be less prevalent in this group, potentially due to reduced corneal sensitivity from prolonged exposure (Sacchetti and Lambiase 2014). Additionally, vascular anomalies, such as subconjunctival haemorrhages, were observed in 1.7% of cases, which may be linked to anticoagulant therapy commonly used to manage cardiovascular risk factors post-stroke (Bodack 2007).

The neuro-retina and optic nerve are embryologically and anatomically similar to the tissues of the central nervous system, having a shared embryologic origin and similar physiology (Girach et al. 2024). The supporting retinal vasculature shares a number of features with the cerebral small vessels and allows insight to the development of cerebrovascular anomalies, as well as changes that occur following ischaemic or haemorrhagic insult (Ikram et al. 2006a; Ikram et al. 2006b; De Silva et al. 2011).

Several studies have investigated the link between retinal vessel anomalies with stroke. Consequently alteration of retinal blood vessels are frequently encountered when examining subjects who have experienced stroke. The presence of a decreased arterial diameter (De Silva et al. 2011; Vuong et al. 2015; Hughes et al. 2016), increased veinous diameter (Ikram et al. 2006a; McGeechan et al. 2009; De Silva et al. 2011) and resulting alteration of the arterio-veinous ratio have been found to be independent risk factors for the development of stroke. Damage to the blood vessel walls can lead to the formation of microvascular anomalies such as microaneurysms on the retinal capillaries or even retinal haemorrhages either superficially or deeper within the retina. Reduced and erratic blood flow may lead to ischaemia, the formation of retinal infarcts, and congregations of axoplasmic debris within the nerve fibre layer (McLeod 2005; Chui et al. 2009; Pula and Yuen 2017). The formation of such cardiovascular retinopathy serves as a risk factor for the development vascular insults such as stroke (Baker et al., 2010; Wang et al., 2011; Wong et al., 2001), and are frequently comorbid findings (Vuong et al. 2015) on examination of the stroke patient.

Following neurologic insult, a number of possible pathologies can result in optic nerve damage. Atrophic degeneration of the optic nerve has been found to be present in between 2% and 10% of stroke patients (Rutner et al. 2006; Shrestha et al. 2012). This may result in a number of visual issues, such as loss of acuity, reduction in contrast sensitivity, reduction of colour sensitivity as well as pupil anomalies (Ciuffreda et al., 2007; Hepworth et al., 2016; Munk et al., 2023; Rowe et al., 2017; Rowe et al., 2019; Suchoff et al., 2008). Retrograde degeneration of the optic nerve has been observed to occur in several studies (Jindahra et al. 2012; Keller et al. 2014; Herro and Lam 2015; Yamashita et al. 2016), resulting in thinning of retinal ganglion cell and nerve fibre layer (Tatsumi et al. 2005; Park et al. 2013; Hokazono and Ribeiro Monteiro 2019; Newman-Wasser et al. 2019; Bianchi Marzoli et al. 2023). The integrity of the peripheral retina is crucial to maintain the physiological functions of vision. While increased age gives rise to an increase in peripheral and vitreous anomalies, these have been found to be more prevalent in subjects who have suffered a stroke and are present in around 6% and 10% of these subjects respectively (Rutner et al. 2006). This would suggest that these subjects are more at risk of subsequent retinal damage, indicating a higher eye care requirement for this group from their eye care providers.

Other visual issues encountered by patients following stroke include a reduction in reading performance (Rowe et al. 2011), light sensitivity and pattern glare (Beasley and Davies 2012), a shift of the perceptual visual midline (Barton et al., 1998; Darling et al., 2003; Padula & Argyris, 1996) and visual inattention (Ting et al. 2011).

Disorders of eye movements are a common finding in acute stroke and have been estimated to affect 23-54% of stroke survivors (Ciuffreda et al., 2007; Pedersen & Troost, 1981; Rowe, 2011; Rowe et al., 2013b; Rowe et al., 2022; Rutner et al., 2006; Simon et al., 2003). Stroke affecting the brainstem or the oculomotor, trochlear and abducens nuclei can also affect the actions of the extraocular muscles, resulting in manifest deviations, gaze palsies, internuclear ophthalmoplegia, nystagmus and saccadic dysmetria. Strabismus has been reported in 23-36% of stroke survivors, with anomalies of eye movements present in around 5% (Ciuffreda et al. 2007; Rowe 2011a).

Reading is a complex skill that integrates visual information processing, top-down attentional control, and higher-level linguistic functions involving complex neural networks. While the role of vision in developmental reading difficulties remains a topic of debate (Ray et al. 2005; Legge et al. 2010; Handler et al. 2011; Rowe et al. 2011; Hulme and Snowling 2016; Stein 2022; Loh et al. 2024), the disruption of binocular systems, loss of vision and the presence of field loss have all been reported to impact on reading ability (Rowe et al. 2011; Stein 2022). Studies in acquired reading anomalies in stroke survivors have observed that parafoveal vision plays a role in the coordination of accurate eye movements and decoding (Gall et al. 2010). Impairment of parafoveal vision, such as in hemianopia may disrupt eye movements and textual decoding, resulting in difficulties in reading. The loss of peripheral and saccadic function has been proposed to impact upon reading anomalies through difficulties in visual search, decoding, and processing (Leff et al. 2000), as well as potentially impacting upon function of the auditory, somatosensory, proprioceptive and motor system (Stein 2001; Stein 2014; Stein 2019)

Various perceptual anomalies have been reported to occur following stroke. Sensitivity to light and visual stimuli have been reported (Digre and Brennan 2012; Wu and Hallett 2017; Thielen et al. 2023; Thielen et al. 2024), including sensitivity to patterned stimuli (Beasley and Davies 2012; Beasley and Davies 2013b). Beasley & Davies (2013a) undertook further investigation to the impact of coloured spectral filters on reading rates in stroke survivors, finding improved reading rates and accuracy with these filters. While this work supports the use of coloured filters in stroke survivors presenting with symptoms of visual stress, these symptoms have been attributed to a range of causes, though their origin remains unclear.

Another perceptual phenomenon that may be observed following unilateral neurological events is where following insult the patient's perceptual understanding of egocentric space was altered. These subjects when tested using a moving wand would consistently report an altered position of the perceptual midline (Barton et al., 1998; Darling et al., 2003; Padula & Argyris, 1996) and reported symptoms such as dizziness, balance issues and visual discomfort. In these cases the projection of the perceptual 'straight ahead' is a function believed to be mediated by the praecuneus region of the parietal lobe (Cavanna and Trimble 2006; Zaehle et al. 2007; Loayza et al. 2011). In the absence of neurological or developmental abnormalities, the midline is typically egocentric lying between the interocular axes with small variation towards the sighting eye (Porac' and Coren 1986) and entirely foveo-centric in monocular viewing (Suter and Harvey 2011). It has been suggested that following neurological insult, especially in the presence of homonymous field loss, alteration of the visual midline represents an attempt from the visual system to adapt to the loss, re-centering the visual midline to the subjective centre of perceived field (Suter and Harvey 2011).

Following damage to the right cerebral cortex, neglect of the visual space to the left of the midline has been reported (Sahraie et al. 2010; Ffytche and Zeki 2011; Kletenik et al. 2022). Patients with this phenomenon may have difficulty in many day-to-day tasks, behaving as if the left of their visual world is absent, giving rise to issues of navigation and even self-care (Azouvi et al. 2006; Bartolomeo 2021). Frequently where damage has spared the thalamic pathways, these patients may present a phenomenon known as blindsight, where the patient is able to respond to visual stimuli within the affected field of vision, despite no perceptual awareness of the stimuli (Mazzi et al. 2019).

1.6 Visual examination

Many stroke survivors have difficulty accessing appropriate primary eye care services (Rowe et al. 2009; Rowe 2010b; Rowe et al. 2016; Stalin et al. 2024a; Stalin et al. 2024b), while damaged optical appliances and those using appliances with inaccurate/inappropriate lens power may lead to non-pathological reduction in vision. In a hospital-based study Lotery *et al* (2000) undertook visual assessments with 77 consecutive stroke patients admitted to a rehabilitation unit. This study found that of those patients that required refractive correction, 25% did not have their spectacles with them on admission, and of those that had spectacles 27% presented spectacles that were unserviceable due to damage or poor maintenance. Of those that did have serviceable refractive correction 30% had impaired visual acuity (considered as VA<6/12). This figure was found to drop to 13% when those patients with reduced acuity were refracted and acuity measured through an appropriate refractive error.

The majority of primary eye care services in the UK are provided by optometrists (Shah et al. 2007). Optometry is an autonomous healthcare profession regulated in the UK by the General Optical Council (GOC). There are over 17,000 optometrists (Europe Economics 2023) practising in the UK, the majority of these working in the primary eyecare setting. The traditional practice of optometrists has centred on refraction and the examination of the eye to detect abnormalities of the eyes and visual system. This changed dramatically in 2006 following the introduction of therapeutic prescribing rights for optometrists (Cartwright and Handley 2015) and the introduction of the Minor Eye Casualty Service (MECS), a community eye and visual triage service by the Wales Optometry Postgraduate Education Centre (WOPEC). Many NHS areas now operate MECS pathways and it is anticipated that the scope of practice will continue to expand.

Optometrists are often required to rely on their professional judgement in the provision of care to their patients. While guidance on the appropriate examination techniques to prioritise when examining patients with traumatic brain injury (Goodrich et al. 2013), and dementia (Bowen et al. 2016) have been developed, there is a paucity of evidence in the literature regarding the best practice for examination and long-term optical care and management following stroke. Indeed, a best practice statement for the management of vision problems following stroke produced by the University of Glasgow advises a protocol to assess eye movement disorders and field loss but omits measurement of acuity or refraction (Fisher et al. 2013), while guidance for professional practice provided by the College of Optometrists discusses the requirements for practitioner flexibility in examination,

Within health care it is essential to have a robust evidence base to inform practice and direct care. Much work has been done to improve the assessment of new diagnostic tests being introduced to clinical practice (Ferrante Di Ruffano et al. 2012). The historic absence of a formal framework for diagnostic tests (Knottnerus et al. 2002; Knottnerus and Muris 2003) has however led to the routine use of many clinical tests without a rigorous evaluation of their diagnostic accuracy, and optimal utility in practice. In a recent evaluation carried out by the American Optometric Association (2015; 2023), many of the diagnostic procedures conducted were found to have limited evidence supporting their use in routine primary eye care provision - leading to the agreement of a consensus-based recommendations. Similarly, while a range of studies have reported on the presence of gaze palsies and strabismus following cerebrovascular accident (Ciuffreda et al. 2007; Rowe 2010a; Rowe 2011a), little attention has been placed upon the typical binocular vision profile and orthoptic measurements following stroke.

It is well established that many patients have attention difficulties following brain injury, with the potential for fatigue to influence the results of an extensive battery of tests (Green et al. 2010b). Though there is an option to split the initial assessment into multiple sessions this may lead to patient non-attendance and being lost to follow up (Marzolini et al. 2016). To provide effective visual care, it is important that the diagnostic tests undertaken are appropriate in scope and duration and identify the salient visual issues affecting those who have suffered stroke without placing an undue burden upon them.

Legislatively (Opticians Act, 1989) the chief role of the sight test is to detect physiological anomalies, ocular and systemic pathology and injury to the eye and associated structures. The requirements of this legislation are outlined in broad terms leaving clinicians with scope to practise beyond the minimum requirements outlined by legislation and regulators.

A lack of standardisation in practice has the potential to cause difficulties, especially where clinician continuity is limited. A new practitioner when introduced to the clinical records of a predecessor with a different mode of practice may find that the records do not contain information that they feel should be included, while details that some clinicians may consider superfluous may be present (Shah et al. 2007). This difference in practice could lead to confusion and the belief that one clinician had provided sub-optimal care. Standardisation of diagnostic testing brings about a consistent approach between clinicians, improving continuity of care for the patient. The optometric examination consists of a number of test procedures used to identify the visual, refractive, binocular and ocular health status of a patient, with the information gathered being considered and its results integrated into the clinician's understanding of the patient's visual state. The tests selected by optometrists must be considered appropriate in terms of their clinical purpose and produce relevant information. The test must also be considered in terms of its burden on the patient (such as fatigue, nausea, adverse reactions to diagnostic medications), and the clinician should consider whether the test is truly necessary or whether an alternative would be sufficient.

Difficulty arises though in the development of a standard eye examination due to the subjective nature of what constitutes a "gold" standard eye examination. In a series of studies Shah and colleagues reported that there is a wide range of assessment styles of various rigour practised among primary care optometrists (Shah et al. 2008; Shah et al. 2009a; Shah et al. 2009b; Shah et al. 2009d). To conduct a comprehensive examination assessing all possible visual, binocular and perceptual anomalies with patients who have experienced a stroke requires a more specialised, and time-intensive approach compared to standard vision testing. Clinicians in both community and hospital settings often face significant time constraints, which can limit their ability to conduct this type of examination. While in some cases this may be required, in others access to enable provision of routine ophthalmic care would be expected to address their visual requirements. While several visual screening tests have been developed to identify the presence of various visual deficits following stroke (Hanna et al. 2017a), no formalised ophthalmic test battery has been designed to examine patients with a history of stroke.

This project will seek to assess the literature on the optimal diagnostic approaches to use when conducting the visual examination on a patient with a history of stroke and seek to develop an evidence-based instrument outlining the essential examination procedure for the visual examination for this group. If successful, this instrument could be utilized to support clinicians in the detection and diagnosis of visual anomalies observed in these patients following stroke, identifying the patient's visual prognosis, monitoring the anomalies over time, and in patient management - identifying suitable interventions to support rehabilitation. This instrument could also be used in the research setting to offer a standard baseline on which to assess the effectiveness of various interventions.

Chapter 2 Examination for visual dysfunction post-stroke: A systematic search and literature review

2.1 Introduction

Stroke is a leading cause of morbidity and mortality worldwide. It is characterised by acute focal deficit of the central nervous system (CNS) by a vascular cause with a duration greater than 24 hours (Sacco et al. 2013). While the prevalence of stroke is decreasing (Truelsen et al. 2006; Lee et al. 2011; Johnson et al. 2019), the number of individuals living with the effects of cerebrovascular disease is increasing (Rowe 2011b). While many of the ocular sequelae of stroke are well documented, the incidence of some elements and their impacts remain unknown (Chang et al. 2007; Suchoff et al. 2008; Hepworth et al. 2016).

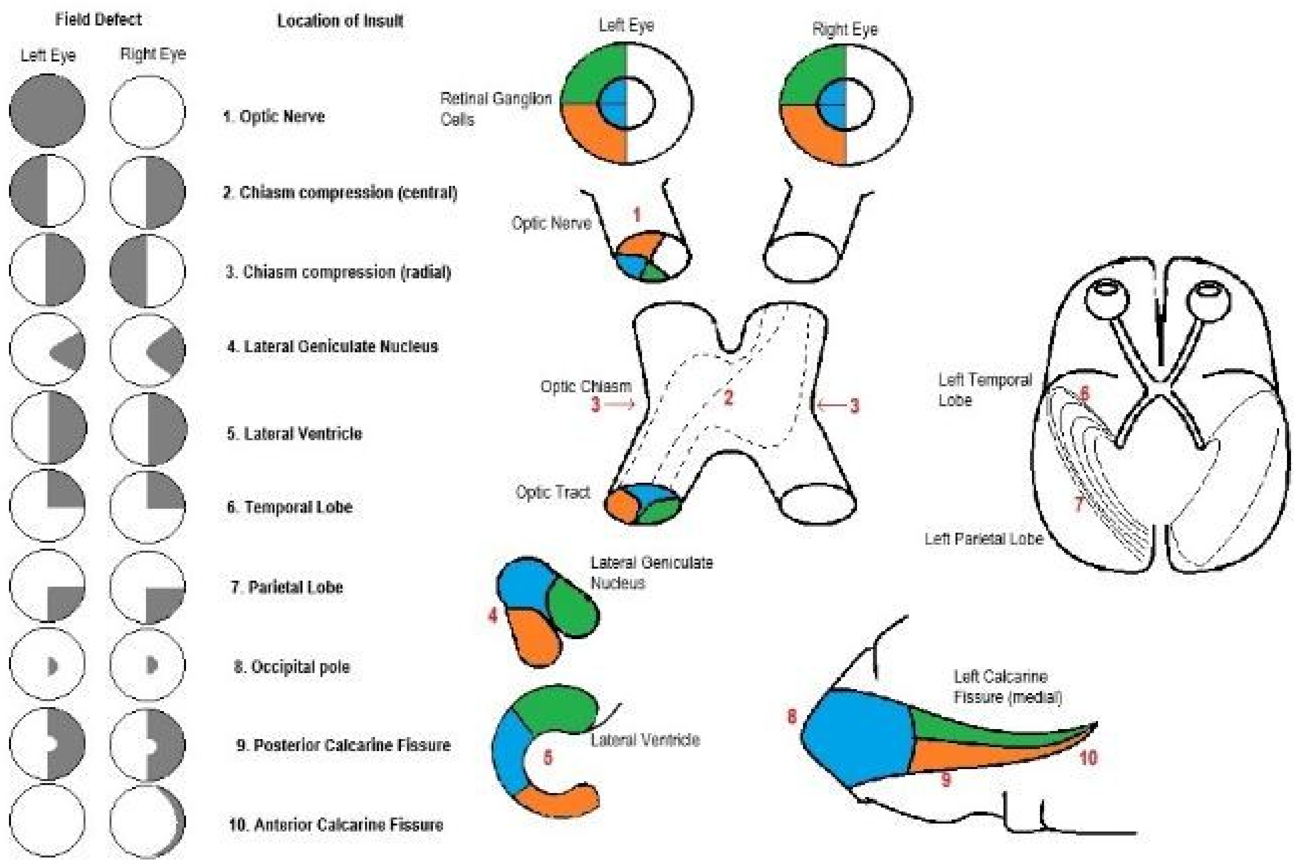


Figure 1. Typical patterns of visual field loss derived from anatomic location of damage. Lesions anterior to the optic chiasm typically give rise to monocular field loss. Lesions of the chiasm itself being heteronymous in nature, while post-chiasm lesions give rise to homonymous field defects secondary to the partial decussation of nerve fibres that occurs at the chiasm (adapted from Suter & Margolis, 2005; Uretsky, 2014).

As visual processing and oculomotor control are well distributed through the cortex, with interruption affecting normal visual processes the visual consequences of stroke can be diverse; including central and peripheral visual loss, homonymous and non-homonymous defects (**Figure 1**), accommodative dysfunction, convergence dysfunction, saccadic dysmetria (**Figure 2**), cranial nerve palsies, and perceptual deficits (Ciuffreda et al., 2007; Hepworth et al., 2016; Rowe et al., 2019; Suchoff et al., 2008). Moreover, individuals who have suffered a stroke are reported to be more likely to have other ocular conditions such as ptosis, epithelial keratitis, lid lesions, pinguecula, lagophthalmos, optic atrophy, and peripheral retinal degeneration (Rutner et al. 2006).

Despite this it has been reported that significant discrepancies exist in post-stroke visual care, with Rowe (2017b) reporting that ophthalmic assessment (within a hospital eye department setting) was sometimes immediate (especially where symptoms of diplopia were present), and in some instances, including many patients with visual field defects, were directed to primary care.

Optometrists are primary healthcare specialists trained to examine the eyes to detect defects in vision, signs of injury, ocular diseases or abnormality, and ocular signs of problems with general health (College of Optometrists 2023b) and are responsible for the delivery of the majority of primary eyecare within the UK (Shah et al. 2007; Hawley et al. 2010). As such, outside a hospital setting it is likely the first professional to undertake an ocular assessment will be an optometrist.

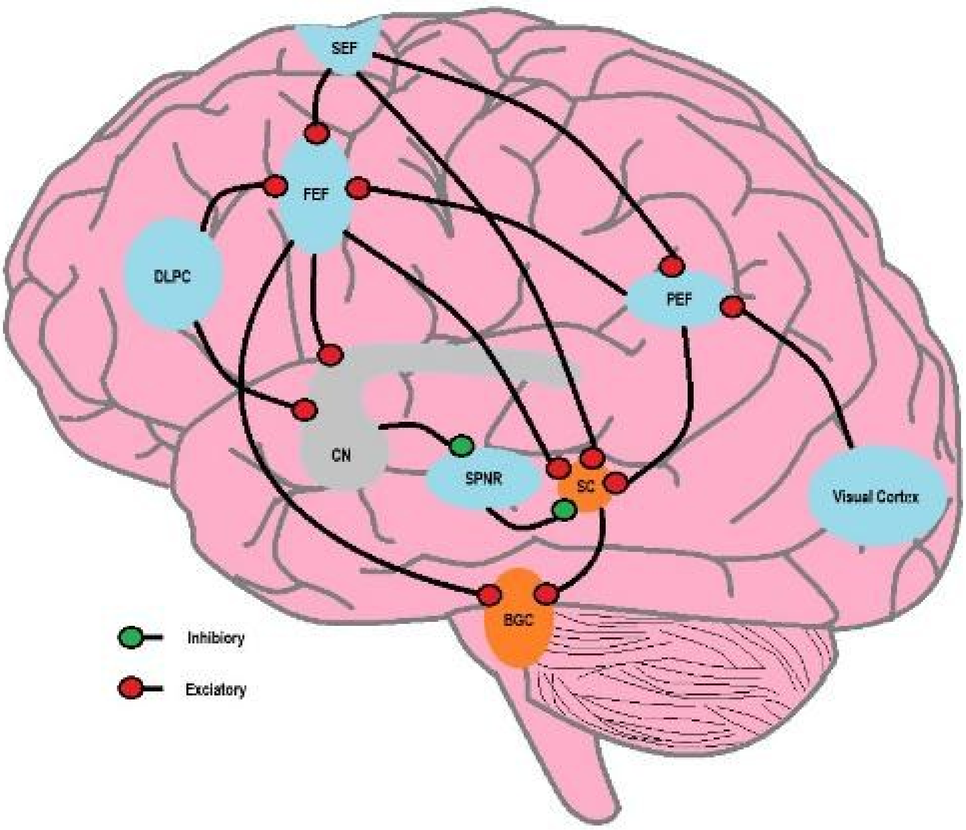


Figure 2. Cortical centres responsible for eye coordination and movement, connecting pathways highlighting excitatory and inhibitory influence on saccade generation (Ventura et al, 2014). Saccades are initially triggered in the frontal eye field (FEF), parietal eye field (PEF) send signal to the superior colliculus (SC) which passes these signals to the brainstem gaze centres (BGC) in the paramedian pontine reticular formation (PPRF). A secondary projection also occurs from the FEF to the BCG. Additional inhibitory pathways are present via the caudate nucleus (CN) to inhibit the action of the substantia nigra pars reticulata (SNPR). **Pursuit** movements are initiated at centres in the tempero-parieto-occipital junction and FEF that project to the pons to innervate the cerebellum, triggering cranial nerve centres. By contrast the cortical control of **vergence** movements are poorly understood beyond the oculomotor nerve reflex pathway (adapted from Ventura et al. 2014).

Identification of visual or ocular disorders in stroke patients requires optometrists to use diagnostic tests of suitable discriminatory power to best detect disorders of the eyes or vision. Optometric assessment plays an important role in the detection and management of ocular conditions or visual sequelae in these patients. To determine the investigations that should be undertaken during a routine assessment, it must first be clear to the examining clinician what anomalies are being assessed for.

During training optometrists undertake a significant period conducting the various assessment procedures used as part of a routine eye examination, as well as a number of further investigative techniques. Upon completion, many choose to work in community practice, where much of their time is spent undertaking examinations on patients. Unlike a number of conditions, there is not at present a standardised, evidence-based approach to the provision of primary refractive care to patients with a history of stroke, so some degree of variability is likely to be encountered in the receipt of care by these patients.

As discussed in **Chapter 1**, the chief role of the sight test is to detect physiological anomalies, ocular and systemic pathology and injury to the eye and associated structures (Association of Optometrists 2015; College of Optometrists 2023b). While it is expected that all eye examinations meet the minimum requirements of the Opticians Act (1989), selection and discretion to use these tests is left to the optometrist's judgement of clinical necessity. Within their professional guidance the College of Optometrists recommends several tests that should be normally included but may not be carried out if the optometrist has good reason to do so as part of a routine examination (**Table 2-1**). These include a complete oculo-visual history, measuring habitual vision and corrected visual acuity, undertaking an assessment of oculomotor balance and providing the patient with advice on the outcome of their examination.

A patient may present for an eye examination for a variety of reasons, which are typically revealed in the history taking process (Pointer 2014). This information influences the approach the clinician takes in conducting the examination, as well as accommodations made for patient comfort. This may lead to clinicians prioritising some tests or procedures based on their interpretation of the patient symptoms and the clinician's preferred approach, rather than that which may effectively benefit the patient, potentially resulting in a suboptimal examination. This may also give rise to variability in the consistency and quality of eye care services provided from one eye care provider to another, a feature identified in other areas (Shah et al. 2008; Shah et al. 2009d; Shah et al. 2009a; Shah et al. 2009b; Margolis et al. 2024), that, should a critical test or series of tests be overlooked, could give rise to differing diagnoses and management strategies.

The aim of this study is to investigate the reported diagnostic accuracy of recognised methods of visual examination of patients with a history of stroke; to identify the optimum combination of visual examination methods for the primary care optometrist to use with this patient group to provide optimal visual care.

You Should:	● Ask for and accurately record: ○ Full name ○ Address ○ Other contact details ○ Date of birth ○ Reason for visit ○ History including description of the onset, character and duration of signs and symptoms ○ History of ocular and general health if relevant ○ Current general health ○ Medication ○ Family history of ocular and general health ○ Occupational and recreational visual needs ○ Driver status ■ If correction is worn for driving ○ Details of previous ocular examination ■ Patient's best estimate if unknown ● Unaided and/or aided vision ○ Habitual correction worn and recorded ● Habitual ocular muscle balance ○ Minimum cover test distance and near ● Examine the anterior eye ○ Using slit lamp if required ● Examine the internal eye ○ Minimum direct ophthalmoscopy in undilated eye ● Establish prescription required ● Measure visual acuity in each eye
If you feel it is clinically appropriate you may:	● Measure convergence ● Assess ocular motility ● Assess pupil reflexes ● Determine objective refractive findings ● Using autorefractor and/or retinoscopy ● Use fundus and other imaging ● Measure intraocular pressure of patients at risk of glaucoma ● Repeat tests to eliminate spurious results ● Perform binocular balancing ● Measure binocular visual acuity ● Assess fixation disparity ● Assess accommodation

Table 2-1. Guidelines to the procedural content of the routine eye examination. Adapted from Guidance for Professional Practice (College of Optometrists 2023b).

2.2 Methods

A systematic search of the literature was undertaken to identify the optimum methods of diagnostic visual assessment of individuals who had suffered a stroke.

The following types of studies were included: systematic reviews, controlled trials, randomised controlled trials, cohort studies, case series and retrospective note reviews. Studies were included where adult participants (18 years and over) had been identified as having previously suffered a stroke. Participants were not required to have been diagnosed as having suffered visual disturbance post stroke to be included in this study.

A Boolean strategy was used to search the following key electronic databases: MEDLINE (1948 to September 2017), SCOPUS (1823 to September 2017), CINAHL (1937 to September 2017) and PsycINFO (1887 to September 2017). Search terms included a variety of MESH terms and alternatives in relation to visual examination and stroke (**Table 2-2**). In order to identify further sources a hand search was conducted of the journals Ophthalmic and Physiological Optics, Journal of Optometry, Clinical and Experimental Optometry and Optometry and Vision Science. The title and abstracts of reference lists of included articles were also searched.

Articles assessing the diagnostic accuracy of recognised visual tests used in optometric practice on stroke survivors were included in this study. Articles related to the ocular sequelae of stroke but not addressing diagnostic process were considered to be outside the scope of this review and were excluded. Assessment of the diagnostic accuracy of visual tests commonly used in optometric practice where the primary study group participants had not experienced stroke were excluded. Titles and abstracts identified from the search strategy outline were reviewed by the author using the search strategy outlined above. Where it was not possible to identify if the study met the inclusion criteria from the title and abstract, the full published paper was reviewed. Articles were evaluated using the QUADAS-2 instrument for assessment of diagnostic accuracy studies (Whiting et al, 2011).

Stroke* Infarction* Cerebrovascular accident* Intracranial arteriovenous malformation Intracranial embolism Intracranial thrombosis Cerebral haemorrhage	**Refraction Keratometry Corneal topography Vision screening Visual acuity Contrast sensitivity Colour vision Amsler Stereopsis Near vision Visual impairment Vision, binocular Fixation disparity Eye movements Tonometry, ocular Pupil test Visual fields Perimetry Slit lamp microscopy Ophthalmoscopy Indirect ophthalmoscopy Visual stress**
OR	**OR**
AND	

Table 2-2. Search terms employed within the Boolean strategy, * MESH

2.3 Results

Search of the electronic databases identified 3915 studies, reducing to 391 after the removal of duplicates. An additional 14 studies were identified by journal search. Review of title and abstract removed a further 356 studies as not relevant to this review, resulting in 49 articles that were reviewed in full. Of these only two were found to be relevant to the review question, a summary of the findings of the systematic search are outlined in **Figure 3**.

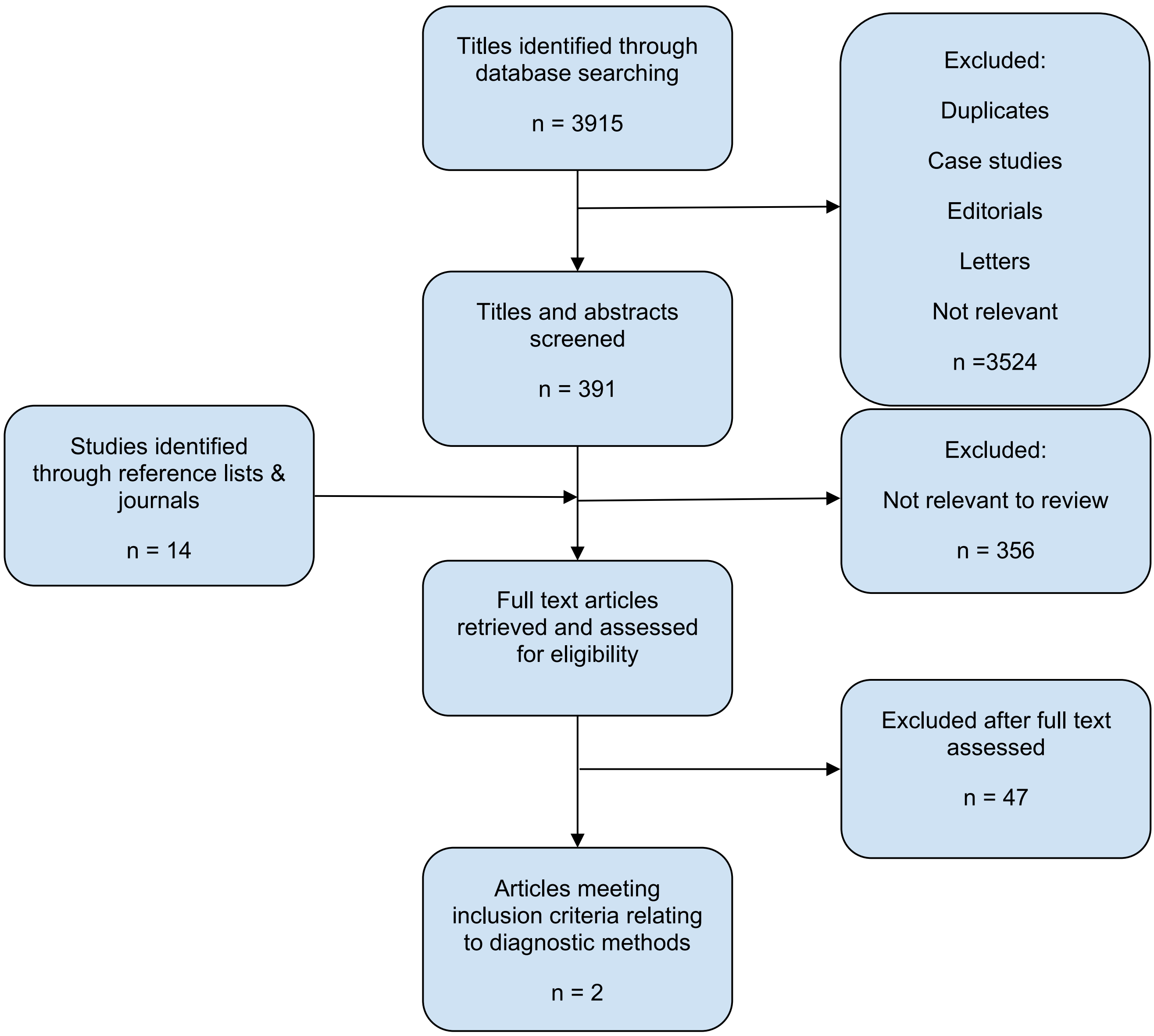


Figure 3. Flowchart for the pathway of included articles

Wong & Sharp (2000) present a prospective study where Goldmann, Humphrey (30-2) and Tangent Screen perimetry were compared and correlated with MRI images of post stroke participants. This study reported completion of field assessments within 1 month of each other and 3 months of MRI assessment (**Figure 4**). Twelve participants completed this study (time since stroke 4-20 months) and no controls were present. The results of perimetry were then assessed to predict the expected location of the cranial lesion which was compared with the location of the lesion on MRI. Ad hoc macular 10-2 fields were conducted on participants who exhibited macular sparing on Goldmann/Tangent screen perimetry that was not observed on 30-2 threshold testing. No details of masking were provided.

This study found that Tangent screen and Goldmann perimetry were found to correlate well with lesion location and low degrees of discrepancy were found between them. By contrast automated perimetry using the Humphrey Visual Field Analyser were found to not correlate well with either Goldmann, Tangent Screen or MRI location of the lesion. Even where further ad-hoc macular threshold fields were undertaken these were found to be of limited sensitivity in localising lesion. The presence of a visual pathway lesion was detected by all three methods of perimetry employed, but Humphrey perimetry was found to not correspond to the other perimetry forms or MRI in just under half of participants, resulting in inaccurate localisation of lesion and failed to reveal macular sparing in a third of participants.

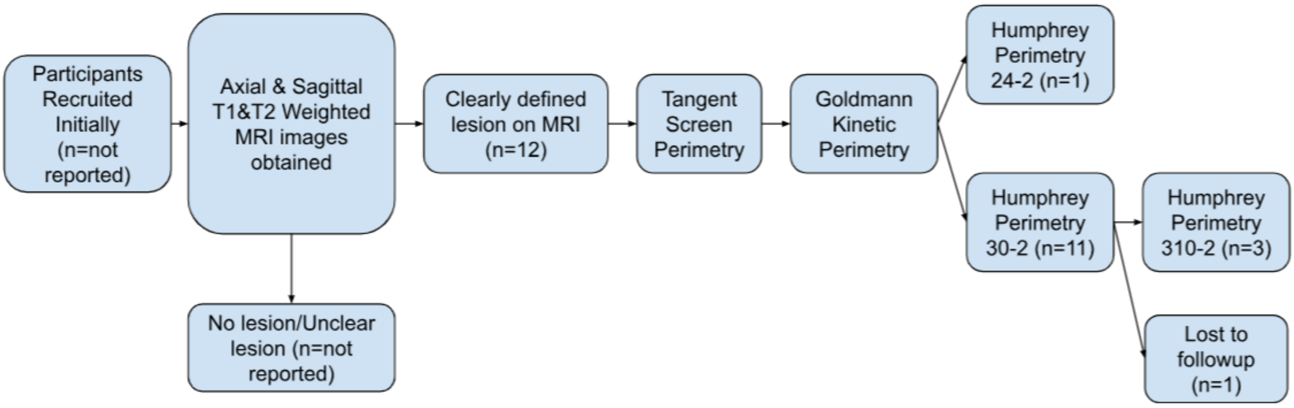


Figure 4. Flow diagram outlining the study process reported by Wong & Sharp, 2000

Townend et al (2007) presents a prospective study assessing the detection of post-stroke homonymous visual field loss comparing confrontation field assessment outlined by the National institutes of Health Stroke Scale (Goldstein and Samsa 1997) with automated threshold perimetry 9 months post stroke (**Figure 5**). The study suffered from a high attrition rate (65/151 completing the study) reporting a large number of participants being unable to proceed due to reduced consciousness, aphasia, cognitive impairment or inability to travel to the test site. Additionally, no control group was present for this study. The study consisted of patients undergoing full field 121-point threshold assessment on the Humphrey Visual Field Analyser II, following which patients were asked about their awareness of visual field loss before proceeding to a second confrontation assessment with an assessor who was blinded to the results of the threshold assessment.

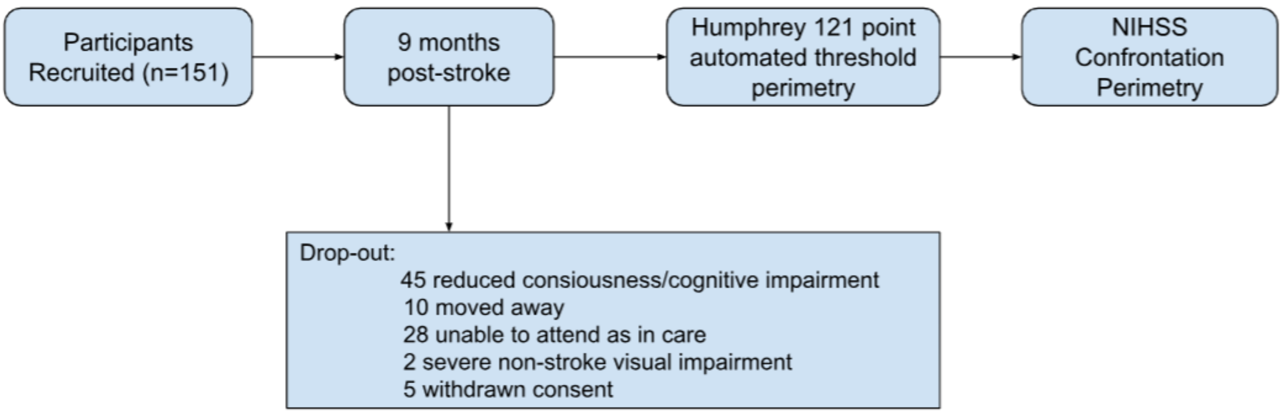


Figure 5. Diagram outlining flow of study as reported by Townend et al, 2007

It was reported that detection of field defects by threshold perimetry in 10/65 (16%) cases, with equal representation of hemianopic defect and quadrantanopia. 70% of defects were reported to affect the right field, though the split between hemianopia/quadrantanopia was not reported, and no participants reported symptoms of field loss. NIHSS confrontation identified field loss in three participants, only two of which exhibited field loss on threshold perimetry. From their findings, Townend et al report a sensitivity and specificity of NIHSS confrontation perimetry of 20% (95%CI=4-56%) and 98(95%CI=88-99) respectively.

2.4 Discussion

Systematic search and review of the literature identified two studies that evaluated the accuracy of vision assessment tools used in the examination of individuals post stroke. The first of these reports the accuracy of Goldmann, Tangent screen and Humphrey 30-2 threshold visual field assessment compared to an MRI localisation of the lesion. This study found that all methods were sensitive to the presence of a visual pathway lesion, but that Humphrey field assessment was not accurate in localisation of the lesion. By contrast Goldmann and Tangent screen were found to be consistent with one another and with MRI location of the visual pathway lesion. The second study sought to assess accuracy of NIHSS confrontation testing against 121-point threshold perimetry assessed using the Humphrey perimeter.

The studies identified suffer a number of quality issues in their design, implementation and reporting, a summary of the QUADAS-2 results are presented in **Table 2-3**. Wong & Sharp's (2000) recruitment is unclear, as participant numbers are confirmed after identification of a discrete lesion on T1 & T2 weighted axial and sagittal MRI. The process followed makes it unclear if researchers were masked, though the ad-hoc administration of 10-2 threshold fields to participants with macular sparing would suggest this was not the case, risking influence of the other examination techniques employed. This work reviews visual field defects as performed by different methods with the anatomical lesion location as identified on MRI. While anatomical mapping of brain areas does enable modeling of expected visual field defects from lesion location, it is important to note that some variation in cortical and pathway structure does exist in the healthy brain (Aguirre et al., 2016; C. Song et al., 2015), which may limit this approach as a benchmark of function, indeed it has been reported that specific field defects do not always map as anticipated to anatomical lesion location (Zhang et al. 2006; Tao et al. 2012). This approach may have been improved had functional MRI been used for mapping (Brown et al. 2016), allowing direct assessment of functionality. This raises a question on the use of MRI lesion location as a benchmark against which to assess the field accuracy, as an objective baseline of the impacted visual pathway, and as a structural surrogate for the integrity of visual field processing. The methodological variation reported, with ad-hoc 10-2 fields being undertaken on Humphrey on participants to investigate the instrument's sensitivity to macular sparing highlight a lack of consistency in the research process, highlighting the apparent absence of masking and exposure to potential observer bias in the course of this project. The final major limitation of this work relates to the small number of participants recruited to the study. This study was operated out of a Neuro Ophthalmology unit of Toronto Hospital, as a large population centre it is surprising that such a small sample size is reported upon, given the expected number of patients being reviewed. This small number weakens the impact of this report, raising questions to how representative of the wider population of stroke survivors with hemianopic type defects this is.

Townend et al (2007) identifies a structured approach to their investigation, identifying masking, and detailed inclusion/exclusion criteria. This study suffered from a small sample size, with significant dropout present. While widely employed within the clinical setting, considering the findings identified in Wong & Sharp (2000) the use of Humphrey perimeter as a reference test raises questions of validity of its use for assessing other field tests.

STUDY	RISK OF BIAS				APPLICABILITY CONCERNS		
	Patient Selection	Index Test	Reference Standard	Flow & Timing	Patient Selection	Index Test	Reference Standard
Wong and Sharp, 2000	−	−	−	−	−	−	−
Townend et al, 2007	+	+	?	+	+	+	?

Table 2-3. QUADAS 2 Risk of Bias results: + Low risk − High risk ? Unclear risk

The studies identified here are of low quality and contain a low number of participants. This reduces confidence in how representative they can be of the wider demographic of stroke survivors. Despite these issues they do highlight the variability in different testing methods within stroke survivors with visual field defects, highlighting challenges that may arise around the use of different methods of assessment of field loss in this group, an approach that has been used in some larger studies (Rowe et al., 2019). This review has, like the American Optometric Association Guideline on Adult Eye Examination (2015; 2023), identified a shortage of evidence on the optimal approach to examining the eyes and visual system of stroke survivors that could be applied in optometric practice.

Within health care it is essential to have a robust evidence base to inform practice and direct appropriate care. Much work has been done to improve the assessment of new diagnostic tests being introduced to clinical practice (Ferrante Di Ruffano et al. 2012; Cohen et al. 2016). The historic absence of a formal framework for diagnostic tests (Knottnerus et al. 2002) has however led to the routine use of many clinical tests without a rigorous evaluation of their diagnostic accuracy. It is well established that many patients have attention difficulties following brain injury, with the potential for fatigue to influence the results of an extensive battery of tests (Green et al. 2010b). Though there is an option to split the initial assessment into multiple sessions this may lead to patient non-attendance, and this may even result in the patient being lost to follow up (Marzolini et al. 2016). To provide effective visual care, it is important that the diagnostic tests undertaken are appropriate in scope and duration and identify the salient visual issues affecting those who have suffered stroke.

The assessment of individuals who have experienced a stroke necessitates a more comprehensive and time-intensive approach than standard visual testing (Hanna et al. 2020). Many practitioners in both community and hospital settings may be under time constraints to undertake an appropriate assessment and management before moving on to their next patient. While several visual screening tests have been developed to detect the presence of various visual deficits following stroke (Hanna et al. 2017a) within a secondary care setting this has not translated to an equivalent diagnostic approach for primary eye care practice.

The studies reported upon highlight the paucity in evidence for the most effective methods of undertaking a diagnostic visual examination in a patient with a history of stroke. While an absence of studies of diagnostic accuracy is present in this group, a short-term solution would be the use of a consensus-based approach to propose a minimum diagnostic test battery to assess visual function in these individuals. Such a battery could be used in several ways; It could support clinicians in the detection and diagnosis of visual anomalies caused by the stroke, aid in identifying the patient's visual prognosis, support monitoring the presence/absence of anomalies over time, and in patient management - identifying suitable interventions to support rehabilitation. This instrument could also be used in the research setting to offer a standard baseline on which to assess the effectiveness of various interventions.

These findings have previously been presented as a poster at Optometry Tomorrow 2018:

Maciver M., Markham C., & Stores R. (2018, March) *Methods of visual examination following stroke: A systematic review*. Poster presented at Optometry Tomorrow, the annual conference of the College of Optometrists. Birmingham

Chapter 3 Developing a diagnostic visual test battery for stroke patients: A Delphi study

3.1 Introduction

Strokes are responsible for around 10% of all deaths in the western world and are the second most common cause of death globally (Donnan et al. 2008), stroke can be broadly classified into two major subtypes, ischaemic and haemorrhagic. Ischaemic strokes result from cerebral vascular occlusion and represent around 80% of all strokes, with the more serious haemorrhagic strokes being encountered less frequently. The resulting cerebral damage from stroke can lead to a number of difficulties, affecting an individual's social, functional and cognitive performance (Hafsteinsdóttir and Grypdonck 1997).

The visual effects of stroke include central vision loss (Rowe et al. 2009), visual field loss (Gray et al. 1989; Donahue et al. 1995; Townend et al. 2007; Rowe et al. 2009; Larson 2015; Rashid et al. 2021), accommodative dysfunction (Ciuffreda et al. 2007; Green et al. 2010b), vergence dysfunction (Ciuffreda et al. 2007; Smaakjær et al. 2018), eye movement dysfunction (Suh et al. 2006; Rowe 2010a; Mullen et al. 2014), and a reduction of binocular performance (Bridge 2016). Other visual issues encountered by patients following stroke include a reduction in reading performance (Rowe et al. 2011; Dickens et al. 2021), light sensitivity and pattern glare (Beasley and Davies 2012; Beasley and Davies 2013a; Clark et al. 2017; Wu and Hallett 2017), a shift of the perceptual visual midline (Barton et al., 1998; Darling et al., 2003; W. V Padula & Argyris, 1996a) and visual inattention (Ting et al. 2011). Loss of vision or visual function can have a major impact on the quality of life (Vu et al. 2005) and can also be a major risk factor in falls (De Boer et al. 2004; Lord 2006). As the incidence of stroke increases with increasing age (Lee et al. 2011), falls resulting from visual loss can represent a risk factor for increased morbidity following stroke. Optometrists are often required to rely on their professional judgement in the provision of care to their patients. A best practice statement for the management of vision problems following stroke produced by the University of Glasgow (Fisher et al. 2013) advises a protocol to assess eye movement disorders and field loss but omits measurement of acuity or refraction, while guidance for professional practice provided by the College of Optometrists discusses the requirements for practitioner flexibility in examination (College of Optometrists 2023b). The aim of this study was to propose a minimum diagnostic test battery to provide a standard assessment of visual function to patients with a history of stroke. Such a battery would serve a number of uses; It would support clinicians in the detection and diagnosis of visual anomalies caused by the stroke, identifying the patient's visual prognosis, monitoring the anomalies over time, and in patient management - identifying suitable interventions to support rehabilitation. A Delphi method was used to seek the views of the content of a standard ophthalmic diagnostic battery for use when examining patients with a history of stroke who present for eye examination.

The Delphi technique is an iterative consensus driven methodology that uses expert opinion to establish consensus. This method, using iteration and anonymised group feedback, allows a group of selected experts to develop a consensus response to the problem posed (Keeney et al. 2006; Keeney et al. 2011). The technique is well established and has been used within medical and allied health disciplines for the establishment of competency frameworks (Holmes & Myint, 2018; Masud et al., 2014; Myint et al., 2010; Sue Hoyt et al., 2010), optometry curricula (Shah et al. 2016; Davey et al. 2017) and approaches to visual examination (Goodrich et al. 2013; Evans et al. 2017).

3.2 Methodology

In order to identify appropriate ophthalmic diagnostic tests for use in this group an electronic Delphi technique was used. The end point for this study was set at three rounds to reduce participant attrition (Cantrill et al. 1996). Questionnaires were designed and disseminated online using the questionnaire software BOS(www.onlinesurveys.ac.uk). Data analysis was undertaken by the principal investigator (MM). The panel was chosen using an opportunity sampling method to provide perspectives from eye care providers with experience of examining and managing patients with a history of stroke in primary and secondary eye care settings. Prominent researchers in this field were approached and invited to participate and details of the study were distributed to the Royal College of Ophthalmologists, College of Optometrists, British and Irish Orthoptic Society, and Stroke Association for dissemination to members who may be interested in participating. Interested potential participants were issued with detailed study information, and consent was implied by completion and submission of Delphi questionnaires.

In round 1, participants were invited to provide their responses to fourteen questions on the techniques to be employed to conduct an examination on a patient with a history of stroke that presents for an eye examination. The questions in this round were open, giving participants the opportunity to outline the participant’s personal practice when examining a patient with a history of stroke that presents for a routine eye examination.

In round 2 participants were issued with a questionnaire outlining the benchmark tests that should be conducted during a comprehensive ophthalmic examination on a patient with a history of stroke, this questionnaire consisted of 170 items. The questions presented as part of this round were derived from the responses of from round 1 of the study. In this round participants were instructed to respond to this questionnaire with the guidance they would give to a less experienced or confident colleague who had this patient booked for examination with them.

Questions in this round were closed, with most questions requiring participants to respond to case history questions and investigative techniques on a 5 point Likert scale, ranging from 1 - Unimportant to 5 - Very Important. Multiple choice options were available for participants to respond to length of examination, methods of oculomotor examination, methods of external and internal examination of the eye, perimetry, tonometry, and functions to be delegated to auxillary staff. For each of the Likert-type questions, a median figure and interquartile range was calculated. Items with an interquartile range of

1 or less were considered to have achieved consensus (Kay Rayens and Hahn 2000). Items that fulfilled this criterion and achieved a median of 4 (Important) or above were included in the comprehensive ophthalmic examination recommended.

For round 3 participants were again issued with a questionnaire outlining the benchmark tests that participants would recommend to a less experienced or confident colleague to be conducted during the ophthalmic examination on a patient with a history of stroke. In this round participants were instructed to consider the tests that should be prioritised for such a patient in a 25 minute examination. Participants were also given the option to outline tests to be conducted in a follow-up appointment as necessary. The questions that made up this questionnaire were derived from the responses to round 2 of the study, with any element that received a median score of less than 4 being removed from the primary examination section and offered to participants as an optional test for a follow-up examination. Consensus and inclusion in the recommended primary examination was followed as outlined above.

At each stage of the study, participants were issued with a summary of responses. Feedback from round 1 was delivered thematically whilst feedback from rounds 2 and 3 were presented as histograms to show group responses. This study was conducted in accordance with the requirements of the Declaration of Helsinki (2013) and received ethical approval from the Science Faculty Ethics Committee of the University of Portsmouth.

Participant	Practice Setting	Area of Specialisation
1	Community	Primary eye care
2	Community	Primary eye care
3	Community	Primary eye care
4	Community	Therapeutic Optometry
5	Hospital Eye Department	Low Vision
6	Academic/Community	Stroke
7	Community	Behavioral Optometry
8	Community	Behavioral Optometry
9	Community	Behavioral Optometry
10	Community	Behavioral Optometry
11	Community	Behavioral Optometry

Table 3-1. Demographic information on participants of the Delphi study. All participants were UK registered Optometrists.

3.3 Results

Following opportunity sampling there were 17 expressions of interest, of which 11 chose to participate within the Delphi study. The Delphi panel was made up of eleven optometrists with experience of providing care to patients with a history of stroke. The panel consisted of an optometry academic, a hospital based low vision optometrist, three community based optometrists, one community based therapeutic optometrist and five community optometrists with a specialist interest in behavioral and neuro-optometry (**Table 3-1**). All members of the panel were UK based GOC registered optometrists. Response rates for the study were 10 of 11 (91%) for round 1, 10/11 (91%) for round 2 and 7/11 (64%) for round 3 of the study.

3.3.1 Round 1

Responses to the first round reported on contemporary practice. Clinicians indicated a range of examination times ranging from 30 minutes to 3 hours, with most participants indicating an examination time under an hour. Responses from participants indicated that a thorough case history should be undertaken, seeking to identify clinical symptoms affecting distance and near vision, central and peripheral vision, spatial awareness, diplopia, pattern sensitivity and how these impact quality of life. Other key features of clinical history related to the presence of cardiovascular disease, medical and medicinal history and details relating to the stroke.

To examine the external and internal eye, most participants indicated a preference for slit lamp biomicroscopy examination to assess the external eye, and slit lamp indirect examination to assess the internal eye, though one respondent indicated a preference for direct ophthalmoscopy to assess the external eye. In addition to a physical examination of the eye most participants indicated that they would conduct a pupil assessment, peripheral vision assessment and intraocular pressure testing.

In assessing the visual system respondents were uniform in their suggestion of distance acuity (aided and unaided). Other tests suggested included colour vision testing by Ishihara and red desaturation, and contrast sensitivity testing. Retinoscopic objective refraction was the preference for most practitioners, followed by conventional Jackson Crossed Cylinder refraction with binocular balancing. Many practitioners also sought to undertake testing of the accommodative system (especially in pre-presbyopic subjects) and assessment of vergence ranges.

To assess ocular alignment, respondents were evenly split between the use of the objective cover test and the use of a Maddox rod. Most respondents also indicated a preference for fixation disparity findings to support their prescribing as well as near point convergence testing. Tests of fusion were rare and less than half of respondents chose to measure stereopsis. Physiological X/H testing of ocular motility was near universal with many practitioners also testing patient's saccadic accuracy through observation and tests of inferred saccadic accuracy (eg the Developmental Eye Movement Test [Bernell Corporation, IL, USA] or King-Devick Test [King-Devick Technologies, IL, USA]). In addition, a range of other procedures were identified by individual participants as useful during assessment, notably; the Wilkins Rate of Reading Test (Institute of Optometry, London, UK), Pattern Glare Test (Institute of Optometry, London, UK), alpha-omega pupil testing, optokinetic nystagmus testing, jump vergence, effect of typoscope on reading and dilated fundus examination. Two participants responded that due to the variable sequelae of stroke, their examination would be fluid and tailored to the visual requirements of the patient. While some responses indicated a preference for clinicians to conduct all diagnostic testing, non-contact tonometry, visual field testing, fundus imaging and OCT were frequently delegated to auxiliary staff to undertake prior to examination with the optometrist.

3.3.2 Round 2

Participants indicated that a comprehensive examination should take upto 75 minutes (1/10, 10%), with most opting for between 30 and 45 minutes (3/10, 30% and 4/10, 40% respectively) with 20% (2/10) suggesting a period of around an hour. In response to clinical questions to be included in case history, consensus was achieved in 77/79 questions, with participant's identifying 4 questions that should not be included in the comprehensive case history (**Table 3-2**).

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
How is the patient's distance vision?	Yes - Include	5	0.75	4.7	0.48
How is the patient's near vision?	Yes - Include	5	1.00	4.6	0.52
Does the patient experience variability in vision?	Yes - Include	4	1.00	4.3	0.67
Does the patient experience asthenopia?	Yes - Include	4	0.75	4.1	0.88
Does the patient experience headaches?	Yes - Include	4	1.00	4.4	0.52
Does the patient experience diplopia?	Yes - Include	5	0.00	4.8	0.42
Does the patient experience flashes & floaters?	Yes - Include	4	0.75	3.7	0.82
Does the patient have difficulty in coordination?	Yes - Include	4	0.75	4.1	0.88
How is the patient's balance?	Yes - Include	4	0.75	4.2	0.63
Does the patient experience any dizziness?	Yes - Include	4	0.75	4.1	0.74
Does the patient experience sensitivity to motion?	No - Include	4	2.00	3.9	1.10
Does the patient experience car sickness?	Yes - Exclude	3	1.00	3.4	1.17
Does the patient notice any reduction in their peripheral vision?	Yes - Include	5	0.75	4.7	0.48
Does the patient leave food on their plate when eating?	Yes - Include	4	0.75	3.7	1.06
Does the patient walk/bump into things?	Yes - Include	4.5	1.00	4.5	0.53
Do faces appear to be distorted to the patient?	Yes - Include	4	1.00	4.4	0.52
Does the patient experience visual hallucinations?	Yes - Include	4	1.00	4.3	0.67
Does the patient have difficulty maintaining focus?	Yes - Include	4	0.75	4.1	0.88
Does the patient have difficulty changing focus?	Yes - Include	4	0.00	4	0.82
Does the patient experience visual difficulty when reading?	Yes - Include	4.5	1.00	4.5	0.53
Does the patient have trouble with comprehension when reading?	Yes - Include	4.5	1.00	4.5	0.53
Does the patient have trouble when using VDUs?	Yes - Include	4	0.75	4.1	0.88
Is the patient sensitive to bright light?	Yes - Include	4	1.00	4.2	0.92
Does the patient suffer from sensitivity to glare?	Yes - Include	4	1.00	4.2	0.92
Does the patient experience pattern related discomfort?	No - Include	4	1.50	3.9	0.99
How is the patient's general health?	Yes - Include	5	0.75	4.7	0.48
Has the patient been diagnosed with any medical conditions?	Yes - Include	5	1.00	4.6	0.52
Does the patient suffer from hypertension (high blood pressure)?	Yes - Include	4.5	1.00	4.5	0.53
Does the patient suffer from diabetes?	Yes - Include	4.5	1.00	4.5	0.53
Does the patient suffer from hypercholesteremia (high cholesterol)?	Yes - Include	4.5	1.00	4.4	0.70

Does the patient undertake regular exercise?	Yes - Exclude	3.5	1.00	3.5	0.85
Does the patient smoke?	Yes - Include	4	0.75	4.3	0.48
Does the patient drink?	Yes - Include	4	0.00	3.7	0.67
Does the patient take non prescription drugs?	Yes - Include	4	1.00	3.3	1.06
Has the patient been diagnosed with any mental health conditions?	Yes - Include	4	1.00	3.5	0.97
Does the patient take any medications?	Yes - Include	5	1.00	4.6	0.52
Does the patient take any nutritional supplements?	Yes - Exclude	3.5	1.00	3.2	1.03
Did you ever have any surgery to straighten the eyes as a child?	Yes - Include	4	1.00	4.3	0.67
Did you ever have to wear an eye patch as a child?	Yes - Include	4	1.00	4.3	0.67
Have you ever been given exercises for your eyes?	Yes - Include	4	0.00	3.8	0.79
Do you routinely use refractive correction?	Yes - Include	5	1.00	4.6	0.52
Have you ever had an injury to the eye?	Yes - Include	4	0.75	4.3	0.48
Have you had eye surgery for any other problems?	Yes - Include	5	1.00	4.6	0.52
Have you been diagnosed with any eye conditions?	Yes - Include	4.5	1.00	4.5	0.53
Do you ever experience dry/gritty eyes?	Yes - Include	4	0.00	4.1	0.57
Do you ever experience itchy eyes?	Yes - Include	4	0.00	4	0.67
Do you ever experience eye pain?	Yes - Include	4	0.75	4.2	0.63
Do you ever experience watery eyes?	Yes - Include	4	0.75	4.1	0.74
Do you take any eye drops?	Yes - Include	4	0.00	4.1	0.57
Do you experience pain when moving your eyes?	Yes - Include	4	0.75	4.1	0.74
Do you experience any flashing lights?	Yes - Include	4	0.00	4	0.67
Have you experienced any distortion in your vision?	Yes - Include	4	0.75	4.3	0.48
Have you experienced any changes in how you see colours?	Yes - Include	4	0.00	4	0.47
Date of the stroke?	Yes - Include	4	1.00	4.1	1.20
Time of onset of stroke on the day of the episode?	No - Exclude	3	1.75	2.7	1.16
Severity of stroke symptoms at onset?	Yes - Include	4	1.00	4.3	0.67
Severity of stroke symptoms now?	Yes - Include	5	1.00	4.6	0.52
Severity of visual symptoms at onset?	Yes - Include	4	1.00	4.4	0.52
Severity of stroke symptoms now?	Yes - Include	5	0.75	4.5	0.97
How many previous episodes were experienced?	Yes - Include	4	0.75	4.1	0.88
Brain areas affected by the stroke?	Yes - Include	4	0.75	4.1	0.88
How has the stroke affected the patient physically?	Yes - Include	4.5	1.00	4.5	0.53
How has the stroke affected the patient emotionally?	Yes - Include	4	0.75	4.1	0.88
What rehabilitation is the patient currently receiving?	Yes - Include	4	1.00	4.3	0.67
Any previous brain injury?	Yes - Include	4	0.00	3.9	0.57
Is the patient currently under the care of a stroke clinic?	Yes - Include	4	1.00	4.4	0.52
What prognosis has the patient been given?	Yes - Include	4	1.00	4.4	0.52
How is the patient's mobility?	Yes - Include	4	0.75	4.3	0.48
Is the patient still working? if so, what is their occupation?	Yes - Include	4	0.75	4.3	0.48
Is the patient able to undertake tasks on their own without a carer?	Yes - Include	4	0.75	4.3	0.48
How is the patient's hand-eye coordination?	Yes - Include	4	0.75	4.2	0.63
What are the patient's hobbies?	Yes - Include	4	1.00	4.4	0.52
Is the patient able to undertake their hobbies without visual impediment?	Yes - Include	4	1.00	4.4	0.52
Does the patient read for pleasure?	Yes - Include	4	1.00	4.4	0.52
Is the patient able to read with good comprehension?	Yes - Include	4	1.00	4.3	0.67
Does the patient use VDU/tablets/smartphones?	Yes - Include	4	0.75	4.3	0.48
Does the patient experience losses of concentration?	Yes - Include	4	1.00	4.2	0.79
Does the patient drive?	Yes - Include	5	0.00	4.9	0.32
Has the patient been advised not to drive?	Yes - Include	5	1.00	4.6	0.52

Table 3-2. Case history questions - responses to questions identified by participants as important for inclusion within comprehensive evaluation.

For diagnostic items assessing the visual system, consensus of assessments to be undertaken was reached in 16/16 items presented - identifying 5 tests to be included in a comprehensive visual test battery (**Table 3-3**). Participant's responses were mixed, with most indicating that distance acuity should be assessed using LogMAR (6/10, 60%), while the remainder indicated preference for the more traditional Snellen (4/10, 40%) assessment. All participants indicated that corrected distance acuity should be measured, while most indicated that they would collect unaided distance acuity (9/10, 90%) and habitual distance acuity (8/10, 80%). Near vision assessment was similarly split, with many indicating a preference for the traditional N point acuity measure (9/10, 90%) with a minority indicating a near LogMAR (1/10, 10%) should be used. All participants agreed that corrected near acuity would be measured, with the majority indicating that habitual (8/10, 80%) and unaided (9/10, 90%) near acuity should be assessed.

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Pelli-Robson Contrast Sensitivity	Yes - Include	4	1.00	3.5	0.71
Ocular Dominance (Sensory)	Yes - Include	4	1.00	3.4	0.82
Pattern Glare Test	Yes - Include	4	0.75	3.6	0.70
Wilkins Rate of Reading Test	Yes - Include	4	1.00	3.5	0.71
Colour Vision Screening (Ishihara, City III)	Yes - Include	4	0.75	3.8	0.63

Table 3-3. Tests of the visual system - Tests of the visual system identified as required within a comprehensive visual examination.

For diagnostic assessment of the refractive system, consensus was reached 14/21 items presented, identifying 8 refractive diagnostic tests (**Table 3-4**) to be included in the comprehensive diagnostic battery.

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Retinoscopy	Yes - Include	4	1.00	4.4	0.52
Jackson Crossed Cylinder Refraction	Yes - Include	4	0.75	3.9	0.74
Binocular Balancing	Yes - Include	4	0.00	4	0.67
Amplitude of Accommodation	Yes - Include	4	0.75	3.8	0.63
Determination of Near Addition	Yes - Include	4	1.00	4.4	0.52
Determination of Intermediate Addition	Yes - Include	4	1.00	4.4	0.52
Pin-hole test	Yes - Include	4	1.00	4.3	0.67
+1.00DS Blur test	Yes - Include	4	0.00	3.8	1.14

Table 3-4. Tests of the refractive system - Tests identified by the panel as being required as part of the comprehensive evaluation.

Assessment of the binocular vision system consensus was achieved in 14/18 items presented, identifying 8 binocular vision tests (**Table 3-5**) to be included in the battery. On questioning the preference of methods of oculomotor assessment, most participants indicated a preference for the cover-uncover test for distance (7/10, 70%) and near (6/10, 60%) assessment. Other methods used included the Howell Card for distance (2/10, 20%) and near (2/10, 20%) assessment, assessment using the Maddox Rod for distance (10%) and near (1/10, 10%) assessment and the Maddox Wing for near oculomotor evaluation (1/10, 10%).

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Near point of convergence testing	Yes - Include	4	0.00	4.1	0.57
Jump vergence to 15cm	Yes - Include	4	0.75	3.7	1.16
Distance Fixation Disparity	Yes - Include	4	0.00	3.8	0.79
Near Fixation Disparity	Yes - Include	4	0.00	3.8	0.79
Ocular Motility (Physiological H/X)	Yes - Include	5	1.00	4.5	0.71
Ocular Saccades	Yes - Include	4	0.75	3.6	1.26
Ocular Pursuits	Yes - Include	4	0.75	3.6	1.26
Stereopsis	Yes - Include	4	0.00	4	0.47

Table 3-5. Tests of the binocular system identified as being required as part of the comprehensive evaluation.

To undertake an assessment of ocular health, all participants indicated a preference for the slit lamp biomicroscope to assess the anterior eye, whilst the majority (9/10, 90%) choosing to use this instrument with a condensing lens to assess the posterior eye, rather than a direct ophthalmoscope (1/10, 10%). To assess the anterior eye, consensus was reached on 7/15 items presented, with 3 tests of the anterior eye to be conducted in the battery. In the assessment of ocular health and complementary tests consensus was reached on 9/12 items presented identifying a further 7 tests to be undertaken (**Table 3-6**). Of those using the slit lamp with condensing lens to view the posterior pole there was an even split between participants who would undertake a dilated examination and those who would undertake the test undilated. The largest group (5/10, 50%) chose to use a wide field 90D lens, while the remainder were evenly split between the 60D (2/10, 20%) and 78D lenses (2/10, 20%).

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Van Herrick's test	Yes - Include	4	0.75	3.9	1.20
Sodium Fluorescein staining	Yes - Include	4	0.00	4.0	0.67
fBUT	Yes - Include	4	0.75	3.7	0.48
Colour Retinal Photography	Yes - Include	4	1.0	3.5	0.97
Macular OCT Imaging	Yes - Include	4	0.75	3.6	1.07
Optic Nerve Head OCT Imaging	Yes - Include	4	0.00	3.7	1.06
Measurement of Pupil Diameter	Yes - Include	4	1.00	3.4	1.17
Pupil Reflex testing	Yes - Include	4.5	1.00	4.5	0.53
Marcus Gunn Swinging Flashlight test	Yes - Include	4.5	1.00	4.4	0.70
Perimetry	Yes - Include	5	1.00	4.5	0.71
Tonometry	Yes - Include	5	1.75	4.3	0.95
Amsler test	Yes - Include	4.5	1.00	4.3	0.82

Table 3-6. Tests of ocular health identified as required as part of the comprehensive evaluation.

Of note, only one test met the requirement of achieving the requirement for inclusion but without consensus being reached, that being assessment of intraocular pressure. To conduct this test participants were split, reporting Goldmann Applanation Tonometry (GAT) (4/10, 40%), pneumatic tonometry (3/10, 30%) and rebound tonometry (2/10, 20%) as their preferred method, with one participant (10%) viewing this test as being unimportant in this case.

3.3.3 Round 3

When considering the clinical case history in the third round, participants reached consensus for 54/73 questions to be included in the case history, identifying two questions not to be included in the minimum battery. When undertaking assessment of the visual system consensus was reached on all items presented (**Table 3-7**) identifying 4 tests of the visual system to be included on the diagnostic battery.

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Habitual Distance Acuity (LogMAR)	Yes - Include	5	0.0	4.86	0.38
Habitual Near Acuity (N Point)	Yes - Include	5	0.5	4.43	1.13
Corrected Distance Acuity (LogMAR)	Yes - Include	5	0.0	4.86	0.38
Corrected Near Acuity (N Point)	Yes - Include	5	0.0	4.86	0.38

Table 3-7. Tests of the visual system identified as required as part of the essential diagnostic battery.

Similarly, consensus was reached for all presented items in the assessment of the refractive system, confirming 6 diagnostic tests to be used in the final battery (**Table 3-8**). Participant's responses were mixed in response to binocular assessment for the minimum test battery. Consensus was reached in 6/10 items presented, identifying 3 diagnostic tests to be included in the minimum test battery (**Table 3-9**).

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Retinoscopy	Yes - Include	5	1.00	4.57	0.53
Jackson Crossed Cylinder Refraction	Yes - Include	4	1.00	4.43	0.53
Binocular Balancing	Yes - Include	4	0.00	4.00	0.58
Determination of Near Addition	Yes - Include	5	0.50	4.71	0.49
Determination of Intermediate Addition	Yes - Include	4	1.00	4.43	0.53
Pin-hole Test	Yes - Include	4	0.50	4.14	0.69

Table 3-8. Tests of the refractive system identified as required for the essential diagnostic battery.

In the examination of ocular health, the majority (6/7, 86%) indicated that they would use the slit lamp biomicroscope during the minimum test battery, while the remaining participant opted to use the direct ophthalmoscope. Consensus was achieved in 2/3 tests presented identifying two anterior eye assessment techniques for the minimum battery. For assessment of the posterior eye and ocular health most participants (5/7, 71%) indicated that the most appropriate technique would be slit lamp indirect assessment using a 90D lens, the remaining participants were split between the use of slit lamp assessment with a 78D lens (1/7, 14%) and direct ophthalmoscopy (1/7, 14%). For ocular health and complementary assessments, consensus was reached for 5 / 11 techniques presented, identifying diagnostic tests (**Table 3-10**) to be included in the minimum battery. Of note, automated perimetry was rejected from the final battery (Median 3, IQR 1.5).

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Distance Cover Test	Yes - Include	5	0.00	4.86	0.38
Near Cover Test	Yes - Include	5	0.00	4.86	0.38
Near Point of Convergence	Yes - Include	4	1.00	4.28	0.75
Distance Fixation Disparity	No - Exclude	4	1.50	3.71	1.11
Near Fixation Disparity	No - Exclude	4	1.50	3.71	1.11
Ocular Motility (Physiological H/X)	Yes - Include	4	0.50	4.14	0.69

Table 3-9. Tests of the binocular system identified as part of the essential evaluation. Note that while agreement was not reached for three of these tests.

When offered the opportunity for prospective tests for follow-up examination, six (86%) participants indicated diagnostic procedures that would be undertaken not covered in the initial examination, with consensus being reached for 20/42 items presented, identifying 4 diagnostic tests that should be considered for follow-up assessment, only one of which (Wilkins Rate of Reading Test - Median 4, IQR 1.00) was not included in the main examination.

Question	Agreement?	Median	Inter-quartile range	Mean	Standard Deviation
Van Herrick's test	Yes - Include	4	1.00	3.71	1.38
Sodium Fluorescein Staining	Yes - Include	4	1.00	3.29	1.25
Pupil Reflex testing	Yes - Include	5	0.50	4.57	0.78
Marcus Gunn Swinging Flashlight test	Yes - Include	5	0.00	4.86	0.38
Amsler test	Yes - Include	4	0.50	3.86	0.69

Table 3-10. Tests of ocular health identified for inclusion to the essential test battery.

3.4 Discussion

This study is the first investigation to construct a visual diagnostic test battery for the examination of patients with a history of stroke. This study utilised a Delphi methodology, bringing together experienced eye care providers to construct a standardised test battery to examine the ocular health and visual system of this group (**Figure 6**).

While access to hospital-based eye care services for patients who have suffered acute stroke have improved over the last decade, there are a number of areas where patients still are without access to these services (Hepworth and Rowe 2019; Stalin et al. 2024a). The picture of accessibility to community services are less clear, with many studies investigating access not recruiting optometrist participants, and an absence of commissioned community eye care services dedicated to stroke patients. This is further confounded with perceptual barriers limiting patients to seek out community eye care services. A national report produced for the RNIB (Hayden 2012) identified that many patients report barriers in accessing primary eye care services, based upon knowledge of eye health issues and financial barriers to accessing primary eye care services.

In the course of this study it was identified that consistency and the provision of eye care provided by participants would alter depending upon the patient's ability to pay for a private comprehensive exam or access to a dedicated further investigation pathway. While several participants indicated that eligibility for NHS testing would not influence their exam, half of participants indicated that they would not be able to provide their desired level of care due to time and financial constraints. This suggests that while hospital-based eye care services have improved, significant barriers exist in the accessibility of comprehensive community eye care services for patients with chronic stroke, even among experienced practitioners. When confronted with a time limitation, or a subsequent follow-up appointment some clinicians chose to alter their approach, reducing the diagnostic tests employed:

"What is the reason for a follow-up appointment? If I was looking for something specific I may use specific exam techniques to confirm or rule out a potential diagnosis."

While one participant suggested that remote review of symptomatology may be more appropriate in lieu of further diagnostic evaluation.

"I would recommend a follow-up phone call rather than another examination. The phone call would establish whether the visual needs of the patient had been addressed in a 'real world situation' more appropriately than endless quantity of testing."

This suggests that while practitioners seek to provide a high level of patient centred care, they are often unable to provide this due to financial and time constraints. It is perhaps unsurprising therefore that the minimum battery identified within this group shares many features with the College of Optometrists' guidance (2023b) on the content of a routine eye examination. This aligns with the findings of Shickle et al (2015) that identified that frequently the NHS sight test fee is viewed as a loss leader, with costs recouped from the sale of other services or appliances. The report of these experienced participants highlights that inequality in the provision of comprehensive care exists and may be wide ranging especially among less experienced or confident colleagues.

A recent update to the College of Optometrists guidance on professional practice included guidance on the examination of patients with acquired cognitive impairment. This edition of the guidance highlighted the importance of clinicians in maintaining flexibility in assessment, communicating with the patient in the presence of cognitive impairment and emphasises the importance of the patient's capacity to consent to examination and management of visual anomalies. While this guidance does not specify diagnostic testing, indicating that patients with cognitive impairment may have a similar range of problems as the general population, it directs clinicians to review their patient's colour vision and contrast sensitivity to consider these factors when determining the suitability of coloured lenses in this group, with the clinician satisfying themselves to the appropriateness of the interventions prescribed. The findings of this study are at variance with the professional guidance in this area, though it should be noted that the guidance has been heavily influenced by the findings of the PrOVIDe study (Bowen et al. 2016) investigating the prevalence of visual issues in a dementia population.

While many cognitive issues may be common to dementia and stroke, with dementia arising as a sequela to stroke in some instances (Hu and Chen 2017), the difference in aetiology and pathogenesis may lead to different clinical requirements for these patient groups. Like dementia, visual problems following stroke are likely to be underreported (Cockburn 1983; Rowe 2011b; Baxter et al. 2013; Rowe 2013), with even many visual screening tools lacking sensitivity due to their reliance upon patient reported symptoms (Hanna et al. 2017a). It is therefore likely that the prevalence of visual impairment following stroke may be higher than reported in the literature. Optometrists represent the largest group of eye care providers in the UK and optometrists provide the majority of primary eye care services (Shah et al. 2007). With the ageing UK population, and improved management of stroke, optometrists will increasingly be required to provide care to patients with chronic stroke. The development of a visual diagnostic battery that may be employed by a trained eye care professional would serve as a useful benchmark for the clinician, while providing support to neophyte practitioners.

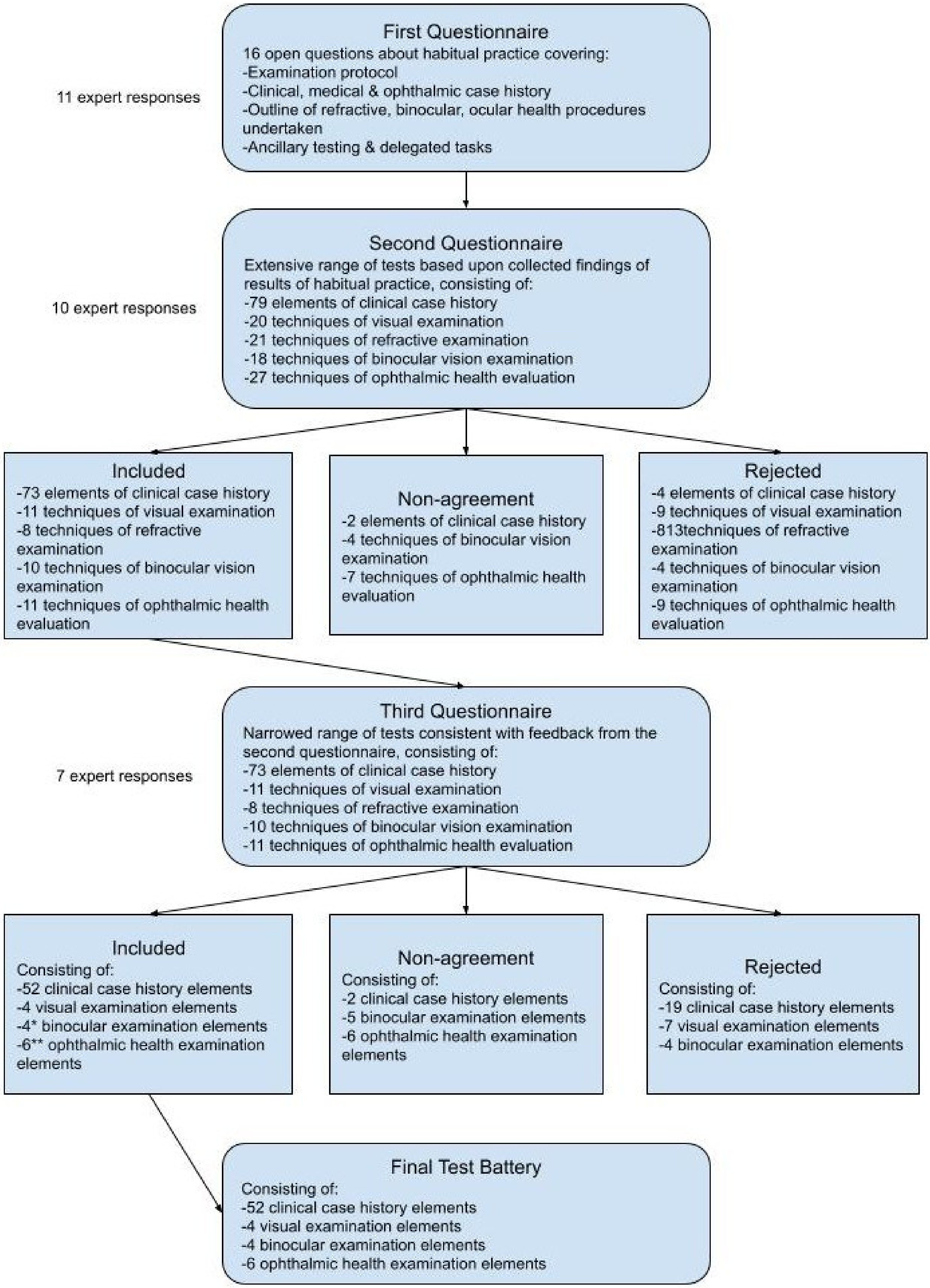


Figure 6. Summary of the Delphi protocol used in the development of the standardised clinical battery. *3 clinical items included, and ** single item included where median score was 4 or greater was found but no consensus found with interquartile range >1.

In making use of the Delphi approach in this study expert opinion was able to be collated to develop a diagnostic instrument for use in patients with chronic stroke. While the Delphi approach has been employed in a number of areas within both optometry and wider health care, the method has some notable limitations. *The Delphi technique has been described "as a method of structuring group communication process so that the process is effective in allowing a group of individuals, as a whole, to deal with a complex problem"* (Linstone and Turoff 1975)*. This method, using iteration and anonymised group feedback, allows a group of experts to develop a consensus response to the problem posed* (Dalkey and Helmer 1962).

Challenges arise in defining what constitutes the 'expert', as although several studies have examined different approaches to defining expertise (Hasson et al. 2000; Hanafin 2004; Keeney et al. 2006; Hasson and Keeney 2011), there remains no universally accepted definition of what constitutes an expert (Hanafin 2004). In this study participants were recruited using opportunity sampling. Participants self-selected based on prior expertise in the provision of eye and vision care services to patients with chronic stroke. As a self-selecting panel, these participants were likely to have an interest and understanding of the visual sequelae of stroke. These participants were able to call upon their previous experience to identify further lines of examination and diagnostic testing that less experienced practitioners may not consider. *The Delphi approach is reliant upon the skills and experience of the panel recruited. While there is no standard sample size for Delphi studies* it has been suggested (Delbecq et al. 1975; Linstone and Turoff 1975) that a smaller group of 10-15 participants may be feasibly managed. While larger groups have been found to improve the range of experience, it has been suggested that significant increases in sample sizes add little to the findings of a Delphi study (Black et al, 1999). This issue is compounded around the lack of inter-panel reliability.

It has been reported in the literature (Williams and Webb 1994; Walker and Selfe 1996) that variability of outcome may exist between panels, though this has been disputed elsewhere (Duffield 1993; Ono et al. 1994). By its nature, the Delphi method utilises a qualitative approach and is reliant upon the opinion of participants. To minimise bias, the Delphi approach limits communication between panel members by having a facilitator control communication with the expert panel. However, bias may be observed in applying this method especially in an attempt to conform to expected norms. This was identified in the first round of the study where one participant identified that their method of internal examination of the eye "*... is defined in the GOC guidelines*". While variety in methods of care is to be expected between any two eye care professionals, it is likely that even with inter-participant masking that a desire to be seen to conform to professional standard (real or perceived) will have influenced responses.

Despite the variety of procedures employed by participants of this study, it is perhaps surprising that the tendency was observed for the selection of examination procedures that largely aligned with the elements of the College of Optometrists' (2023b) recommendations for an eye examination. While the participants of this study ranged in the nature of their practice, including some whose scope involved different philosophical approaches, it is likely that this convergence arose due to the homogeneity of the participants as practicing optometrists. A more diverse panel may have resulted in an instrument more tailored to stroke specific visual issues. Despite many cognitive and communication difficulties may arise following stroke, no consideration was given to the complexities of procedures employed, or the relevance to ongoing care.

One area not appraised within the battery was the examination of stroke survivors for visuospatial neglect. While some clinicians in the first round of the Delphi did report undertaking tests for visual neglect these were selected out in subsequent stages. Present in 20 to 80% of stroke survivors, visual neglect has the potential to impact functional outcomes such as mobility, reading and other activities of daily living (Ten Brink et al. 2017; Esposito et al. 2021; Bosma et al. 2023; Durfee and Hillis 2023). The failure to detect this anomaly (especially where it has not otherwise been detected) may compromise any rehabilitation effort the patient seeks to undergo. This likely resulted from the homogeneity of the participants of the test battery, with subjects possibly viewing the evaluation of perceptual deficits as beyond the scope of their care provision. This likely would not have been the case had input been present from specialists outside optometry such as occupational therapists, Neurologists, Neuro-ophthalmologists or orthoptists. The exclusion of visuospatial neglect screening underscores a wider issue in the test battery – namely, a tendency to favour established optometric tools, even where their diagnostic utility may be limited.

The selection of the Ishihara test of colour vision may have arisen from a similar concern. While sensitive for the detection of protoanomalous and deuteranomalous defects (Birch 1997), this instrument was initially designed for the screening of congenital colour vision deficits, and would be ill suited to the determination of colour anomalies where perceptual anomalies may affect a wide range of the colour spectrum (Munk et al. 2023). It was likely that this was chosen due to its familiarity to clinicians and its relative ease and speed of use. While other tests such as the Farnsworth D15 Dichotomous Colour Blindness Test or City III test may be more suitable, these procedures are less widely used and less familiar to many clinicians. As such, while this battery may be able to detect defects colour perception affecting similar areas of the colour spectrum as the common congenital anomalies, it is insensitive to anomalies of the blue-yellow colour pathway.

Although the Maddox rod may provide a quantitative measure of any deviation present, this technique is of limited use in isolation. For instance, it is inadequate to determine a latent and manifest deviation or deriving insight to the degree of compensatory control a patient may exhibit - tasks that the cover-uncover test is better suited (Evans 2022). Similarly, while assessments such as the Developmental Eye Movement (DEM) test are frequently employed to infer saccadic accuracy (Facchin 2021), their clinical utility remains contested. While individuals with reading difficulties may perform poorly on the DEM test, this has been found not to correlate with poor eye movements or symptoms of oculomotor dysfunction (Ayton et al. 2009). Indeed, when controlling for poor reading ability the test's predictive value for reading speed diminishes dramatically (Webber et al. 2011), with one study's findings suggesting that the anomalous eye movements may be more likely to be the effect of poor reading rather than the cause of these difficulties (Medland et al. 2010). While less widely used within eyecare, given the similar design it is likely that the King-Devick Test may suffer similar limitations.

One surprising omission from the final developed test battery was that of field assessment. As highlighted in **Chapter 1** and **Chapter 2**, field loss affects a large number of stroke survivors and may have significant impact on quality of life. While it may seem unusual that some form of perimetry (beyond Amsler testing) was omitted from the final test instrument, this is likely to have resulted from the anticipated examination time frame proposed in round 3 of the Delphi. It is possible that clinicians chose to forgo perimetry in order to use this time on other procedures. While this may appear appropriate when considering the provision of basic refractive care, it presents a major gap in capability of the provision of wider visual care to stroke survivors, with the absence of detection of field defects potentially impacting on aspects of daily living (Rubin et al. 2001), increasing risk of falls (Rowe et al. 2013a), and where coincident with neglect presenting a risk of harm to the stroke survivor or others around them.

Due to its iterative questionnaire approach, the Delphi method is at risk of low response rates (Keeney et al. 2006). While reminders were sent to non-responding participants, and feedback designed to be accessible to participants the low response rate of the final round of the study limited the input of the wider panel in the final battery design and risks limiting the validity of the outcome due to the reduced sample input.

Over the course of the study several participants highlighted the importance of a symptom led examination. Identifying that their approach, and that recommended by them would be directed by the symptoms experienced by the patient.

"I feel tests performed should be symptom dictated. Each patient will be very different and some tests won't be possible to perform on every person."

"Some symptoms would require certain tests. I would be led by patients' symptoms as to what is important to test."

Given this approach, it is perhaps unsurprising that variation exists between these experts at a clinical level. Conducting a symptoms-based exam would lead to variation in diagnostic procedures used on a patient-by-patient basis. Another source of diversity could be the different approaches to different aspects of ocular assessment. There is a paucity of evidence around many ophthalmic diagnostic methods employed in primary eye care practice (American Optometric Association 2015; American Optometric Association 2023) especially in patients with a history of stroke. It is likely that clinicians select diagnostic procedures based on familiarity rather than inherent accuracy, which may result in variation of patient outcomes and subsequent management.

These findings have previously been presented as a poster series:

Maciver M., Markham C., & Stores R. (2019, March) *A minimum dataset for the ophthalmic examination of patients with a history of stroke: a Delphi study*. Poster presented at Optometry Tomorrow, the annual conference of the College of Optometrists. Birmingham

Maciver M., Markham C., & Stores R. (2018, September) *The development of a diagnostic battery for the comprehensive optometric examination of stroke: a Delphi study.* Poster presented at the University of Portsmouth Research and Innovation Conference 2018. Portsmouth

Maciver M., Markham C., & Stores R. (2018, June) *Ophthalmic examination of patients following stroke: A Delphi study.* Poster presented at Portsmouth Hospital Trust - University of Portsmouth Health and Technology Research & Innovation Conference 2018. Portsmouth

Chapter 4 Clinical Procedures

Following the development of the diagnostic test battery for the visual examination of stroke survivors, the next phase was to test its use in a clinical setting. This involved testing the instrument's findings beside the findings of a typical sight test undertaken in primary eye care practice. Following enrolment participants would be scheduled for two separate assessments at the research site. During one visit, the participants underwent the components of the trial battery assessment (**Table 5-2**), and binocular vision assessment (**Chapter 6**). Following a brief break of around 5 minutes pattern glare testing and rate of reading assessments were undertaken (**Chapter 7**). The participant was then led to the practice's imaging room where they undertook automated perimetry. Following this pupil dilation was then initiated and following a period of around 20m the participant returned to the imaging room to have retinal imaging completed (**Chapter 8**), with the entire episode lasting between 75 and 90 minutes.

At the second appointment, participants received the reference standard examination, a typical sight test undertaken by another optometrist. This visit was much shorter, lasting in the range of 25-35 minutes. To reduce potential learning effects the order in which the reference and trial test were undertaken was randomised. In all cases, clinicians were masked to the findings of the initial test when conducting the second test.

A number of clinical procedures were employed during this study, encapsulating a wide range of the investigations used in primary eye care settings. While some degree of overlap is present across a number of these procedures, the techniques outlined may be considered to examine ocular health, refractive status, visual status and binocular vision. While a full account of these procedures may be found in several authoritative texts (Carlson and Kurtz 2004; Benjamin 2006; Elliott 2013; Evans 2022), a concise summary of the procedures employed in the course of this study can be found below.

4.1 Case History

The typical examination begins by undertaking an ophthalmic case history. This serves to collect essential information and support the building of rapport between clinician and patient. The first important feature of an ophthalmic history is the establishment of the patient's reason for presenting. For many patients their presentation may be in response to a routine recall from a previous examination, or for review due to pre-established risk factors such as family history of glaucoma, or the presence of diabetes. For others they will present in response to the emergence of new symptoms that have impacted on daily living. Following discussion of any presenting issues it is important to consider the patient's general and ophthalmic history. As a structure with significant neurological innervation and vascular supply a number of systemic issues may give rise to ocular complications from these causes. Given the eye's unique position as a location for direct, non-invasive viewing of several key neurological as well as vascular structures several anomalies may present ocular complications some of which may be the origin of a patient's presenting symptoms.

A thorough medical history should be undertaken including review of systemic medication use and history of previous treatments for eye conditions. The patient's ocular history is an important aspect of case history taking, as the presence of previous anomalies or treatments may alter the course of an examination, as well as providing insight to potential anomalies that may be present. While the content of this history should be systematic and structured, it should also be responsive to the patient's concerns and presenting symptoms, with the clinician practising active listening, giving opportunity to the patient to discuss their unique visual concerns. Following a comprehensive ophthalmic history, the clinician is able to provide a series of likely differential diagnoses, upon which to their examination.

4.2 Ocular health examination

One of the core functions of the eye examination is the examination of the health of the internal and external eye to determine anomalies of the eye or signs of problems elsewhere in the body (Opticians Act, 1989). A comprehensive overview of the anatomy and pathology of the eyes may be found in several authoritative sources (Levin et al. 2012; Salmon 2019; Miller et al. 2020), a summary can be found here.

The eyes each sit within the orbit, a pair of hollow, cone shaped cavities that also contain the extraocular muscles, vascular and nervous support, as well as fat and associated viscera. The ocular surface is protected by the eyelids, thin folds of skin that can close over the eyes to protect them (**Figure 7**). These eyelids serve a number of other functions, their motion serving as trigger to lacrimal secretion and drainage, as well as housing the Meibomian glands, modified sebaceous glands responsible for secretion of the superficial layer of the tear film.

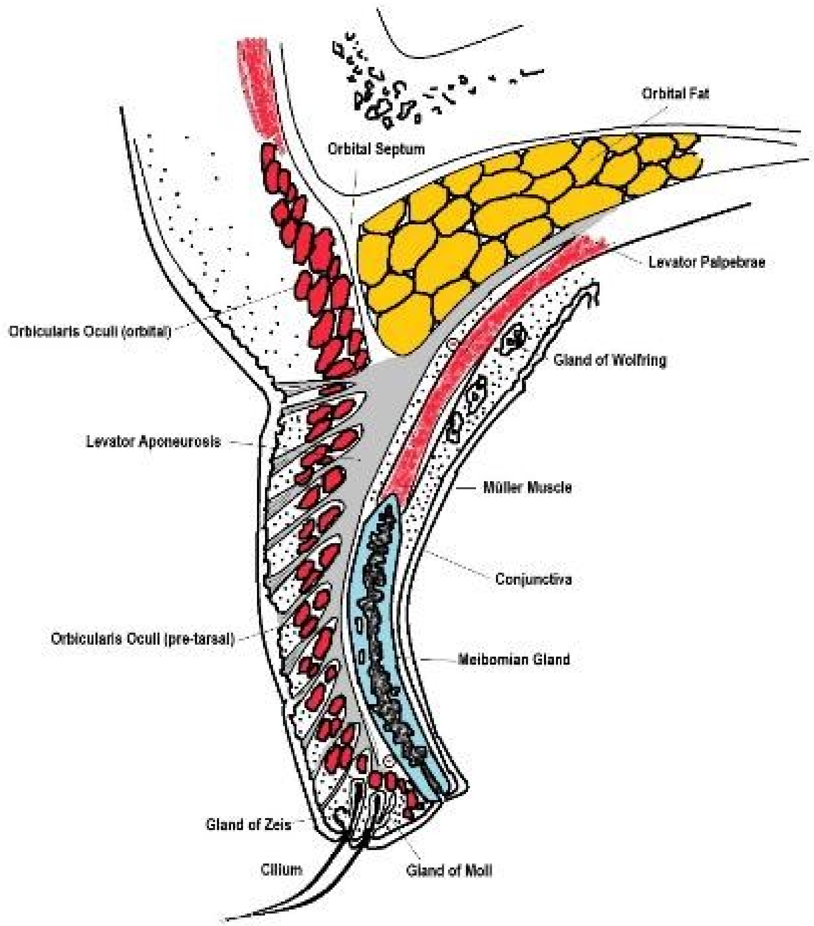


Figure 7: Cross-section of the upper eyelid

Overlying the anterior sclera, lining the fornices and inner eyelids to the eyelid margin lies a thin clear mucoid tissue called the conjunctiva. The conjunctiva contains a high density of goblet and mast cells aiding in the immune protection of the eye, as well as supporting ocular lubrication. As the conjunctiva approaches the cornea, the conjunctiva thins, becoming continuous with the superficial epithelial layer of the cornea.

The cornea is a multi-layered structure consisting of a central stroma, two collagen lamellae and an outer and inner superficial epithelial layer. The external superficial epithelium supports the tear film, a thin superficial layer of fluid that nourishes the cornea, provides a smooth refractive surface, aids in the removal of debris and cellular waste, provides anti-microbial protection to the eye, and lubricates the movement of eyelids over the surface of the eye. The internal endothelium consists of a single squamous layer of cells that operate as a 'leaky' barrier, allowing leakage of aqueous from the anterior chamber to nourish the inner cornea, whilst pumping fluid out of the cornea to avoid break down of stromal lamellae and subsequent corneal haze. The transparency of the cornea along with the crystalline lens and ocular media described later, facilitates the refraction of light onto the light sensitive retina, with the cornea accounting for around 43 dioptres of refractive power (Courville et al. 2004). To maintain this transparency, no blood vessels are present within this tissue, instead the cornea derives its nutrient support and excretion of waste via the superficial tear film and aqueous humour.

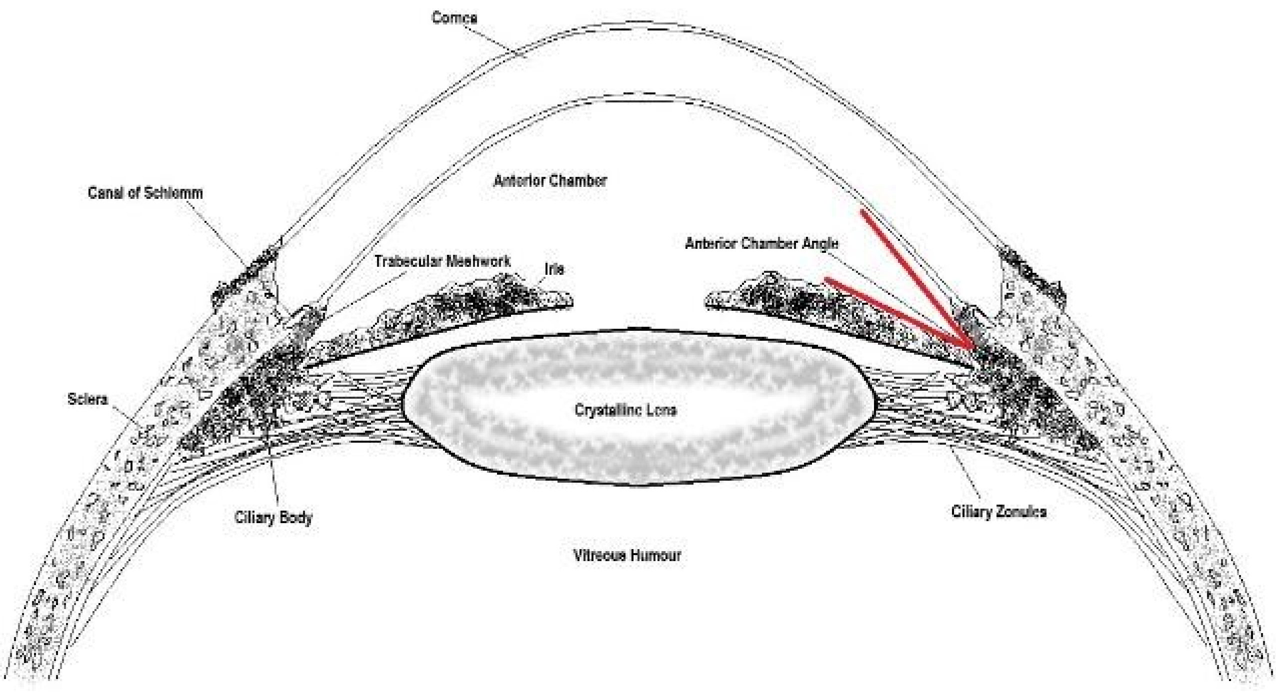


Figure 8. Diagram of the anatomical structures forming the iridocorneal angle.

The peripheral corneal stroma is continuous with the anterior sclera, with the translation between tissues occurring in a region described as the anterior chamber angle. The angle describes an area of the anterior eye where the posterior cornea, sclera, and iris meet. The angle describes the orientation of the coloured iris in relation to the position of the cornea (**Figure 8**).

The trabecular meshwork, a sponge-like structure in the apex of the anterior chamber angle is the location of drainage of aqueous humour, the fluid that occupies and nourishes the anterior chamber.

From the trabecular meshwork this fluid passes into the Canal of Schlemm and into the ciliary venous drainage. The posterior trabecular meshwork connects to the scleral spur, the anterior projection of the sclera, to which posteriorly sits the ciliary body, and the iris. The iris is a thin annular structure that may alter its structure via contraction of the smooth iris sphincter and dilator pupillae muscles. Through this action the iris may alter the amount of light entering the eye as well as the depth of field of the image viewed. Posterior to the iris sits the ciliary body, an annular muscular structure that secretes aqueous humour, and via radial zonules suspends the crystalline lens.

The crystalline lens is a biconvex structure that sits immediately behind the iris, with its centre in close proximity to the centre of the pupil, the aperture in the middle of the iris. The lens is encapsulated within a collagen capsule, with a thin epithelial layer anteriorly that produces lens fibres and grows throughout life. In youth, the crystalline lens may alter its focal power by changing the curvature of the anterior and posterior surfaces, via contraction and relaxation of the ciliary zonules in a process called ocular accommodation. With age, the lens loses this elasticity, resulting in a relatively fixed focus, clinically manifesting as presbyopia.

Posterior to the crystalline lens sits a semi-rigid jelly like substance known as the vitreous humour. While this provides initial structure to the eye during gestation, in later years this degenerates resulting in fluid pockets with suspended collagen fibrils, frequently observed as floaters.

Lining the interior surface of the eye is a thin, light sensitive structure known as the retina. The retina is a multi-layered structure that absorbs light, and through the process of phototransduction converts the light to electrical signals, to be processed by retinal interneurons that project to the thalamus and onward to the visual centres of the brain.

At the posterior pole a central avascular area is present known as the macula, the centre of which lies the fovea, where retinal cone density is highest resulting in the greatest spatial resolution. The fovea exhibits thinning relative to the tissue surrounding it due to the displacement of interneuronal layers, facilitating high acuity. Around 15^0 nasal to the posterior pole of the eye sits the optic nerve, a circular structure of around 1.5mm diameter marking where the optic nerve enters the eye. Through this structure, the central retinal arteries and veins pass from the nerve to form the inner retinal vasculature. This location is also where the nerve axons from the retinal interneurons exit the eye, passing through fenestrations in the sclera. This structure has no overlying photoreceptors, resulting in a physiological blind spot manifesting around 15^0 temporal to fixation in each eye. In a clinical examination, the structure of the optic nerve serves as a reference point from which to conduct examination of the inner eye. The retinal vasculature passes from the nerve to support the inner retina along four arcades, with arterioles and venules passing to support the inferior nasal, inferior temporal, superior nasal and superior temporal portions of the retina. The outer layers of the retina receive their vascular support from the choroid, a highly vascularised tissue that sits between the neuroretina and the sclera of the posterior eye.

4.2.1 Slit lamp examination

Examination of the anterior eye may be undertaken using a number of different methods, the most common being the examination using the slit lamp biomicroscope. The slit lamp can be used to examine a range of structures of the anterior eye and adnexa.

For the studies undertaken in **0** examination was undertaken using the SL-D4 slit lamp (Topcon Healthcare). This instrument uses 12.5x magnification in the eyepieces and has the option of variable 6x, 10x, 16x, 25x and 40x magnification. Illumination is provided by an LED lamp and is variable from 1-14mm. The instrument has filters providing blue, red-fee, amber, UV & IR filtering and neutral density filter, and has an incorporated barrier filter (Wratten 12) for use with sodium fluorescein.

Width of shadowed space compared to corneal thickness	van Herick Grade	Angle status
No shadowed space observed	0	Closed
< ¼ Corneal thickness	1	Extremely narrow
¼ of corneal thickness	2	Narrow
> ¼ to ½ of corneal thickness	3	Open
> ½ of corneal thickness	4	Wide open

Table 4-1. Results of the the van Herick test: The examiner view's the shadowed space behind the cornea to appraise the distance between the cornea and iris surface. From this an estimation of iridocorneal angle may be made (adapted from Källmark and Sakhi 2013).

When undertaking slit lamp examination, the Van Herick technique can be used to appraise the nasal and temporal iridocorneal angle and screen for the necessity of further investigation (Källmark and Sakhi 2013). To conduct the procedure, the subject is directed initially to look ahead and the illumination arm is moved to 60^0 temporal to fixation. The beam is narrowed and the examiner assesses the temporal cornea just within the limbus. An apparent cross section of the cornea is observed with a space behind before illumination of the iris is seen, with the relative apparent thickness of the cornea and shadow compared to infer angle status (**Table 4-1**). The technique is undertaken in the nasal cornea by moving the microscope system temporal to the subject's midline and instructing the subject to direct their gaze to the microscope system. The illumination system is then moved to a position 60^0 from the microscope system towards the subject's midline and the examination repeated.

Dry eye is a multifactorial disorder affecting the tear film and ocular surface (Bron et al. 2017). Diagnosis requires a thorough assessment of the ocular surface, an appraisal of symptoms and an examination of lid or ocular surface anomalies. In practice this examination is facilitated using sodium fluorescein eye drops (Chen et al. 2017). Fluorescein drops when applied to the cornea and anterior eye aid the detection of anomalies by aiding the imaging of the tear fluid, as well as issues of corneal integrity. Where a cobalt blue (494nm) light source is applied, these drops fluoresce green (521nm) with greater fluorescence visible where disruption of the corneal surface occurs. This agent is readily absorbed by cells undergoing apoptosis (Bandamwar et al. 2014) giving an indicator of areas of stress or damage to the ocular surface. Pooling of the agent within conjunctival folds can also give an indication of conjunctival wrinkling, an anomaly that is frequently observed to coincide with dry eye conditions

(Chhadva et al. 2015). The use of this agent can also be used to better observe the ocular tear film, as the fluorescence enables better visualisation of tear film disruption, a phenomenon that can be observed as interruption to the smooth surface.

Examination of the eye following installation of sodium fluorescein centres on three areas. First the overall profile of the corneal surface is viewed, observing for areas of fluorescence on the corneal surface indicating epithelial disruption, with clinically significant dessication being recorded by one of several grading methods. The conjunctiva is observed likewise to observe for evidence of epithelial disruption or the presence of folds in the conjunctiva. Finally the coverage and stability of the tear film is assessed. This may be done by observation of disruption to the surface after blinking or by asking the subject to hold their eyes open until disruption of the tear film is observed. The time for the tear film to destabilise is frequently used as a screening tool for potential dry eye, with greater suspicion of dry eye in cases where disruption occurs in under 5 seconds, and with most subjects exhibiting a physiological tear film exceeding 10s before disruption is noted (Pflugfelder et al. 1998; Wolffsohn et al. 2017). For this study all anterior surface grading was undertaken using the Efron grading scale (Efron et al. 2001).

4.2.2 Pupil examination

The pupil reflex test is a test of the integrity of the optic nerve. Pupil reflexes are mediated by the autonomic nervous system, with pupil dilation occurring because of sympathetic innervation, while pupil constriction occurs with parasympathetic innervation. The pupil test is a useful assessment of the integrity of the visual pathway, with unilateral damage giving rise to anomalies of the physiological pupil response, while damage to the autonomic innovative pathways gives rise to uneven pupil sizes, known as anisocoria.

To examine the integrity of the pupil pathway the subject is directed to view a distant, non-accommodative target such as a spotlight. The examiner initially observes the subject's pupils, measuring their diameter with a millimetre ruler or pupil size gauge, noting any asymmetry present. The examiner then using a transilluminator or pen torch illuminates one of the eyes. The examiner observes for the presence of pupil reflex of the illuminated eye, as well as reflex of the fellow eye. The process is repeated for each eye in turn, noting any deficits of response. Where uneven pupil size is observed, the procedure is repeated in low lighting to aid classification.

The Marcus-Gunn swinging flashlight test is a test of relative signal strength from the optic nerves. The test is undertaken by assessing the relative pupillary contraction between the eyes, which is most readily done by direct observation. In a healthy subject when the flashlight is passed from one eye to the other, an equal constriction is observed as the first eye, due to equal afferent signalling. In a subject with an anomaly of the afferent pathway, whilst a normal response is observed from the unaffected eye, a relatively reduced response is present in the affected eye. As a result in the presence of an anomaly when the flashlight is passed from the unaffected eye to the affected eye pupil constriction is not observed but instead a paradoxical pupil dilation is observed, this anomaly is known as an afferent pupillary defect. This occurs as when the flashlight is passed from the unaffected eye to the affected eye a reduced stimulus to pupil constriction is received from the affected eye. At the same time the stimulus to pupil dilation from the unaffected eye outweighs the stimulus to pupil constriction from the affected eye to bring about pupillary constriction.

4.2.3 Tonometry

The internal pressure of the eye is an important physiological measure that can identify the risk of developing chronic disorders. While elevated intraocular pressure (IOP) is widely associated with glaucoma, it can be used to support the diagnosis of other ocular anomalies. A range of options may be employed to measure intraocular pressure, with clinicians most frequently employing non-contact or contact methods.

4.2.3.1 Non Contact Tonometry

Non-contact tonometry (also known as air puff or pneumatic tonometry) is a minimally invasive technique to measure the internal pressure of the eye. The Keeler Intellipuff (Keeler Ltd, Windsor) operates by using a columnated pulse of air to applanate (flatten) the front surface of the eye, deriving the pressure of the eye by the pressure of air required to applanate the cornea. Due to the instantaneous nature of the measure and the variability of ocular pressure between systole and diastole, an average of multiple measures is recommended to improve accuracy. It is recommended that up to 4 puffs are undertaken each eye and an average derived, though where two consecutive puffs are within 1mmHg of each other the instrument identifies this, indicating that further measures may not be needed. While some studies have indicated consistency of pressure measured using this approach with contact methods (Erdogan et al. 2018), non-contact methods frequently report elevated measurements compared to contact methods (Harada et al. 2008; Farhood 2012; Lee and Ahn 2016)..

4.2.3.2 Applanation Tonometry

Goldmann Applanation Tonometry (GAT) is the gold standard approach for measuring IOP (Brusini et al. 2021). It derives the intraocular pressure through applanation of the cornea with a calibrated probe, relying upon the Imbert-Fick principle to derive the internal pressure of the eye (Mark 2012). Standard technique was employed with anaesthesia in this study completed using combination of lidocaine hydrochloride 4% w/v & sodium fluorescein 0.25% w/v.

4.2.4 Indirect Ophthalmoscopy

Indirect ophthalmoscopy is undertaken to examine the internal structures of the eye. The technique is undertaken using an instrument that illuminates the internal eye in combination with a high-power convex condensing lens which is used to produce an image of the internal eye that may be viewed with the illuminating instrument. For the studies outlined where indirect ophthalmoscopy was undertaken, this was done using the slit lamp in combination with a high power volk lens, while different clinicians will have preferences to their preferred instrument, the author favours the Volk Digital Widefield (Volk Optical, OH, USA), which was employed for indirect ophthalmoscopy assessment during the trial battery. While other techniques are available to examine the internal structures of the eye, indirect ophthalmoscopy provides improved resolution with the ability to minimise the impact of media opacities and gain a high magnification image of the inner eye. The procedure is undertaken by setting the slit lamp to view the eye with an illumination arm aligned with the observation system. The high-powered condensing lens is then placed in front of the eye and the slit lamp pulled back until a clear image of the internal eye is observed. Through manipulation of lens and slit lamp position different areas of the retina may be viewed. This procedure is more easily undertaken with dilation of the pupil.

4.2.4.1 Dilation

Physiologically pupil size varies by age and refractive error (Guillon et al. 2016), with many older subjects exhibiting smaller pupil diameters. Smaller diameter pupils restrict the view gained by the examiner and so the use of pharmacological agents to dilate the pupil can facilitate the examination. Pupil dilation facilitates direct examination of structures such as the crystalline lens, as well as techniques to view the posterior structures of the eye such as indirect biomicroscopy. Pupil dilation may be undertaken using either anti-muscarinic medication, inhibiting the uptake of acetylcholine, within the sphincter pupillae, or sympathomimetic medication, stimulating the sympathetic action of the muscle fibres of the dilator pupillae. For all subjects in this study the anti-muscarinic drug Tropicamide hydrochloride 1% w/v was used.

4.2.5 Retinal imaging

A range of imaging procedures may be employed to facilitate the ocular examination. Two commonly employed methods are scanning laser ophthalmoscopy (SLO) and optical coherence tomography (OCT). SLO operates using a confocal laser imaging system. Where multiple laser imaging is used, this can enhance the image quality, enabling imaging of both superficial and deep structures within the eye (Stevenson et al. 2016; Mainster et al. 2022). OCT scanning utilises low coherence interferometry to image the layers of the retina (Roorda et al. 2002; Popescu et al. 2011; Nolan et al. 2015). This approach enables viewing of subtle anomalies that may not be visible by conventional imaging techniques, with possible detection of anomalies up to several years in advance of conventional examination (Goździewska et al. 2023).

In the course of this study, the Optos Monaco (Optos Ltd, Dunfermline, UK) instrument was used to conduct retinal imaging. The Optos Monaco is a combination SLO and OCT intended for in-vivo imaging of the structures of the inner eye. The instrument uses a dual red and green confocal laser imaging to achieve widefield imaging of up to 200^0 of the retina in a single image (**Figure 9**). As the light from each wavelength penetrates to different depths, a composite image viewing from the superficial retina to the choroid may be assessed by the examiner through the instrument's imaging software. Using the green laser for illumination, the instrument is also able to measure retinal autofluorescence.

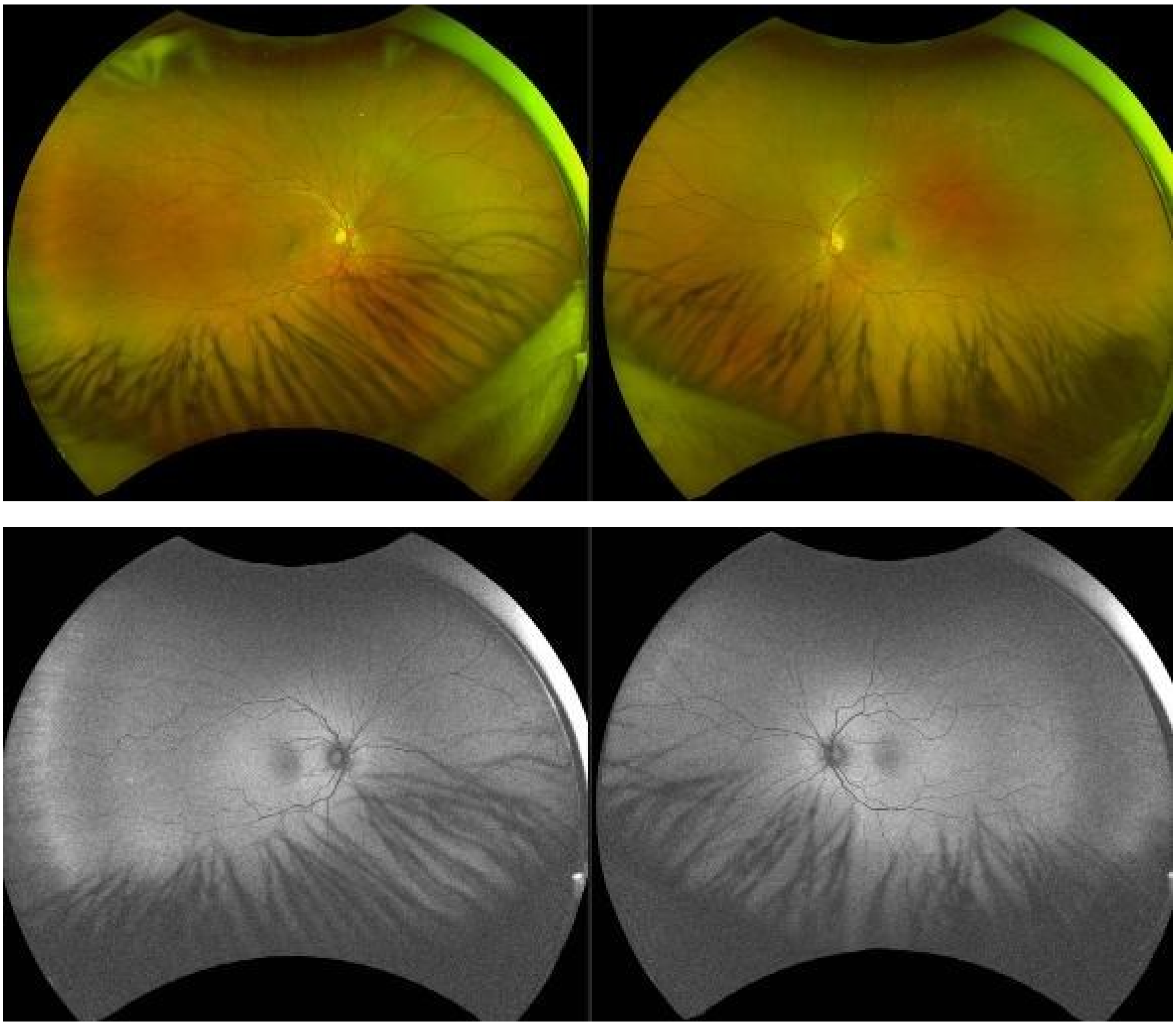


Figure 9. Scanning laser ophthalmoscope [top] and Autofluorescence [bottom] imaging of the retina captured by the Optos Monaco instrument.

When conducting OCT assessment, the Optos Monaco can undertake up to 70,000 scans per second to enable high resolution imaging of the posterior eye. The Monaco is capable of undertaking a high-resolution line scan of the retina of 12mm in length within the posterior 12mm by 9mm of retina (**Figure 10**). The instrument is also capable of undertaking volume scanning of the central retina, capturing an area centred on the fovea of 8mm x 8mm field of view, and centred on the optic nerve head of 5.28mm x 5.28mm each comprising of 97-line scans. From these scans retinal, ganglion cell, optic nerve head and neuro-retinal rim parameters may be derived (**Figure 11**).

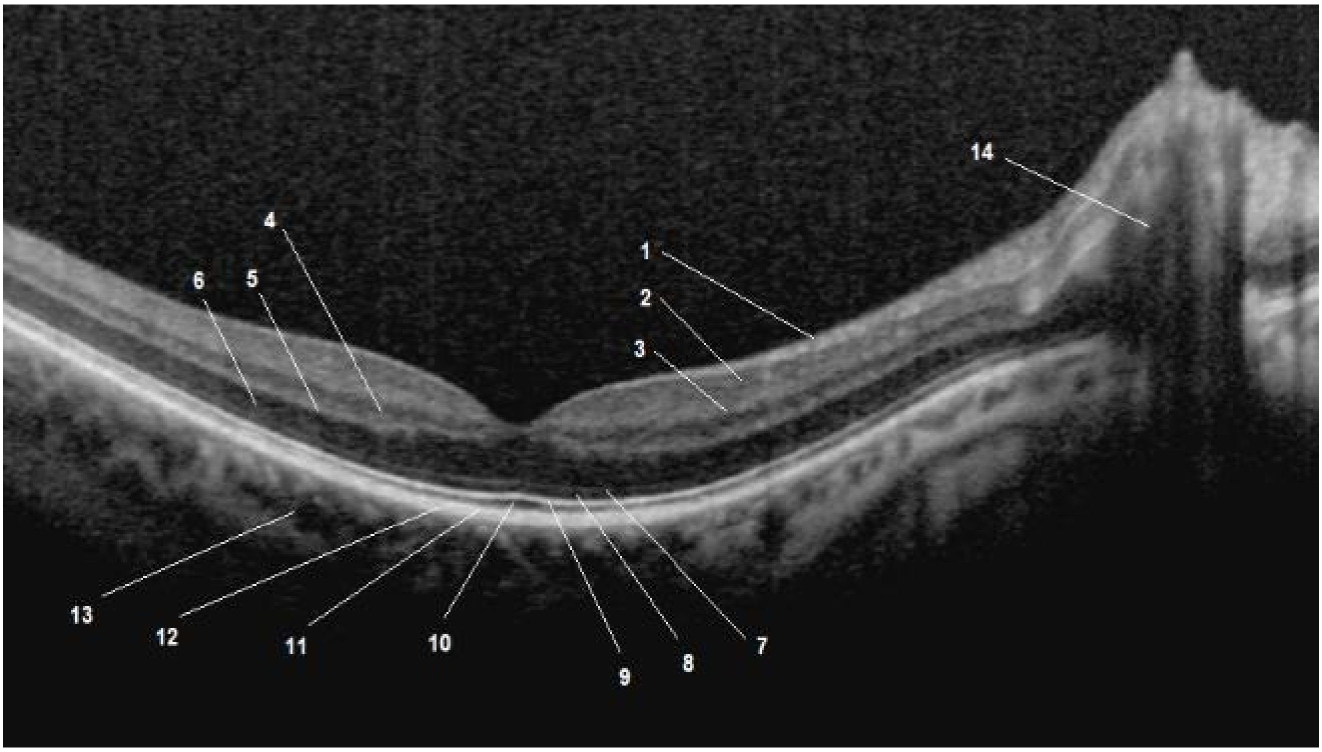


Figure 10. High resolution Raster line of the central retina, with differentiation of retinal layers. 1: Retinal nerve fibre layer, 2: Ganglion cell layer, 3: Inner plexiform layer, 4: Inner nuclear layer, 5: Outer plexiform layer, 6: Outer nuclear layer, 7: External limiting membrane, 8: Inner photoreceptor segment, 9: Inner/outer photoreceptor junction, 10: Outer photoreceptor segment, 11: Retinal pigment epithelium interdigitation zone, 12: Retinal pigment epithelium/Bruch's membrane complex, 13: Choroid, 14: Optic nerve.

Within the imaging software segmentation algorithms are used to analyse the measures and compare to an internal normative database of 355 patients aged 22-95 years. The analysis software codifies the data measured against the internal database providing a comparison of the measure against its location within the database. It should be noted that this database is not matched for gender, race or refractive error, which must be accounted for when undertaking analysis.

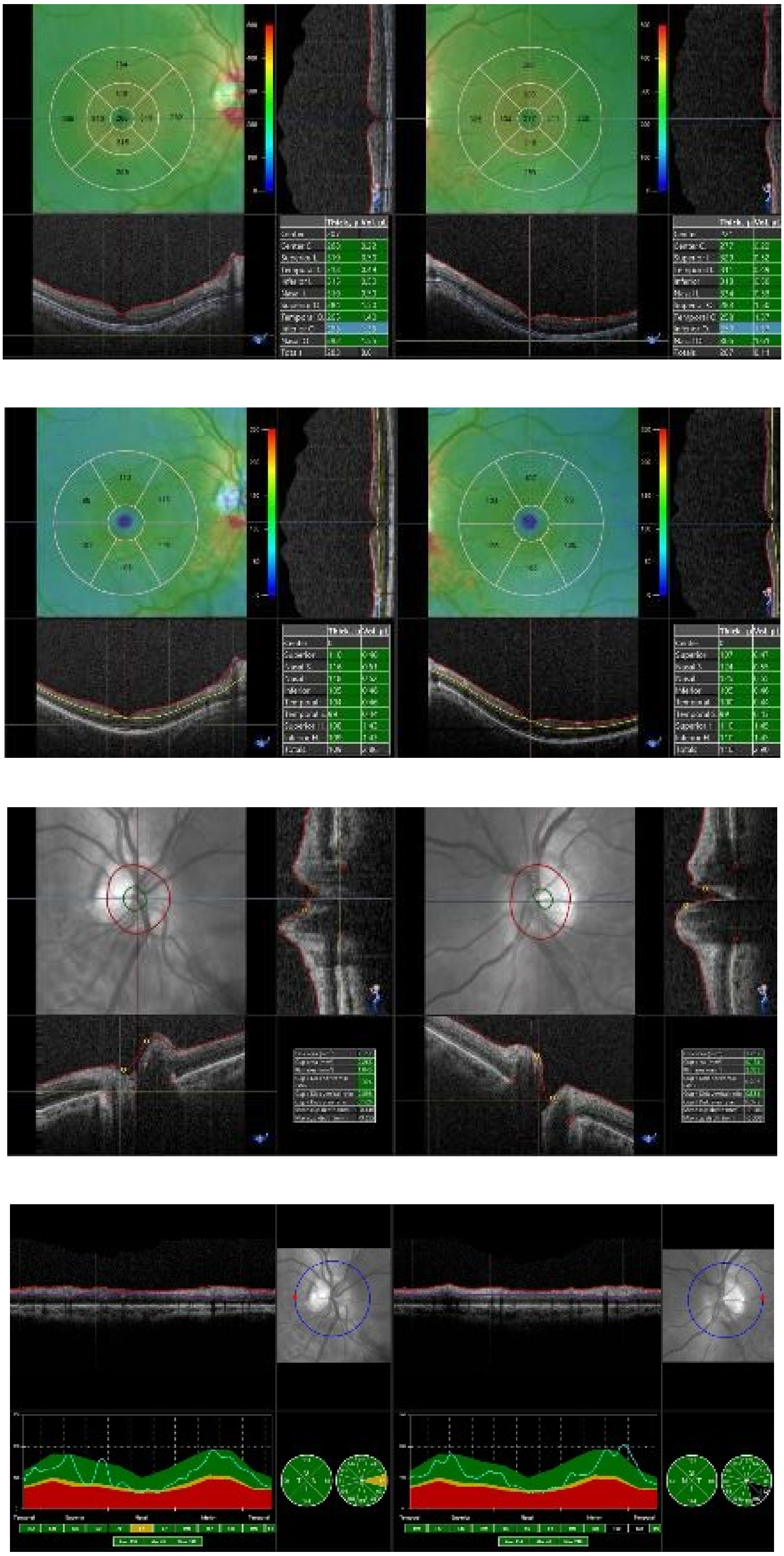


Figure 11. OCT Analysis segments of the Optos Monaco instrument. Four separate analyses of data are undertaken by the instrument, two of the posterior pole reviewing retinal thickness against the ETDRS segment zones (Early Treatment Diabetic Retinopathy Study Research Group 1991), as well as review of ganglion cell layer thickness and two analyses of the optic nerve, assessing optic disc and neuroretinal rim parameters. Data output is analysed against the internal database, with output graded against the database using a traffic light scheme.

4.2.6 Common ocular anomalies

In the range of ophthalmic examination, a range of ocular anomalies may be commonly encountered, a summary of some common ocular anomalies is outlined below.

4.2.6.1 Blepharitis

Blepharitis describes a series of conditions that affect the eyelids resulting in red, inflamed, irritated lids and frequently associated with dry eye. Blepharitis is defined by the area of the eyelid affected, with a build-up of debris around the eyelash margin being defined as anterior blepharitis, while inflammation secondary to blockages of the meibomian glands being defined as Meibomian gland dysfunction or frequently as posterior blepharitis. While this may arise from a range of factors, frequently this occurs secondary to response to the skin’s flora (Schaumberg et al. 2011). A range of options for management of this are available (Geerling et al. 2011; Jones et al. 2017). In the absence of systemic pathological causes, first line therapy consists of lid hygiene to remove the debris and attempt to clear the glands, along with the use of topical lubricants for comfort.

4.2.6.2 Dry eye

Dry eye disease is a condition affecting the ocular surface that gives rise to symptoms of ocular irritation. While blepharitis is frequently associated with the presence of dry eye (Bron et al. 2017; Stapleton et al. 2017), the condition is often multifactorial. In this condition the stability of the physiological tear film is impaired, with alteration of the osmolarity profile of the remaining tear film, neurosensory anomalies and increase in the presence of inflammatory biomarkers factor into the condition, with frequent disruption of the ocular surface itself (Bron et al. 2017). This condition is typically chronic, with a range of management options available. Typical first line therapy for this condition consists of alleviation of predisposing factors and treatment of any coexisting ocular surface disease, though a range of options may be considered in more severe cases (Jones et al. 2017).

4.2.6.3 Eyelid malposition

Physiologically the eyelids should be in position against the ocular surface, passing smoothly over this surface with each blink action. Where there is a loss of eye lid elasticity, the eyelids may be prone to move to an anomalous position, turning inwards towards the eye (entropion), or outwards away from the eye (ectropion). While the presence of an outward turn may give rise to exposure of the ocular surface, resulting in symptoms like those exhibited in dry eye, an inward turn of the eyelid can result in scratching of the eyelashes against the cornea - giving rise to more significant symptoms.

4.2.6.4 Fuch’s endothelial dystrophy

Fuch’s dystrophy is a progressive disorder of the corneal endothelium, in this condition, the cells of the endothelium experience a loss of function, which results in corneal swelling secondary to loss of the fluid pump function of these cells. While mild cases may be asymptomatic, more severe cases may give rise to blurred vision, with blurring upon waking that improves throughout the day.

4.2.6.5 Cataract

Cataract is the description given to a clouding of the crystalline lens. This condition is commonly encountered, with increasing prevalence with increasing age. While a number of different presentations are possible, this condition is described by the area of the lens affected. Common classifications exist for nuclear sclerotic cataract, a yellowing of the central lens, cortical cataract where wedge-like opacities project from the edge of the lens to the central portion, and posterior subcapsular cataract, where opacities may be observed beneath the lens capsule at the posterior pole (Chylack 1993). With the progression of cataracts individuals experience symptoms of blurred vision, changes of ocular prescription, glare, visual discomfort, and difficulties in colour perception.

4.2.6.6 Glaucoma

Glaucoma is a group of progressive diseases of the optic nerve that results in characteristic excavation of the optic nerve head with accompanying visual loss. While historically this has been heavily associated with elevated ocular pressure, it may exist with eye pressure within the normal range. Despite this, intraocular pressure remains a key risk factor, with all interventions for the condition acting to reduce ocular pressure. While pressure is a key risk factor, elevated eye pressure beyond the typical range can exist without damage to the nerve, a condition known as ocular hypertension. Glaucoma may be classified as being either open angle or closed angle, depending on the configuration of the iris with respect to the peripheral cornea. Where the angle narrows to the point where the iris occludes aqueous outflow from the eye, the ocular pressure can increase rapidly, resulting in a painful, red eye with loss of clarity of vision, that if not treated quickly will result in permanent vision loss. The more common type of glaucoma is that of the open angle. These are frequently asymptomatic, with progressive loss of peripheral vision typically identified during examination of the eyes (Shah et al. 2007; Evans et al. 2021). While there are a range of clinical signs may be associated with glaucoma (Salmon 2019; European Glaucoma Society 2021), one of the more commonly used measures is the cup to disc ratio. This measure is a surrogate measure of thickness of the neuroretinal rim, measuring the ratio of the central ‘cup’ against the total diameter of the optic nerve. Any loss of nerve fibres would result in expansion of the cup. While readily employed within practice, this measure has limitations of reliability and may vary between measures and clinicians (Harper et al. 2000). This may be supplemented through OCT imaging, though this has limitations related to the limitations of the embedded databases (Bussel et al. 2014; Dong et al. 2016; Mehta and Waheed 2020a; Banc and Ungureanu 2021a; Bradley et al. 2023; Nakayama et al. 2023a).

4.2.6.7 Blood vessel anomalies

During examination of the retina, the vascular supply is inspected to assess for anomalies. Anomalies of the blood vessels such as tortuosity or microaneurysms and haemorrhages can give insight to vascular disorders elsewhere in the body. During assessment as well as recording major anomalies, it is typical to note the ratio of the thickness of the retinal arterioles to the venules. This ratio may be monitored to identify any alterations over time, with conditions such as atherosclerosis giving rise to thickening of vessels. In subjects with a history of stroke, it has been observed that retinal arteries thin, while retinal veins thicken (Ikram et al. 2006a; McGeechan et al. 2009; De Silva et al. 2011; Vuong et al. 2015; Hughes et al. 2016; Wang et al. 2025), additionally other anomalies such emboli in the retinal vasculature may be observed that require further investigation.

4.2.6.8 Age related macular degeneration (AMD)

Age related macular degeneration (AMD) is a progressive degenerative disease of the macula, the central region of the posterior pole. Macular degeneration results in deterioration of central vision, impacting acuity, colour perception, and in many cases giving rise to distortion. AMD may be classified as one of two forms, the ‘dry’ form, where retinal thinning and loss of sensitivity occurs secondary to the development of drusenoid changes, and the ‘wet’ form, where an accumulation of intra and subretinal fluid occurs within the retina following the errant growth of new blood vessels. This gives rise to significant distortion and reduction in vision. While studies are ongoing (Borrelli et al. 2024), to date no successful treatment is available for the dry form of the disease. However, the wet form, if treated promptly may successfully be managed through the use of Anti-VEGF agents (Song et al. 2022).

4.2.6.9 Choroidal naevus

A choroidal naevus is a benign pigmented lesion of the choroid that may be observed upon retinal examination. Due to the common embryologic origin, these are analogous to moles on the skin and are typically harmless. Very rarely these may metastasise and so it is recommended that these be monitored regularly to enable prompt identification and referral if warranted (Roelofs et al. 2020).

4.2.6.10 Peripheral retinal degenerations

Beyond the retinal equator, a range of peripheral degenerative anomalies may be observed, while many of these may be degenerative, rarely these may be pathological, resulting in risks to sight. These are frequently best observed under dilation, enabling the clinician to observe and characterize the nature of these, giving insight to the risks of progression and highlighting the need for further investigation or treatment if required.

4.3 Refractive examination

The most common visual anomaly encountered is refractive error, this occurs where light entering the eye does not focus correctly on the retina, resulting in a loss of vision that may be corrected by the use of supplementary optical lenses.

Hyperopia describes the condition where light is refracted such that the visual image does not fall upon the retina but instead would result in an image location behind the plane of the retina, resulting in a blurred retinal image. This requires the use of convex lenses to bring about correct positioning of the retinal image. Myopia describes the condition where light is refracted such that the image does not fall upon the retina but instead forms in front of the retina, resulting in a blurred image falling onto the retina; this condition requires concave lenses to bring about correct focus. While this may occur due to a mismatch of the focal components with the ocular length, frequently the presence of hyperopia is the result of an ocular length that is lower than the focal length of the refractive components of the eye, while myopia is the result of excessive axial elongation (Troilo et al. 2019).

Astigmatism describes the alteration of the focal profile such that light when refracted by the ocular components of the eye gives rise to more than one focal point. These are typically managed with cylindrical lenses (frequently in toroidal form).

Presbyopia describes the age-related loss of accommodative range that results as the crystalline lens loses flexibility. With this the eye loses its ability to alter its focus to view near objects, and supplementary convex lens powers are required. These additional lenses may be worn in a range of refractive options as a separate reading correction, or in bifocal or progressive options that are available in both spectacles and contact lens forms.

The clinical measurement of these anomalies of ocular focus is known as refraction, and may be undertaken objectively, without input from the subject, or subjectively modifying the lens requirement in response to the subject's preference. Technical details of these procedures may be found in several texts (Carlson and Kurtz 2004; Benjamin 2006; Elliott 2013), a summary of the procedures employed in the determination of refractive error may be found below.

4.3.1 Objective Refraction

While automated refraction instruments have become increasingly popular in primary eye care settings, many clinicians still make use of the retinoscope when undertaking objective refraction. This instrument has the advantage that it enables simultaneous assessment of the quality of the ocular media. It is lightweight and can be used on subjects that struggle with desk-based instruments due to physical limitations, as well as having greater consistency in assessment of astigmatism (Elliott, 2013).

4.3.1.1 Retinoscopy

The retinoscope may be used to investigate objectively the refractive status of the eye through the interpretation of the "red reflex". With the subject viewing a distance fixation target, the clinician undertakes assessment by using the instrument to illuminate the ocular pupil, interpreting the movement of the red reflex when the instrument is moved. Lenses may then be used to manipulate the reflex to bring about neutralisation, at which point the optical far point will be coincident with the instrument's internal mirror. From this the objective refractive power may be derived by modification of the spherical finding to account for the dioptric working distance of the examiner.

4.3.2 Subjective refraction

Subjective refraction may be undertaken starting from unaided vision, previous refractive measurements, habitual correction or using the results of objective measures. Monocular refraction consists of three stages, initially using spherical lenses to move the focal point, or circle of least confusion (the dioptric mid focal point between two astigmatic foci) onto the retinal plane. Following this the presence of astigmatism may be assessed using the Jackson Crossed Cylinder (JCC) test (**Figure 12**). The presence, orientation and degree of astigmatic error may be measured using a series of forced choice tests while viewing a series of circular non-chromatic targets. As modifications to spherical power may be made during the course of JCC assessment, following completion the mean spherical error is reassessed to ensure correct focus of the image on the retina.

Figure 12. The Jackson Crossed Cylinder lens. The lens is a sphero-cylindrical combination lens where the resultant power is equal to the combination of two oppositely powered cylinders placed orthogonal to one another. The design of the JCC is such that the lens can be easily changed by rotation of the to alter the power presented to the subject, deriving power and axis through a series of forced choice presentations.

In the process of assessing mean spherical refraction a number of ancillary tests may be employed to check progress. The Duochrome test is a useful procedure to assess the relative position of the circle of least confusion from the retina and thus estimate the required spherical power (**Figure 13**). While this test's accuracy may be impacted by the presence of lenticular opacities typically found in older age

(Rolandi et al. 2024), it is a useful adjunct to the refractive process and checks for the position of the circle of least confusion.

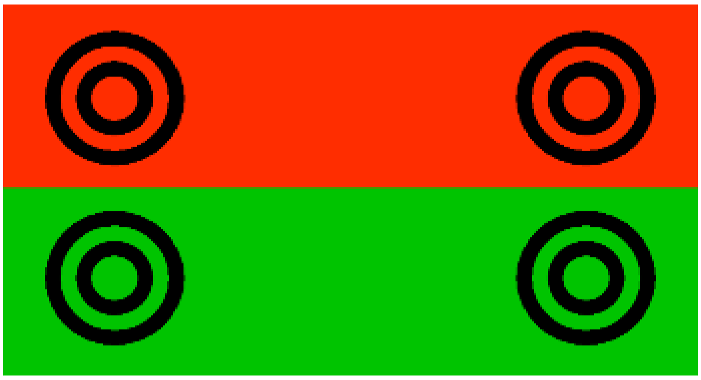


Figure 13. The Duochrome test: The test consists of a series of black targets (typically Verhoff type ring targets as seen here) superimposed upon a red and green field. The test takes advantage of the longitudinal chromatic aberration present within the refractive system of the eye to aid in identifying necessary spherical alteration.

4.3.3 Accommodation and presbyopia

In the juvenile eye the crystalline lens exhibits a flexibility, that upon contraction of the ciliary body, takes up a more convex shape increasing the optical power of the eye. This mechanism is known as ocular accommodation and enables the alteration of focus to achieve comfortable near viewing without supplementary optical aids. As previously described, presbyopia describes the reduction of this near focus to the point where supplementary optical aids are required to undertake near point tasks, and typically arises in the early to mid-40's. This occurs as with increasing age the density of lens fibres within the lens increases resulting in reduced flexibility, this in turn reduces the range of focus. Presbyopia is managed using additional (add) lenses for use in combination with the distance correction to compensate for this loss of focal range. The appropriate addition is most frequently determined by reviewing the subject's desired working distance and selecting a lens that would be expected given the anticipated loss of accommodation with age, this can then be refined manually by the clinician to identify the subjectively preferred option (Elliott 2013). Supplementary tools such as the duochrome on the near vision test unit may be used to refine this finding (Tunnacliffe 1993).

Figure 14. The Thomson XPert 3Di Snellen Chart: This chart is designed to present letters that subtend 5 minutes of arc vertically, scaled for different viewing distances. These letters are then presented at a consistent viewing distance, typically 6m (or 20 feet in USA and Canada). The chart is viewed at the distance required of the instrument, and the subject reads down until they are unable to correctly identify the letters. Scoring consists of a fraction, with the numerator consisting of the viewing distance while the denominator consists of the respective distance where the letters read subtend 5 minutes of arc. Missed or additional letters may be annotated, though due to the uneven scaling and number of letters on each line, results may vary between clinicians.

4.4 Visual examination

During an eye examination a number of procedures are employed to examine the different aspects of the visual system (Carlson and Kurtz 2004; Benjamin 2006; Elliott 2013). The procedures employed during the following studies are outlined below.

4.4.1 Vision / Visual acuity

The most widely recognised and employed test of visual function is the assessment of acuity. This procedure assesses the sensitivity of the visual system to high contrast, high spatial frequency targets. This is frequently undertaken within clinical practice using visual testing charts based upon the principles outlined by Snellen (**Figure 14**), or more recently those based on the logarithm of the minimum angle of resolution (**Figure 15**). Testing is typically undertaken at distances of 4-6m, with charts calibrated to account for testing at the appropriate distance. These charts are readily available, easily understood by patients and familiar to eye care professionals, serving as a useful measure of vision, a medico-legal assessment, and aid to the determination of refractive status. Testing may be performed monocularly or binocularly and subjects are instructed to identify the letters presented until they are no longer able to resolve these, whereupon the examiner records the limit of acuity. Distance acuity measures were undertaken using the distance logMAR chart incorporated within the Thomson XPert 3Di test chart software (Thomson Software Solutions, Hatfield, UK) at a testing distance of 6 meters.

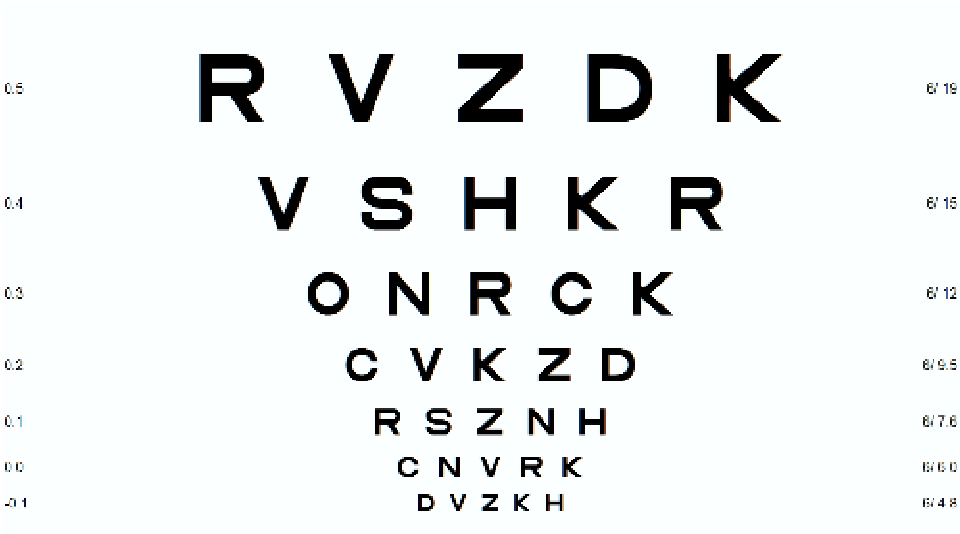


Figure 15. The Thomson XPert 3Di LogMAR letter chart: In this test the stroke width of each letter is scaled to assess the minimum angle of resolution at the testing distance, with the score recorded being the base 10 logarithm of this. Each line consists of five letters, with lines scaled in steps of 0.1 LogMAR differences. Each letter is given a score of 0.02, with this number added to the line scale for each letter missed or incorrectly identified. This enables more consistent quantification of the acuity achieved (Bailey and Lovie 1976; Ferris and Bailey 1996; Raash et al. 1998; Elliott 2016).

While near formats of Snellen and LogMAR type testing are available (Radner 2017), the most encountered instruments for assessing near acuity in the UK do so measuring the size of typeface. These are available from a number of manufacturers and are frequently incorporated into other instruments such as the near vision test unit, and the Saladin Card (**Figure 16**), where a LogMAR near test scaled from 0.0 to 0.7 LogMAR present. It should be noted that while LogMAR scaling is present in this instrument, the structure and spacing are not consistent with the design of other LogMAR instruments (Bailey and Lovie-Kitchin 2013; Sánchez-González et al. 2021).

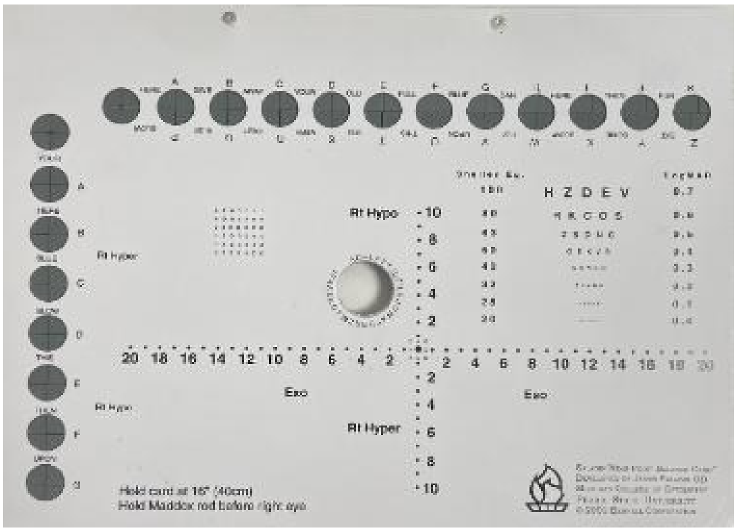


Figure 16. The Saladin Near Point Balance Card (Bernell Corporation, IN): This near point card provides a range of clinical tests that may be used to assess visual and binocular function at near. Along the upper and left side of the card a series of cross polarised circular apertures present offset lines to enable assessment of fixation disparity when the correct polarisers are worn. The chart contains a Modified Thorington scale that in combination with a Maddox rod and spot light may be used to assess near heterophoria as well as a nearpoint LogMAR chart. The chart additionally has a near Hart Chart for accommodative activities as well as a central circular aperture with surrounding accommodative targets for use in dynamic retinoscopy.

4.4.2 Contrast sensitivity

Contrast sensitivity testing evaluates the subject's ability to perceive differences in luminance between a target and its background. The measure is a useful surrogate measure of real-world detection where high resolution is not present. This procedure can also be used to identify the impact of other ocular conditions earlier than may be observed with acuity testing. The principles of this test are like those of the Pelli-Robson test (Mäntyjärvi and Laitinen 2001). Contrast is defined as:

$$\mathrm{Contrast} = \frac{\mathrm{Luminance_{Background}} - \mathrm{Luminance_{Optotype}}}{\mathrm{Luminance_{Background}}}$$

This results in a figure between 0 and 1, with contrast sensitivity being the reciprocal of this. Contrast sensitivity was assessed using the Thomson XPert 3Di (Thomson Software Solutions, Hatfield, UK) test chart software. As many computer monitors take time for their luminance and contrast to stabilise after they have been turned on, it is recommended that the monitor is turned on at least 30m before it's intended use. This test is undertaken monocularly at 1m with the subject wearing appropriate corrective lenses. Letters are presented in groups of three of decreasing contrast from the top to the bottom of the screen (**Figure 17**). Like the assessment of acuity, the subject is instructed to identify the letters presented with the examiner scrolling the screen if required, until the subject is unable to distinguish two out of three letters present. The examiner then records the last complete row as the contrast sensitivity. To ensure contrast is accurately reproduced on screen, it is recommended that the system is calibrated using a light meter. For the work undertaken in **Chapter 7** no calibration was undertaken, limiting the generalisability of contrast findings in this chapter.

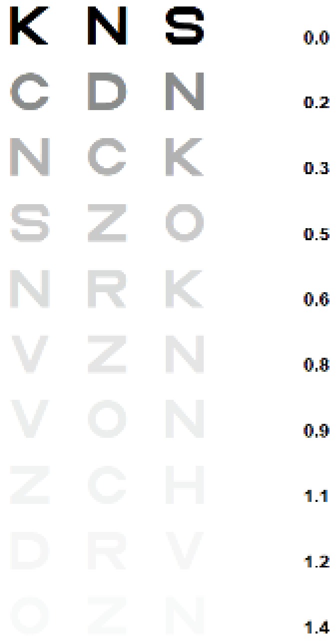


Figure 17. Log Contrast Sensitivity as measured on the Thomson Test Chart. Note that unlike acuity where letters reduce in size, here the letters remain of constant size but exhibit diminishing contrast.

4.4.3 Perimetry

Examination of peripheral vision is an important component of the ophthalmic assessment. The sensitivity of this peripheral *field of vision* is useful in the identification of ophthalmic and neurological anomalies of the optic nerve and the visual pathway. The physiological field extends from around 100^0 temporally, 60^0 nasally, 75^0 inferiorly and 60^0 superiorly. Sensitivity is greatest at the centre of the field, falling rapidly with retinal eccentricity. Around 15^0 temporally a small absolute scotoma around $3\text{-}5^0$ in size can be found resulting from the absence of photoreceptors around the optic nerve head. While different methods of assessment of peripheral vision exist, they can be associated with limitations. While simple confrontation perimetry may be readily accomplished, its accuracy is inferior to automated perimetry, a procedure that many subjects have difficulty with due to fatigue (Cumming et al. 2016). Within this thesis two methods of peripheral vision assessment were used, the Amsler test and suprathreshold automated perimetry using the Henson 7000 field screener.

4.4.3.1 Amsler test

The Amsler test is a subjective test of the central visual field, it was designed primarily for the detection of distortion within a subject’s vision that may be an indication of early maculopathy (Amsler 1953). The test consists of a series of seven charts, based on a grid with a central fixation spot (**Figure 18**). The test is undertaken with the appropriate near correction in place at a working distance of 30cm. At this range each small square represents 1^0 of visual angle, enabling a qualitative assessment of the central 20^0 of visual field (**Figure 19**). The subject is directed to fixate on the central spot and asked a series of questions on the presence of anomalies on the chart.

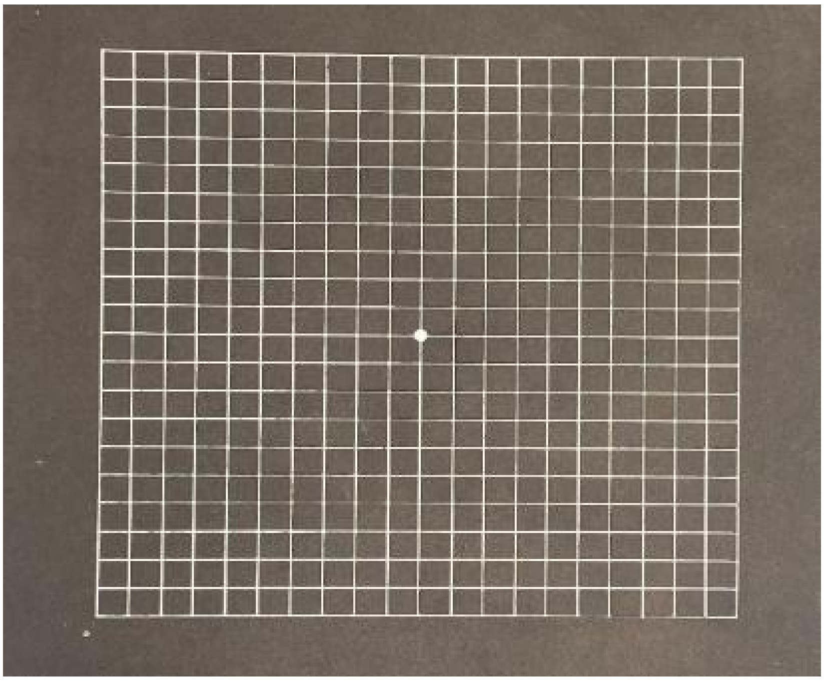


Figure 18. The Amsler chart. While frequently only the first page is utilised, the full Amsler chart book consists of seven charts. Chart 1 is the standard chart for general use. Chart 2 is used in instances where a central scotoma impedes the perception of the fixation point, in this case the subject is instructed to direct their gaze to the anticipated central crossing of the diagonal lines. Chart 3 is a variation of the main chart, but with a red grid, this in theory may be used in cases of colour scotoma secondary to neurological effects. Chart 4 is a chart with a series of spots, revealing only the location of the scotoma. Chart 5 is a chart with parallel lines for viewing metamorphopsia, it should be viewed both horizontally and vertically. Chart 6 is another chart of metamorphopsia, this time in more detail along reading lines. Chart 7 enables a more detailed examination of the central 8 deg x 6 deg of field.

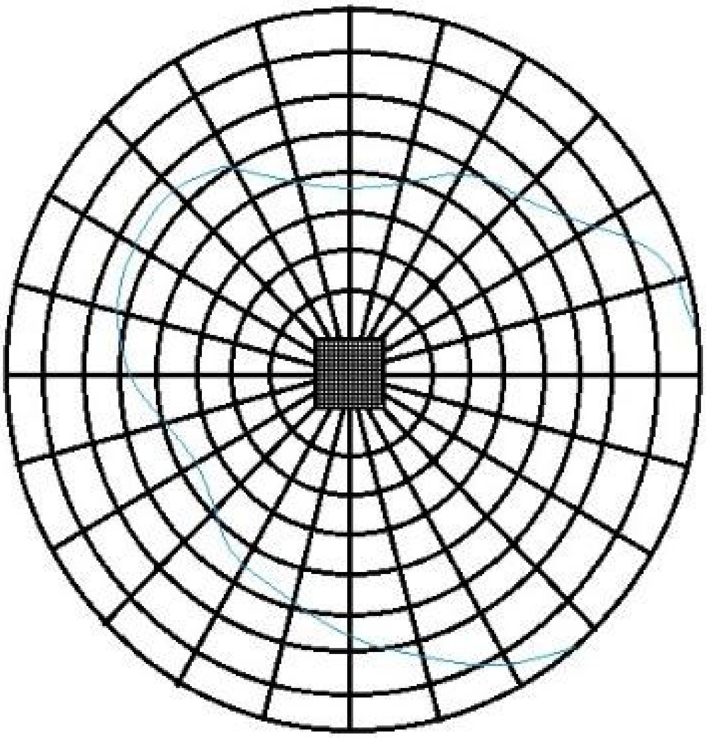


Figure 19. comparison of the field of view tested by the Amsler chart compared to the typical visual field on a subject's right eye. Each concentric circle represents a 100 increment from fixation (adapted from Amsler, 1953)

4.4.3.2 Automated perimetry (Henson 7000)

The Henson 7000 (Elektron Technology, Cambridge, UK) is an automated visual field screener designed to undertake suprathreshold assessment of the central visual field.

The instrument's testing strategy has two levels, consisting of a standard screening test assessing visual sensitivity in 26 points spread across the central visual field, and an extended test for more in-depth investigation assessing 68 test locations across the visual field (**Figure 20**).

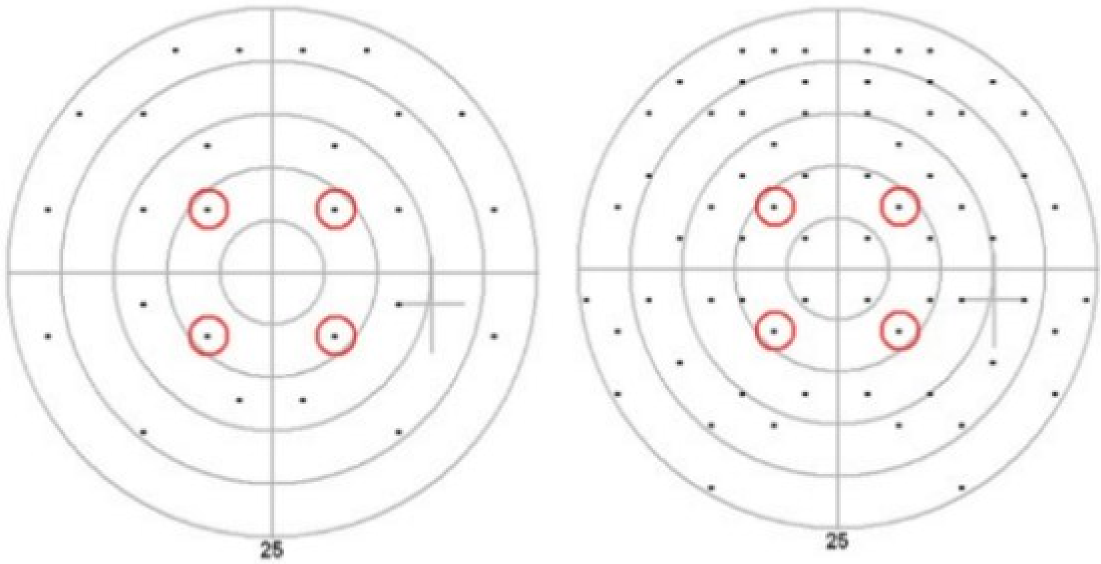


Figure 20. Location of the 26 and 68 test locations on the two test levels of the Henson 7000 suprathreshold field screener.

The Henson 7000 can undertake suprathreshold field screening using a stimulus luminance threshold range from 10dB to 42dB. The test is conducted against an even background illumination of 3.15Cd/m^2 (9.89apostilb), with the threshold for testing being measured at the start of the test. The instrument uses a Heart algorithm initially measuring threshold sensitivity in four test locations, one in each quadrant of the visual field displaced from the vertical and horizontal midlines by 9^0. Each point is tested with a stimulus set 1dB brighter than the anticipated threshold based on the subject's age, using bracketing over six presentations in each of these points, the threshold for the subject is determined by the average of the thresholds measured in the four test locations. Where one point exhibits abnormal depression (outside the 95% confidence limits of normal for the subject's age) the point is excluded from the threshold calculation. Where all four quadrant's measure exhibit abnormal depression, the threshold is automatically set to 4dB below the expected threshold for age. During the test being run, if a stimulus is missed, the instrument will automatically retest at the same point. Where the stimulus is missed again, the point will be tested again with a stimulus of higher intensity. Three levels of increased intensity are tested, at 5dB, 8dB and 12dB higher than the initial test stimulus, recording the intensity of the lowest intensity observed, or marking failure to respond to the 12dB stimulus, the maximum stimulus that may be tested by the Henson 7000 having an intensity of 100Cd/m^2 (314.159 apostilb).

Testing is undertaken monocularly with either refractive correction in place, or with an appropriate supplementary lens installed in the instrument. During the test the fellow eye occluded using a patch or similar. The subject is handed a handset with a response key and instructed to place their eye into the eyepiece and directed to fixate upon the central red spot target. When started, the test presents a series of white light flashes to the subject's peripheral vision. The subject is instructed to press the button on the response key whenever these white light stimuli are observed. The test typically takes around 2 minutes to complete.

Upon completion, the instrument provides a summary plot of the field provided. Additionally, two further pieces of information are given, a summary of the number of stimuli missed across the field and a probability graph comparing the results to a normal eye.

Visual field loss may occur with several ophthalmic anomalies, while field loss associated with damage to areas associated with brain injury tend to respect the vertical visual midline (**Figure 1**).

4.4.4 Colour vision

The human visual system can sample an area of the electromagnetic spectrum ranging from around 380 to 750nm. Colour perception is achieved through the presence of a range of photoreceptors sensitive to short, medium and long wavelengths of light, and transmission of this information is believed to be coded by colour opponency by retinal interneurons (Conway et al. 2023). While colour vision deficits may occur physiologically, frequently being inherited as an x-recessive trait, acquired deficits may serve to indicate damage to the photoreceptors, macular region or optic nerve function. The most frequently employed test for screening for colour vision anomalies is the Ishihara test. First developed in 1916 as a test of congenital colour deficiency, this has been reported to have high sensitivity and specificity for detecting colour vision anomalies (Birch & McKeever, 1993; Birch, 1997). The test is conducted monocularly in good natural daylight by holding the test book at 75cm from the subject. The subject is then asked to report the number observed on the test plate while the examiner compares against the results.

4.4.5 Visual Stress

The term visual stress is used to describe a syndrome of conditions where affected individuals experience symptoms of perceptual distortion and visual discomfort that are either partially or fully alleviated through the use of coloured filters (Wilkins and Evans 2022). For many affected individuals these symptoms are particularly acute when viewing specific repetitive high contrast stimuli such as written text. While frequently associated with dyslexia, a number of neurological conditions have also been observed to exhibit an increased prevalence of these symptoms such as migraine (Wilkins et al. 2007; Vieira et al. 2020), multple sclerosis (Newman Wright et al. 2007), epilepsy (Wilkins et al. 1979), traumatic brain injury (Clark et al. 2017; Bansal and Green 2022), as well as stroke survivors (Beasley and Davies 2013b; Beasley and Davies 2013a). While a number of approaches have been used historically to diagnose visual stress (Evans and Allen 2016; Miyasaka et al. 2019), Diagnostic guidelines were developed using a Delphi technique that identified the key symptoms, signs and behaviours observed (Evans et al. 2017), which could be used to aid in the diagnosis of this anomaly. A range of theories have been proposed to explain these symptoms (see **Chapter 7**), though following the observations of Beasley & Davies (2012, 2013a), cortical hyperexcitability is considered to be the most likely origin of this syndrome in stroke survivors.

4.4.5.1 Pattern Glare

The pattern glare test (Institute of Optometry, London, UK) is an instrument designed to invoke the perceptual distortions associated with visual stress in susceptible patients. The test consists of three high contrast, horizontal periodic grating that when viewed at a testing distance of 40cm samples perceptual responses to low (0.3cpd), medium (2.3cpd), and high (9.4cpd) spatial frequencies.

The procedure is undertaken with the subject wearing their required near point correction. The subject is directed to look at the small square present at the centre of each grating. Following a period of five seconds the patient is asked to report the presence of any visual distortions such as colours within the pattern, bending of the grating lines, blurring of the grating lines, shimmer/flicker in the pattern, fading of the pattern, shadowy shapes within the pattern, or other effects. Where visual disturbances are reported, the subject should be asked whether they occur on both sides of the pattern, or whether they affect one side more than the other. The process is then repeated for the patterns on page 2 and 3. For each page a score is given for the presence of distortions reported (maximum 7 per page), with the total score recorded as the pattern glare score. The difference in results from page 2 and 3 is calculated to identify the mid-high difference score (Evans and Stevenson 2008). Pattern glare score is abnormal if the response to the medium spatial frequency grating exhibits a score over 3, or a difference between the medium and high spatial frequency score of greater than 1.

4.4.5.2 Overlay assessment

Several methods have been developed to identify the optimum colour of filter to reduce the symptoms of visual stress. For this study Intuitive Overlays (Institute of Optometry, London, UK) were used (**Figure 21**). The test consists of nine coloured filters with a neutral grey filter. Each filter has a matt and gloss surface. The test set also comes with a test page of visually demanding text, similar to that found in the Wilkins Rate of Reading Test. To conduct the test, the subject is instructed to view the text on the test page while the examiner places a coloured overlay, matt side up over the left hand paragraph of text. The subject is then asked to report which side of text is most comfortable and clear to view, the side with the filter, or the side without. Where the filter is preferred, the subject is then shown the text with the gloss side up and asked to indicate which side is preferred. Where the side without filter is preferred the filter is removed and the next tested. The order of coloured overlay presentation is designed to avoid the presentation of complimentary colours simultaneously. Colours should be presented in order starting with the Rose overlay, followed by the lime-green, blue, pink, yellow, aqua, purple, orange and finally mint-green overlay. Where multiple overlays are selected, the preferred may be selected by successive elimination. In some instances, multiple overlays may be combined with up to two more filters of neighbouring colours. Where no colours are preferred then the test is over. For this study the grey overlay was omitted as this has been found to rarely improve symptoms of visual stress (Wilkins 2002). Stroke survivors have been observed to exhibit a greater incidence of photophobia. While some degree of overlap may occur between the symptoms of photophobia and pattern glare, the approach employed in **Chapter 7** was undertaken to investigate visual stress specifically, and to maintain consistency with other previous work (Beasley and Davies 2013a) the grey filter was not used in this study.

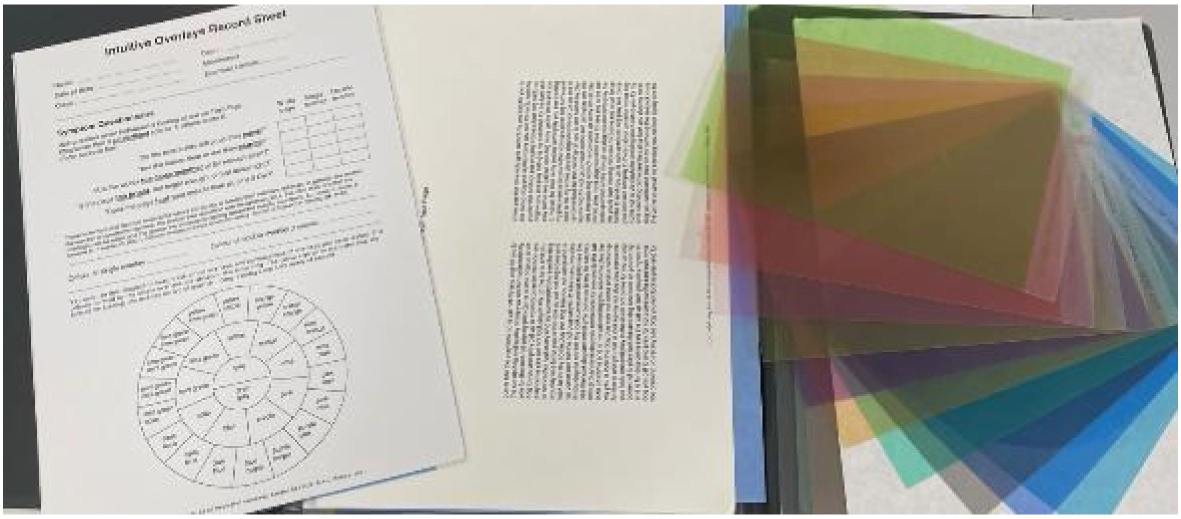


Figure 21. Intuitive overlays test set

4.4.5.3 Rate of reading

A range of methods of assessing reading have been developed and reported upon within the literature (Legge et al. 1989; Hahn et al. 2006; Trauzettel-Klosinski and Dietz 2012; Altpeter et al. 2015; Kingsnorth and Wolffsohn 2015; Morrice et al. 2020; Morrice et al. 2021). The Wilkins Rate of Reading Test (Wilkins et al. 1996a; Wilkins et al. 1996b) was developed to measure the effects of perceptual distortions on reading. This test was designed to be visually stressful and developed to compare one individual's performance under different visual conditions. This test is frequently used to support the assessment of impact of an individually selected coloured filter(s) upon reading performance. Performance is measured by the number of words read and errors made within a set period. The test consists of 4 paragraphs of text, each of which consists of ten lines of 15 words. Simple 2, 3 and 4 letter words that are familiar to a typical seven-year-old and frequently used in the English are used. Each line within the paragraph consists of the same 15 words but in random order. The text is printed in a 9 point Times font, designed to accelerate fatigue when reading. Given the random selection of words, errors may be readily measured and subjects are unable to predict or complete sentences based upon context. The test is conducted with necessary optical correction in place and the patient is instructed to read aloud the text as quickly as possible without errors. As the subject begins the examiner begins a stopwatch recording the number of words correctly read in this time and the number of errors made. Where the subject completes the paragraph in under a minute, the time taken to complete the paragraph is recorded, and an equivalent rate of reading may be calculated by

$$\text{Rate of Reading} = 60\,\frac{\text{Words Correctly Read}}{\text{Time to Complete Paragraph}}$$

Where used to assess the impact of a coloured overlay, the process is undertaken initially with the overlay, then without, repeated again without and finally with the overlay, in an ABBA design. This approach is used to reduce the impact of learning effects and balance for fatigue. The rate of reading and error scores in each visual condition is then averaged to give a rate of reading and error score.

4.5 Binocular vision examination

Binocular vision arises from the sensitivity of the visual system to fuse and detect disparity between the retinal images of the two eyes. This cognitive process enables the visual system to identify relative and absolute depth within the visual field. Binocular vision is described in detail in a number of authoritative sources (Benjamin 2006; Griffin and Borsting 2010; Stidwill and Fletcher 2011; Rowe 2012; Scheiman and Wick 2013; Evans 2022), a summary of this is provided below.

4.5.1 Ocular motility

4.5.1.1 Physiological Motility

The assessment of ocular motility represents an assessment of the ability of the eyes to provide yoked, smooth pursuit movements in the eight positions of gaze. The subject is instructed to view an illuminated target held at 35-40cm in front of the subject held level to the visual midline. The subject is then instructed to follow the target using their eyes without movement of the head. Subjects are instructed to report the presence of diplopia or ocular discomfort on eye movement. The target is moved in a smooth arc-like manner from primary gaze to around 40^0 from the midline, assessing the ocular motility in the eight positions of gaze. During the assessment the clinician should observe the reflection of the illuminated target on the eyes. Where in alignment this should be symmetrical and should be observed to be consistent when assessing the eye positions in the 8 positions of gaze. Any deviation of reflex should raise suspicion of improper movement, warranting further investigation to identify the inadequately functioning muscle. This test may be done monocularly to assess duction movements or binocularly to assess version movements.

4.5.1.2 Northeastern State University College of Optometry Oculomotor Test

A number of methods of assessment have been developed to examine pursuit and saccadic movement (Vinuela-Navarro and Mcoptom 2018), ranging from simple clinical procedures that can be easily used in practice, to specialist psycho-motor tests (Developmental Eye Movement Test, Bernell Corporation, IN) and commercial eye tracking technologies that may be deployed in specialist or research settings. The Northeastern State University College of Optometry (NSUCO) Oculomotor test, sometimes called the Maples' test (Maples 1995) is an objective, standardised chairside test of saccade and pursuit eye movements.

Both tests are undertaken binocularly using small 5mm diameter ball targets typically found as confrontation type tests or commercially available Wolff wands. To test saccades two of these targets are held approximately 10 cm on each side of the subject's visual midline, even with one another, at a distance of 30-40 cm. The patient is instructed to look from one target to the other, and back on the examiner's instruction. Five cycles, consisting of 10 fixations are undertaken. The examiner observes the subject's ability to complete the task, grading the difficulty observed as outlined in **Table 4-2**.

Score	1	2	3	4	5
Ability	Completes <2 cycles	Completes 2 cycles	Completes 3 cycles	Completes 4 cycles	Completes 5 cycles
Accuracy	Large over/undershooting noted	Moderate over/undershooting noted	Constant slight over/undershooting noted (>50% of the time)	Intermittent slight over/undershooting noted (<50% time)	No over/undershooting
Head movement	Large movement of the head at any time	Moderate movement of the head at any time	Consistent slight movement of the head at any time (>50% of the time)	Intermittent slight movement of the head (<50% of the time)	No movement of the head
Body movement	Large movement of the body at any time	Moderate movement of the body at any time	Consistent slight movement of the body at any time (>50% of the time)	Intermittent slight movement of the body (<50% of the time)	No movement of the body

Table 4-2. NSUCO saccade subtest scoring (Maples 1995).

For the pursuit test, the examiner holds a single ball target in front of the subject, at a distance of around 30-40cm. The examiner then traces the path of a 10cm diameter circle centred on the subject's visual midline. Two rotations are completed both clockwise and counterclockwise, during which the examiner observes the subject's response, grading difficulty in completion as outlined in **Table 4-3**. Concerning head and body movement during the test, the test seeks to assess spontaneous responses to eye movements. Test subjects are deliberately not given instruction to maintain head and body posture throughout the test, and unprompted movements of the head and body are assessed as part of the examination of saccade or pursuit movements.

Score	1	2	3	4	5
Ability	Unable to complete ½ rotation in either direction	Completes ½ rotation in either direction	Completes 1 rotation in either direction	Completes 2 rotations in one direction but only 1 in other direction	Completes 2 rotations in each direction
Accuracy	Refixations >10 times	Refixations 5-10 times	Refixations 3-4 times	Refixations <2 times	No refixations
Head movement	Large movement of the head at any time	Moderate movement of the head at any time	Consistent slight movement of the head at any time (>50% of the time)	Intermittent slight movement of the head (<50% of the time)	No movement of the head
Body movement	Large movement of the body at any time	Moderate movement of the body at any time	Consistent slight movement of the body at any time (>50% of the time)	Intermittent slight movement of the body (<50% of the time)	No movement of the body

Table 4-3. NSUCO pursuit subtest scoring .

4.5.2 Ocular alignment

Ocular alignment is under the control of postural, fixational, sensory and motor reflexes. When fixating upon a stimulus in visual space the postural reflexes will serve to bring about close alignment of the eyes to the target of regard. In the normally functioning visual system where both retinas receive similar visual stimulation this information is interpreted as a single percept through a sensory process known as fusion. In addition to the sensory mechanism, a motor fusional reflex is present that where necessary is able to act to alter the function of the extraocular muscles to reduce any retinal disparity present. Where postural and fixational reflexes do not bring about alignment of the visual axes on to the target of regard, motor fusion is required to maintain binocular fusion. In these cases, where fusion is interrupted, the eyes will return to the position of functional rest, any deviation present being called a latent deviation or heterophoria.

When fixation is undertaken, the eyes are orientated to bring about the focus of the target of regard onto the central fovea of each eye. As a stimulus moves away from fixation horizontally it stimulates areas of the temporal retina of one eye and the nasal retina of the other eye. The areas of the retinas stimulated by this are known as having a common visual direction. In the physiological visual system, this is known as normal retinal correspondence.

These corresponding retinal points can be projected forward to establish the Horopter, a region of visual space that represents the projection of the corresponding retinal points relative to a point of fixation. This region represents the field of binocular vision (Ogle 1950; Harrold and Grove 2015). When a stimulus is moved away from the point of fixation in visual space (either proximally or distally) non-corresponding areas of the retina are stimulated, giving rise to the phenomenon of diplopia (double vision). The nature of this double vision is associated with the position of the stimulus relative to the fixation point. Where the stimulus sits within the horopter (with the eyes relatively divergent compared to the stimulus) this gives rise to crossed diplopia, while fixation out with the horopter (with the eyes relatively convergent relative to the stimulus) giving rise to uncrossed diplopia.

Where diplopia is encountered the sensory-motor fusion system is initiated to alter the contraction of the extraocular muscles and bring about alignment of the visual axes onto the object of regard and eliminate the diplopia. While diplopia may arise due to large alterations of ocular alignment in respect to the target of regard, minor differences in proximal location from the point of fixation can give rise to symptoms of ocular discomfort due to the presence of fixation disparity. This is believed to arise as for each point of the retina on one eye corresponds instead of a discrete point but to an area of the retina. This area, approximately 5 arcmin at the fovea and expanding eccentrically is believed to be cortical in origin called Panum’s fusional areas. The visual projection of these areas is known as Panum’s fusional space and represents an area around the horopter where binocular misalignment may be present without diplopia. The degree of misalignment measured without diplopia is known as fixation disparity, while the amount of prismatic correction required to bring about accurate fixation is known as aligning prism.

4.5.2.1 Methods of heterophoria measurement

The measurement of heterophoria may be undertaken by several methods, with the examiner using dissociative techniques to inhibit fusion. The examiner may then determine the presence, size and in some instances infer the degree of compensation of any deviation present across different fixational distances.

4.5.2.2 Cover test

The cover test is an objective test of ocular alignment where the examiner identifies and measures the size and nature of any deviation present. The test is the only method of definitively distinguishing between the presence of heterophoria or heterotropia, though the test requires significant examiner experience before accuracy can be established. This test is typically performed at both distance and near to establish the presence and nature of deviation present and may be used to infer the degree of compensation. The test is conducted in two parts, initially a cover-uncover test is undertaken, which may be followed by a cross-cover test.

The speed and smoothness of recovery can be used to infer whether a heterophoria (where present) is well controlled (Evans 2022), with a poorly controlled deviation exhibiting slow recovery of fixation with difficulty, while a well-controlled deviation will quickly recover with smooth eye movement.

Where small deviation is observed or the clinician is unsure of the deviation observed, the cross-cover (or alternating cover) test may be employed. In this instance, after 1-2 seconds in place over one eye, the cover is quickly removed and placed in front of the fellow eye of the subject for 1-2 seconds and back a number of times. Where this procedure is used, the examiner observes movement of the eye as the cover is removed.

Frequently the size of any deviation observed increases facilitating classification of deviation present. Where doubt remains, the clinician may ask the subject to report their observations of the fixation target. Where a deviation is present the movement of the cover, and subsequent refixation movement will give subjective perception of a change of the fixation target’s location.

The size of the deviation may be estimated based on the degree of movement observed. While useful as a screening test for the presence of a deviation, with movement as small as 2^{Δ} being observed by the majority of examiners the accuracy of this technique for identifying the size of the deviation may be less consistent. Measurement of the deviation using either free prism lenses or a prism bar has been observed to be a more repeatable method (Schroeder et al. 1996; Rainey et al. 1998b; Rainey et al. 1998a), and was employed by the author for oculomotor assessments within **Chapter 5** and **Chapter 6** of this study.

4.5.2.3 Maddox rod

The Maddox rod is an instrument consisting of several parallel high power plano-convex cylinder lenses (**Figure 22**). This lens brings about dissociation through significantly distorting the image of what is viewed to such an extent that fusion is not possible. The procedure is conducted with the subject wearing the appropriate refractive correction for the distance under test.

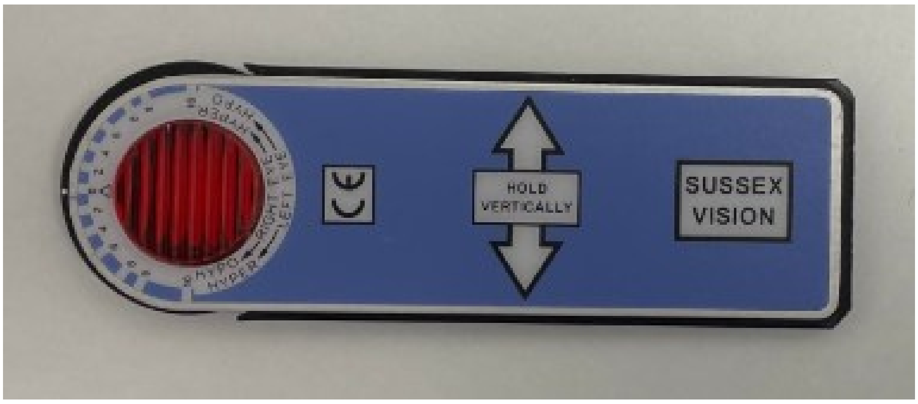


Figure 22. The Maddox rod: Where a point light target is viewed through the instrument, the image of the light is distorted to appear as a bright line, the axis of which being orthogonal to the axis of the cylinders. Convention dictates that this is held in front of the right eye, though where significant degrees of sensory dominance or uneven acuity is present, this may be placed in front of the eye with better acuity. To aid in measurement this particular instrument incorporates a rotary prism, enabling prompt neutralisation of any deviation found without further supplementary lenses.

4.5.2.4 Modified Thorington method

The Modified Thorington method is a technique employed to measure the deviation present at a near point, using the Maddox rod. The Modified Thorington method uses a fixation light source at the centre of a numbered scale. The scale represents the magnitude of deviation of light from fixation at a set distance. During the course of this study, the Modified Thorington method was employed using the heterophoria scale on the Saladin Near Point Card (**Figure 16**), which is scaled for use at 40cm viewing distance.

4.5.3 Fusion

4.5.3.1 Worth 4 spot

The Worth four light test is a dissociative diplopia test to assess the presence of flat fusion. The subject wears a red-green anaglyph visor and is directed to view a target consisting of four lights on a uniform grey background (**Figure 23**). The subject is asked to report how many lights are seen. This test may be conducted at distance and near.

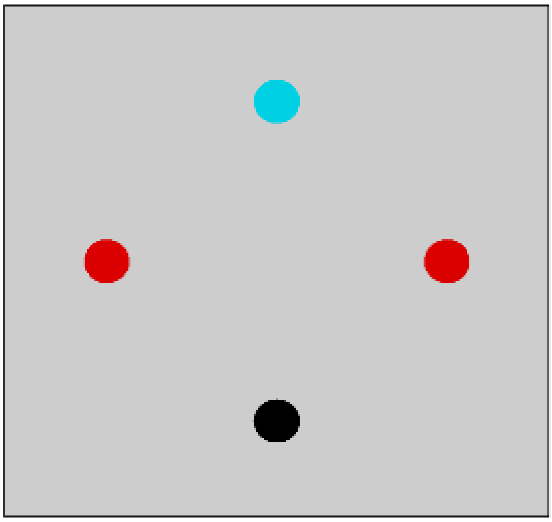


Figure 23. Worth Four Spot Test. With anaglyph filters in place one of the lights (black) is visible to both eyes, while of the remainder one light (turquoise) is visible to only one eye, while the others (red) are visible to the other eye. The presence of four lights indicates fusion, while two or three lights indicates monocular suppression, while five lights indicates diplopia is present.

4.5.4 Vergence

Vergence describes the disconjugate eye movements where the eyes alter their orientation independently from one another. Vergence movements may be undertaken by voluntary control or can be triggered by the presence of retinal disparity. In order to overcome the disparity arising from misalignment of the eyes when viewing the target of regard motor fusion must be used. Motor fusion is then used to bring about a change in the ocular vergence to eliminate the disparity perceived. Convergence movements occur simultaneously with the exertion of ocular accommodation when viewing a near target, and while possibly reduced (Ostadimoghaddam et al. 2017) persists in the presence of presbyopia.

4.5.4.1 Near Point of Convergence

The most commonly used examination to measure vergence in clinical practice is the near point of convergence test. This test is designed to identify the proximal point of ocular convergence before fusion is lost and diplopia (double vision), or outward turn of the eye (objective break of convergence) occurs. While a number of targets may be used to measure convergence in presbyopic subjects (Siderov et al. 2001), the Royal Air Force Near Point Ruler (RAF Rule) is the preferred method of measurement and was used in this study.

4.5.4.2 Jump vergence

Jump vergence describes a clinical technique used to infer convergence facility, the ability of subjects to alter their convergence between proximal and distal targets. To conduct the test subjects are directed to a letter on the distance acuity chart of a size greater than the acuity of the weaker eye or other suitable accommodative target and a proximal target (typically a fixation ruler) held at a point a few centimetres distal to their near point of convergence, which typically is around 15-20cm (Elliott 2013). The examiner instructs the subject to look from one target to the other while observing the eyes as they converge on the near fixation target and diverge to view the distance fixation target. The examiner then records a qualitative summary of the ability and quality of refixation between different distances.

4.5.4.3 Fusional reserves

The measurement of fusional vergence ranges or fusional reserves serves to appraise the subject's habitual motor fusion available, and either alone or in combination with the heterophoria measures be used to identify the necessity for orthoptic management or the addition of prismatic correction to a subject's required optical prescription.

The test may be done in free space using a prism bar (**Figure 24**) or within a phoropter and may be assessed at distance and near (Lança and Rowe 2019). The procedure is undertaken with the subject wearing the necessary correction for the viewing distance being tested and directed to look at an accommodative target larger than their best corrected acuity.

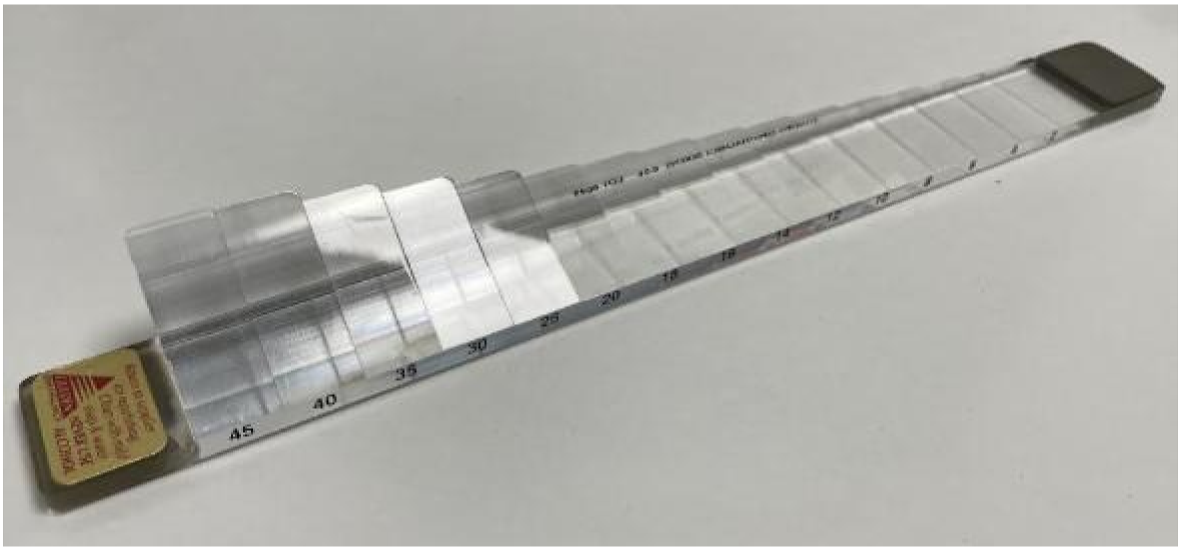


Figure 24. Horizontal prism bar: A series of plano prisms of increasing power that may be used to support the measurement of ocular misalignment as well as assessing horizontal fusional reserves.

The subject is then instructed that the examiner will insert the prism bar in front of the subject's right eye. When this is inserted, the subject is to report whether the target remains clear, whether the target appears to blur, or if it becomes diplopic. The prism is increased steadily until diplopia is reported, with the examiner recording the prism required to elicit blur (if present) and diplopia. Once diplopia is identified then the examiner steadily reduces the prism power until the subject reports that the diplopia has resolved, recording the recovery point. In order to avoid vergence adaption, the fusional reserve measured first is that which opposes the phoria (Rosenfield et al. 1995).

Sheard's criterion describes the principle tthat where a heterophoria is present, the opposing fusional reserve must be double the phoria in order to sustain comfortable binocular vision. Fusional stamina describes a continuous variable based upon Sheard's criterion (Myklebust and Riddell 2016). It is derived by subtracting the heterophoria measured with cover test from half of the opposing fusional reserve. Where this variable is positive Sheard's criterion is met, and negative where this is not met. This variable is simple to calculate and may be used in both clinical and research settings.

4.5.5 Fixation disparity

The term fixation disparity is used to describe the phenomenon of small misalignments of the eyes that occur without binocular suppression or the perception of diplopia. In these cases, minor misalignments of the eye results in the point of fixation sitting either proximal or distal to the horopter, within a region known as Panum's fusional space. This describes a region in space where minor misalignments may occur relative to the horopter without diplopia occurring. While necessary to support the detection of retinal disparity without diplopia and hence stereopsis, misalignments of the eyes within Panum's fusional space may give rise to symptoms of asthenopia.

4.5.5.1 Aligning prism

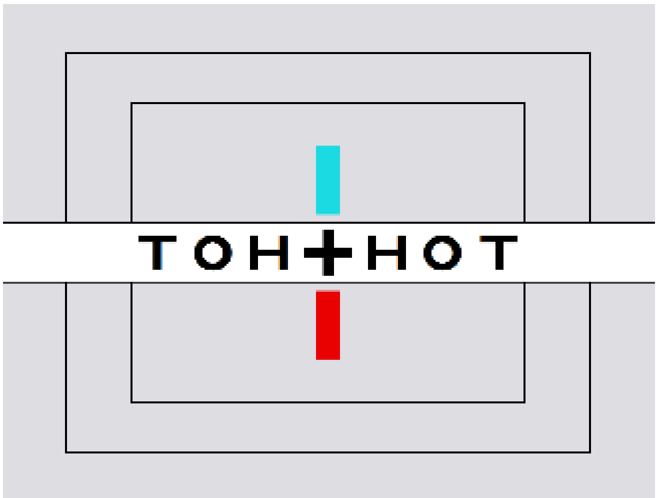


Figure 25. Thomson XPert 3Di test chart Fixation disparity test. This test is undertaken wearing distance correction with supplementary red/green anaglyph filters. The subject is directed to observe the central letters and cross visible to both eyes and the two nonius markers, with one visible to each eye.

The most commonly used test of retinal disparity in the UK is the measurement of aligning prism. This measurement describes the degree of prism required to eliminate fixation disparity. This is most frequently done using the distance and near Mallett Units or similar instruments.

The principle of these instruments is to present a binocular fixation target that serves to lock binocular fusion, while presenting two monocular 'nonius' targets, one perceptible to each eye. Fixation disparity is observed by displacement of one or both of these nonius targets from their original position, with nonius markers crossing the visual midline indicative of exo-slip and moving away from the visual midline indicating eso-slip. The procedure is conducted with the subject wearing the correct optical correction for the viewing distance. The examiner directs the subject to the target and familiarise them with the test. A filter is then inserted to bring about a dissimilar image, this may be done using crossed polarisers or anaglyph lenses depending upon the exact instrument (**Figure 25**). The subject is then directed to observe the central lock, appreciating the presence and location of the nonius markers. The subject is asked to report upon the position of the nonius markers relative to the central lock, and where necessary prismatic lenses inserted to bring about alignment of these markers. In the course of this study distance aligning prism was measured using the Fixation Disparity test on the Thomson XPert 3Di test chart software (Thomson Software Solutions, Hatfield, UK), while near testing was undertaken using the near vision test unit (**Figure 26**).

Figure 26. The near vision test unit. The aligning prism test is similar to that found on the Mallett Unit, with both central and peripheral fusional locks.

4.5.5.2 Forced duction curves

Just as the *aligning prism* may eliminate fixation disparity, the use of other prism powers may be used to induce further fixation disparity. The results of this induced fixation disparity enables the clinician to visualise and further investigate the response of the binocular vision system to stress upon it. The graph of disparity responses to prism is known as a fixation disparity or forced duction curves. These were first described by Ogle (1967) who identified four curve classifications (**Figure 27**).

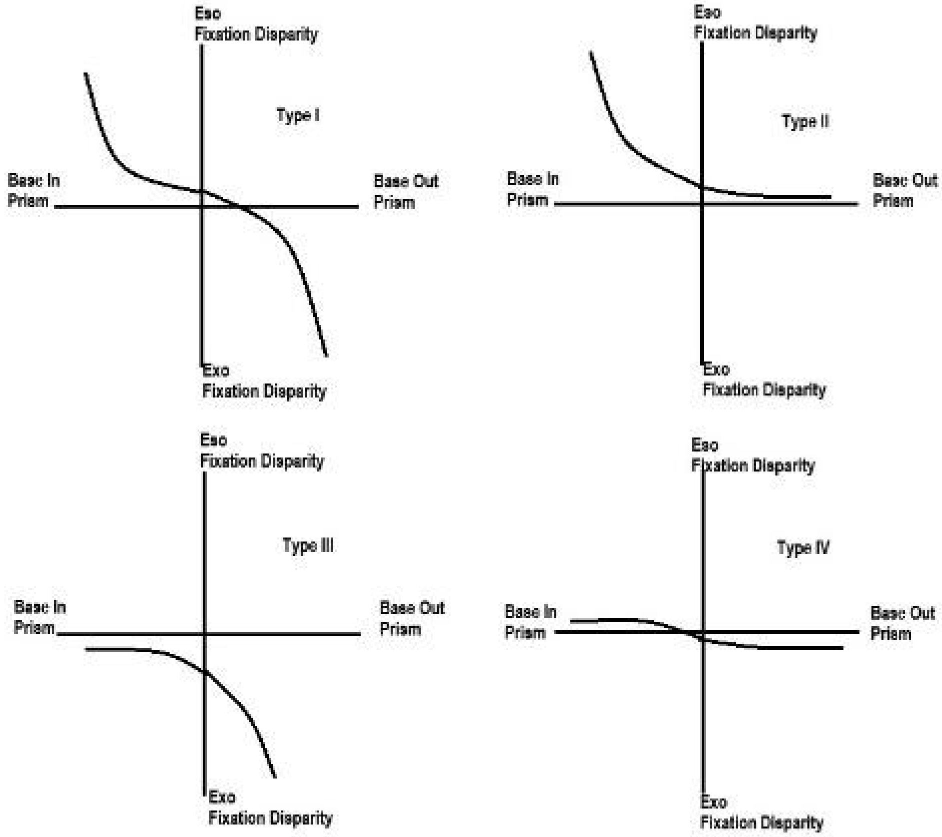


Figure 27: Fixation disparity curve types. Type I curves exhibit the ability to compensate for the induced fixation disparity at low levels of both base in and out prism. Type II curves indicate good adaption to base out prism, but poor adaption to induced base in prism. Type III curves exhibit good base in adaption but poor base out adaption, while Type IV curves are believed to exhibit binocular instability, with subjects possibly maintaining binocularity by their own volition rather than through the accommodative/vergence relationship (London and Crelier 2006).

For this study forced duction curves were derived at near using the Saladin card (**Figure 16**). With appropriate near correction in place subjects were initially familiarised with the card, highlighting the circular openings with lines of varying degrees of misalignment and the letters printed above these. The polarised visor was then added, and subjects asked to identify the circular opening that demonstrates alignment of the two black lines. Subjects are instructed to initially view the letter above the opening before viewing the lines directly. Once achieved the process is repeated with the examiner holding prism lenses before the right eye, of 2^{Δ}, 4^{Δ}, 6^{Δ}, 8^{Δ}, 10^{Δ} and 12^{Δ} initially base in, then base out and recording the subject's response. From these responses the forced duction curve may then be plotted. Notably true fixation disparity is identified by the location of the plotted line crossing the y axis, while the aligning prism is identified by the location of the plotted line crossing the x axis.

4.5.6 Stereopsis

In the absence of amblyopia and other anomalies of ocular coordination the visual system is able to further analyse disparity of the retinal images to infer relative difference of location of a stimulus relative to a plane of regard. This ability to derive information from disparate retinal images to infer the perception of depth is known as stereopsis. Stereopsis is a complex neurosensory mechanism involving several brain areas (Cumming and Deangelis 2001), and widely used within eyecare to assess binocular function.

4.5.6.1 TNO Test for Stereoscopic Vision

The TNO Test for Stereoscopic Vision (Lameris Tech, Veenendaal, Netherlands) is a test of global stereopsis. Using anaglyph filters it can be used to measure stereopsis from 480 seconds of arc to 15 seconds of arc in test subjects. With appropriate near correction and anaglyph worn, subjects are directed to identify the orientation of the missing segment from the stereoscopically perceived discs (**Figure 28**). The examiner records the last correctly identified pair of discs as stereoacuity in seconds of arc. For this study the 10th Edition TNO test for Stereoscopic vision was used (Van Doorn et al. 2014).

Figure 28. The TNO Test for Stereoscopic vision. Wearing appropriate correction and anaglyph filters the presence and depth of stereopsis may be appraised. The subject's task is to identify the missing 'pie' segment in each test plate.

4.5.6.2 Stereo Fly Test

Figure 29. The Stereo Fly Test. The test is conducted wearing appropriate correction and a polarised visor. The test may be used to appraise gross stereopsis (fly), stereoacuity (Wirt circles), and with children (animal targets).

The Stereo Fly test is a clinical test of local stereopsis (**Figure 29**). It is conducted with appropriate near correction worn along with a crossed polarised filter to bring about image disparity. This instrument is able to measure stereopsis from 800 to 40 seconds of arc.

4.5.7 Commonly encountered anomalies of binocular vision

4.5.7.1 Strabismus

Strabismus (manifest squint) describes the phenomenon where in binocular viewing one eye does not fixate and instead is misaligned away from the point of fixation. Strabismus may arise for several reasons such as an anomaly of neuromuscular development, genetic or anatomical origin, or sensory or motor anomalies during the process of the infantile critical period (Bui Quoc and Milleret 2014) as well as secondary to ophthalmic or neuro-ophthalmic origin (Karatas 2009). Where the misalignment has a developmental origin, this is frequently associated with a reduction in the best corrected visual acuity, an anomaly known as amblyopia. Strabismus is most readily identified using the cover-uncover test. The management of strabismus varies depending upon the exact classification, but frequently consists of refractive correction, orthoptic therapy, extraocular muscle surgery or a combination of these (Rowe 2012; Salmon 2019).

4.5.7.2 Decompensating heterophoria

Where the degree of motor fusion is insufficient to maintain control of any heterophoria present, this may give rise to symptoms of eyestrain, headaches, blurred vision and episodes of double vision as the heterophoria breaks down to become an overt eye deviation (strabismus). Diagnosis may be undertaken through assessment of the presence of heterophoria, fusional ranges and through assessment of fixation disparity using the Mallett unit. Management may be undertaken either to improve fusional range using orthoptic exercises, or through the prescribing of prismatic correction to reduce the degree of motor fusion required to maintain comfortable binocular vision (Scheiman and Wick 2013; Evans 2022).

4.5.7.3 Convergence Insufficiency

Convergence insufficiency is a neuromuscular anomaly where the visual system exhibits difficulty in coordination in near-point viewing. It is characterised by greater degrees of exophoria at near vision than at distance vision, a receded near point of convergence and reduced base out fusional ranges. As a low AC/A condition, this responds poorly to near point lenses (Scheiman et al. 2020), management consists of orthoptic exercises to improve the vergence range. While management is well evidenced in a juvenile cohort (Scheiman et al. 2005a; Nehad et al. 2018; Pediatric Eye Disease Investigator Group (PEDIG) 2019; Scheiman et al. 2005b), this is not as well evidenced in older populations (Scheiman et al. 2005a; Momeni-Moghaddam et al. 2015; Alvarez et al. 2021).

4.5.7.4 Cranial nerve palsies

Where damage occurs to one or several of the cranial nerves it may give rise to a number of anomalies as a result of a reduction in or loss of function. These anomalies vary depending upon which nerve is affected but may result in loss of eyelid tonus or misalignment of the eyes with associated symptoms of double vision, watering and irritation of the eyes. While it is important that the cause of nerve damage is identified and managed appropriately, beyond compensatory measures, there is limited evidence of proactive management that may normalise nerve damage.

Chapter 5 An evaluation of a diagnostic test battery to examine the sight of someone who has had a stroke: A diagnostic accuracy study

5.1 Introduction

For many people access to eye-care services following stroke are inconsistent (Rowe 2017b; Rowe 2017a; Stalin et al. 2024a), with specific visual assessment and management advice for visual problems often being overlooked (Rowe 2011b; Stalin et al. 2024b) in specialist settings, while some report difficulty in accessing care from eye care providers in community settings (Rowe et al. 2015; Stalin et al. 2024b; Stalin et al. 2024a). The development of a standardised test battery (**Chapter 3**) has the potential to facilitate access to, and consistency of services received in primary eye care for people with a history of stroke. The test approach utilises procedures routinely employed within primary eye care practice and has the potential to be used by both experienced clinicians in benchmarking their investigations and as guidance to support neophyte practitioners.

The purpose of this study was to examine the relative diagnostic accuracy of the new standardised diagnostic test battery, derived from the Delphi study undertaken in **Chapter 3**, assessing its outcomes against the results of a conventional approach to the testing of sight. Sight testing in the United Kingdom is regulated by the General Optical Council, which enforces the requirements of sight outlined in The Opticians Act (1989). The College of Optometrists provides guidance to optometrists in their professional practice in areas of knowledge, skills & performance, safety & quality, communication, partnership & teamwork and maintaining trust. Within these areas of guidance, the College provides guidelines to optometrists to the expectations of what diagnostic tests should be conducted by the optometrist in the course of a routine examination (**Table 2-1**). It would be anticipated that no significant difference in clinical outcome or findings would be anticipated between the two testing approaches.

5.2 Methods

This study is a prospective observational case-controlled diagnostic study to assess the accuracy and utility of a new diagnostic test battery (**Table 5-2**), with comparison to the findings of a typical examination undertaken in a community practice setting. The decision to use a typical eye examination as a reference standard was taken as it represents the level of care expected to be undertaken in contemporary practice (Knottnerus & Muris, 2003) and would be anticipated that any variation observed would fall within the normal range encountered in typical community optometric settings.

5.2.1 Participants

Potential participants in this study were recruited following response to communication with stroke support groups within the Southampton area, subsequent to social media outreach, in response to practice-based notices outlining the nature and detail of the study, additionally regional colleagues were made aware of the project through communication through the local optometric committee bulletins outlining the study, with details of how to refer potential participants for further information on how to take part. Participants were recruited who had a medical history of stroke (of any type). Controls were identified as an age matched sample. Those who had experienced a TIA without subsequently experiencing a full stroke, and those with the presence of other neurological impairment were excluded **Table 5-1**.

Inclusion Criteria	Exclusion Criteria
• A confirmed diagnosis of stroke as defined by the World Health Organisation (WHO) • Over 16 years of age	• Diagnosis of transient Ischaemic attack (TIA) without stroke • Presence of neurological impairment unrelated to stroke • Unable to consent to participate

Table 5-1: Inclusion & exclusion criteria

Prior to enrolment potential participants were issued a copy of the participant information sheet and consent forms to review before committing to participate in the study. To ensure sufficient power to avoid a type II error and identify a large effect size this study would need to recruit 78 participants when comparing controls, stroke subjects both without and with field defects, 74 participants for comparisons between stroke survivors and control groups, and 20 participants to test measures within each cohort. As the first prospective practice-based investigation of this instrument, in the absence of prior data to anticipate differences a recruitment target was set to recruit 59 subjects, split between stroke and controls (Beasley and Davies 2013a; Viechtbauer et al. 2015).

5.2.2 Test methods

All research undertaken in this study was done within the author's primary place of employment: Leightons Opticians and Hearing Care, 68 The Avenue, Southampton, SO17 1XS, a primary care optometry practice in Southampton. Upon enrolment participants were issued with two appointment times to visit the research venue to undergo examination. At one of these appointments participants would undergo the trial battery examination (**Table 5-2**), binocular vision testing (**Chapter 6**), pattern glare, coloured overlay & rate of reading assessment (**Chapter 7**) automated visual field screening and retinal imaging (**Chapter 8**) following pharmacological pupil dilation with the author. At the other examination, the participant would undergo the reference standard sight test (**Table 2-1**). Details of examination techniques can be found in **Chapter 4**. In order to reduce potential bias, participants had their reference test undertaken by another optometrist from the branch where research was being undertaken, who was initially masked to their status. The optometrists undertaking the reference test all held membership of the College of Optometrists. Additionally, to reduce potential learning effects the order in which the reference and trial test were undertaken was randomised. In all cases, clinicians were masked to the findings of the initial test when conducting the second test.

Where anomalies were identified requiring further investigation and/or treatment within a medical setting, this was discussed with participants at the conclusion of the appointment and where necessary referral undertaken with participant consent.

<table>
<tr><td>Trial battery examination</td><td>

Case History
Habitual distance acuity
Habitual near acuity
Measurement of pupil diameter
Pupil reflex testing
Marcus-Gunn testing
Ocular motility (physiological H/X)
Retinoscopy
Subjective refraction
Jackson crossed cylinder
Corrected distance acuity
Pinhole
Bin Balance
Distance cover test
Determination of near addition
Corrected near acuity
Near cover test
Amsler
Determination of intermediate addition
Near point of convergence
Slit lamp examination
Van Herrick’s test
Sodium fluorescein staining
Posterior Segment Exam
Indirect ophthalmoscopy
</td></tr>
<tr><td>Followup procedures that should be considered.</td><td>

Habitual Distance Acuity
Pattern glare test
Wilkins rate of reading test
Pupil reflex test
Marcus Gunn swinging flashlight test
</td></tr>
</table>

Table 5-2. Summary of the procedures to be undertaken as part of the diagnostic test battery developed by a Delphi panel (See **Chapter 3**).

Given the scope for professional judgment when the reference test examination is being conducted, variability was expected in what clinical information would be collected. For the purposes of this study, data not recorded would be counted as not having been undertaken as part of the reference test.

This study was conducted in accordance with the requirements of the Declaration of Helsinki (2013) and received ethical approval from the Health and Life Sciences Ethics Committee of Aston University (#HLS21005).

5.3 Results

To assess analysis of the diagnostic battery, its ability to determine ocular anomalies across four areas were assessed; refractive, binocular vision, visual and ocular health findings.

Statistical analysis was undertaken using SPSS (IBM SPSS Statistics for Macintosh, Version 29.0.1.0 Armonk, NY: IBM Corp) with analysis of refractive findings completed in accordance with guidance outlined by Armstrong (2013). All quantitative measures were assessed for normality using the Shapiro-Wilk test. Where normality was present parametric tests were applied, with non-parametric approaches used for non-normally distributed results. A significance level of α=0.05 was used for all tests.

Participant	Participant Type	Reason
49	Stroke	Unable to commit to a second visit due to time.
50	Stroke	Completed study. 13 months after completion contacted by the participant's son (holding power of attorney) had seen paperwork and did not want parent involved in study.
51	Stroke	Changed mind after first visit Participant felt the stroke had not been severe enough to justify participation.
52	Stroke	Participant eager for imaging to be done, after the first visit decided they did not want to attend again.
53	Stroke	Participant decided between visits they did not want to have any drops inserted into eyes.
54	Control	Participant unhappy as they felt questions asked at case history felt too personal - refused to participate further.
55	Control	Participant unhappy with interaction with optometrist undertaking College of Optometrists based exam at initial visit - declined to return
56	Control	Participant unhappy with findings of the initial visit, refused to attend for a second visit.
57	Control	No contact after first visit & no response to written communication - lost to followup.
58	Control	After the first assessment participant was unable to commit time for the second visit.
59	Control	Participant raised concern between visit 1 & 2 around risk of interaction of drops with other ocular medication.
60	Control	Participant’s first eye exam in over 10 years. Referral initiated after findings of first visit - participant requested withdrawal due to concern over referral.

Table 5-3. Summary of reasons for withdrawal from study given by participants.

Refractive findings are typically completed using the sphero-cylindrical form, recording the combination of spherical lens power, cylindrical lens power and orientation of this cylindrical lens to record findings. While a useful approach within the clinical setting, this is ill-suited to statistical analysis. To analyse refractive findings, these were transformed to vector format (Thibos et al. 1997) before analysis was undertaken. This approach involved transforming the lens power to be represented by a combination of the mean spherical lens power, and two crossed cylinders, one orientated along the horizontal (J0), and one orientated 45 degrees to this (J45).

Twenty-nine participants with a history of stroke and thirty-one control participants were recruited. All participants with a history of stroke had been discharged from hospital care at the point of enrolling in this study. Over the course of the study 7 participants with a history of stroke and 5 control participants chose to withdraw (**Table 5-3**). In total 22 participants with a history of stroke completed the study

(**Table 5-4**) consisting of 14 males and 8 females, ranging in age from 49-89 years (mean 71.86, SD 10.78), with a mean time since stroke of 5.72 years (SD 3.50years, range 1-15 years) as well as 26 controls (**Table 5-5**) consisting of 10 males and 16 females, ranging from 48-90 years (mean 69.04, SD 11.71). Control subjects were age matched (unpaired t-test; t =0.863 df=46 P=0.392), this distribution of gender was not found to be significantly different (Pearson chi-squared: χ^2=3.021, df=1, p=.082) between groups. Twelve participants from the stroke cohort and fourteen participants from the control cohort underwent the trial examination followed by the reference test, the remainder underwent the reference test initially followed by the trial battery examination (Pearson chi-squared: χ^2=.002, df=1, p=.961), The median interval between visits was 9 days (range 2-38 days), with no significant difference found between cohorts (Mann-Whitney U test: p=.429).

Participant	Sex	Age (years)	Time between first & second visit/days	Order of visits*	Time since stroke (Years)
1	MALE	75	7	1	5
2	MALE	88	7	2	10
3	FEMALE	68	10	1	2
4	FEMALE	86	17	2	7
5	FEMALE	86	7	1	3
6	FEMALE	49	13	2	1
7	MALE	81	2	2	7
8	MALE	89	14	1	2
9	FEMALE	64	4	1	6
10	FEMALE	75	12	2	5
11	MALE	63	6	1	3
12	MALE	68	11	1	8
13	FEMALE	87	5	2	1
14	MALE	74	7	1	6
15	FEMALE	72	6	2	11
16	MALE	63	16	2	2
17	MALE	68	7	1	4
18	MALE	66	7	1	8
19	MALE	55	35	2	7
20	MALE	68	12	1	15
21	MALE	68	7	2	5
22	MALE	68	2	1	8

Table 5-4. Details of participants with a history of stroke that completed the study. Order of visits 1. Participants attended for the trial battery examination initially, followed by the reference standard examination at a later date, 2. Participants attended the reference standard examination followed by the trial examination later.

5.3.1 Case History

Completed questionnaires were returned by 7 subjects from the stroke cohort, and 4 subjects from the control cohort (Pearson chi-squared: χ^2=1.822, df=1, p.177). From those subjects that responded, a similar proportion experienced symptoms suggestive of ocular surface disease (4/7 stroke survivors and 2/4 controls) and glare (5/7 stroke survivors and 2/4 controls). A small number of stroke respondents (2/7) reported difficulty with focus and motion, and a single respondent reported difficulty in reading comprehension.

Participant	Sex	Age	Time between first & second visit/days	Order of visits
23	FEMALE	78	4	2
24	FEMALE	67	3	2
25	MALE	62	38	1
26	FEMALE	76	8	2
27	MALE	54	7	1
28	MALE	70	11	1
29	FEMALE	60	5	1
30	FEMALE	63	6	1
31	FEMALE	72	10	1
32	MALE	90	11	2
33	FEMALE	84	11	2
34	FEMALE	83	18	1
35	FEMALE	58	4	2
36	MALE	84	7	1
37	FEMALE	65	2	1
38	FEMALE	61	18	2
39	MALE	52	13	2
40	FEMALE	63	11	1
41	MALE	53	18	2
42	FEMALE	74	35	2
43	MALE	80	35	2
44	FEMALE	48	3	1
45	MALE	83	11	1
46	MALE	72	12	1
47	FEMALE	82	19	1
48	FEMALE	61	6	2

Table 5-5. Details of control participants that completed the study.

Upon further questioning on visual symptoms, only a single respondent (Participant 17) reported upon visual testing undertaken within the hospital setting, indicating *Well I had all the tests at the time, it must have been a few months* [after the stroke] *I'm not sure.* Subjects otherwise reported no hospital-based checks, or crude nonclinical measures.

[How long after the stroke was it until your vision was checked?] *Well, I didn't I guess, only when I came here* [study participation]. *I think when I was in hospital so many other things going on, so many other priorities, my mobility [was poor], erm.. I couldn't watch tv, couldn't concentrate for anything either, erm of course that affects the eyes, had very good physios. But I couldn't write or remember my own name. (Participant 37)*

They [the hospital staff] gave me a book about Cliff Richard but I couldn't read it, my head couldn't go. Then on New Year's Day had complete stroke - thought my eyes tired, and the only thing said was "can you see?" and I said yes because I could see but I didn't know because the focus wasn't right. Kept saying my eyes weren't right, but they said I can go home but can't give you an eye test until you go home then the week after they let me go [discharged]. *The GP said I was diabetic - I had [diabetic retinal screening] it done over the road, they had a look over eyes and said nothing's damaged or nothing. but I kept saying I can't see properly all i could do was take headache tablets. No follow up after that - I went to* [habitual optometry practice] *I couldn't talk and they tried to do numbers - I knew it* [VA testing] *was an N but I couldn't say N then I got animals children's book.* (participant 15)

Some variability in understanding was observed, within the returned questionnaires only 3 stroke survivors were able to provide some indication of where their stroke had affected, with one subject (Participant 10) reporting that the stroke affected their left optic nerve. Understanding of the visual effects of the stroke were mixed

I noticed something was off right after the stroke, not sure about how long it was [before vision was checked] *after? maybe a year? maybe a little more? Lost all the vision on one side, everything's just a blur there - I can't drive anymore, but its fine otherwise.* (Participant 21)

While one subject (Participant 8) reported:

My vision didn't really change after the stroke, so I didn't rush to get it checked, I went whenever my next check was due. I'm not sure it really was a stroke I had, the doctor says it was but my son thinks it was a mini-stroke. I haven't really noticed any changes in my vision, one eye is worse than the other but that's the cataracts. The doctor says that there's some gaps in my vision, but I don't feel like I have any problems other than the cataracts which are an annoyance.

While all respondents from the control cohort reported regular attendance at an optometry practice, 2 participants from the stroke cohort reported not routinely attending primary eye care services. Where vision was affected, only one subject reported undergoing hospital-based therapy:

I said will it get better? [physios said] no you've got to start again at zero, what you've forgotten won't come back, you've got to start again and learn it. I can't write I can't read, reading was hard, couldn't read along a line. [I was instructed to] *sit down every morning write letters of alphabet, doesn't matter if gets wrong. Straight on Es fairly easily, curved* [letters] *harder. Sounds stupid now writing b's backwards. Because of COVID there's been no speech* [and language rehabilitation] *so I've had to go without that. and the kids got me 'what the children learn'.* (Participant 37)

respondents demonstrated an acceptance of their visual state

I feel that my vision has just deteriorated as a factor of my life, I'm 87 now and i imaging most people will deteriorate. it's a fact of life that i am elderly (Participant 13)

No treatment I just gotta adapt and make the best of it. (Participant 21)

Though one subject, who following attendance at their habitual optometry provider had a different experience:

It was my son that said i needed to get it [vision] *checked. I had a bit of problems with focus when watching TV for any time and my eyes would water. They* [the optometrist] *said my eye muscles weren't working so I was given special glasses and exercises to keep my vision sharp.* [What types of exercises] *all sorts following a finger, blinking and looking all over. (Participant 17).*

Questioning identified this as being a practice focussing on behavioral optometry, despite these activities having been issued, it appears no follow-up had been undertaken and (shortly before data collection) this practice ceased trading.

Of those participants with a history of stroke, 16 (72.7%) were using an optical appliance routinely, upon inspection 1 of these were found to be unserviceable. The remainder used no ophthalmic appliances for day-to-day activities, with one reporting that they had been advised explicitly by another hospital based health care provider to not use spectacles. Of those control participants, 24 (92.3%) presented with ophthalmic appliances, which upon inspection 1 was unserviceable. The remaining two participants utilised over the counter ready made correction. A summary of habitual refractive parameters and distance refractive measures obtained can be seen in **Table 5-6**. Habitual refractive corrections in the right eye were found to have a mean sphere ranging in power from range -9.00D to +4.88D, J0 ranging from -0.94 to +2.74, and J45 ranging from -1.22D to +1.05D. Left eye habitual corrections had mean sphere ranging from range -11.00D to 4.75D, J0 from -1.25D to +2.95D, and J45 ranging from -1.48D to +0.54D. A high degree of correlation was found between the mean sphere (ICC .986 95%CI .975-.922, F[47,47]=71.445, p<.001) and J0 (ICC .948 95%CI .908-.971, F[47,47]=19.390, p<.001) measures, though no correlation was found for the J45 (ICC -2.567 95%CI -5.362- -.999, F[47,47]=.280, p=1.000) of the right and left eyes. No significant difference in distribution of habitual powers were found between the cohorts for mean sphere, J0 or J45 for either the right (Mann-Whitney-U: [mean sphere] p=.320, [J0] p=536, [J45] p=206) or left (Mann-Whitney-U: [mean sphere] p=725, [J0] p=704, [J45] p=108) eyes.

5.3.2 Ocular health findings

During data collection, no adverse reactions were reported to medications or procedures undertaken.

5.3.2.1 Findings: Trial battery examination

A summary of ocular anomalies identified during the trial battery examination can be seen on **Figure 30**.

Anomalies of the eyelids were prevalent within both test cohorts. Eyelid malposition (ectropion) was observed in two participants from the stroke group and one participant from the control group (Fisher's exact test: p=.587). Conjunctival degeneration (pinguecula) was observed in 3 participants from the stroke group and 2 participants from the control group (Fisher's exact test: p=.649).

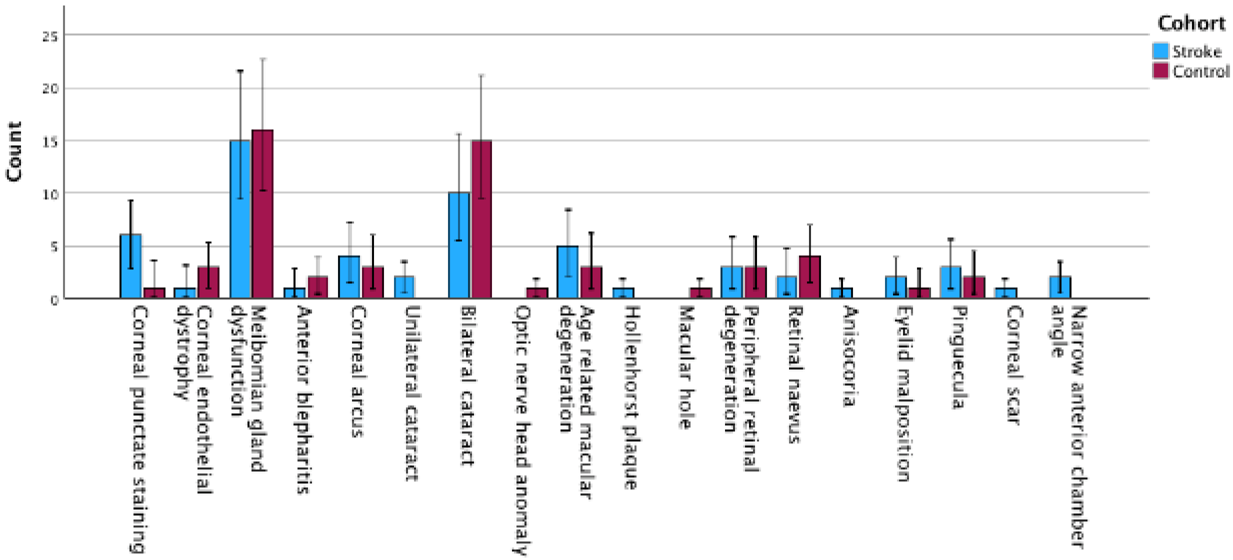


Figure 30. Summary of ophthalmic anomalies identified in participants during the trial battery examination. Error bars represent 95% CI.

Meibomian gland dysfunction was observed in 15 participants from the stroke cohort and 16 participants from the control cohort (Fisher's exact test: p=.765). No significant difference in grading of meibomian gland disease observed between cohorts (Mann-Whitney U test: p=.313) with 11 participants of the stroke cohort and 15 participants of the control cohort exhibiting grade I disease and 4 participants of the stroke and 1 control participant exhibiting grade II disease. Anterior blepharitis was observed in a single participant in the stroke cohort and two participants from the control cohort.

Staining of the ocular surface by fluorescein was observed to occur more frequently within the stroke cohort, with 6 participants from the stroke cohort exhibiting clinically significant ocular surface staining and only one participant from the control cohort (Fisher's exact test: p=.038). The control participant with corneal staining exhibited grade II (Efron et al. 2001; Gomes et al. 2017) in both left and right eyes, while the stroke participant's staining ranged from grade I to III in the right eye (Mann-Whitney U test: p=.012) and grade I to II in the left eye (Mann-Whitney U test: p=.013). Fluorescein break up time was found to have a median of 9 seconds (range 4s to 13s) for the right eye and 7 seconds (range 4s to 17s) for the left eye for the stroke cohort and 9 seconds (range 3s to 15s) for the right eye and 8 seconds (range 4s to 17s) for the left eye of the control cohort. Differences in tear film break up were not found to be significant between cohorts (Mann-Whitney U test: [right] p=.538, [left] p=.143), and between eyes for both cohorts (Wilcoxon signed rank test: z=-.305, p=.760).

Examination of the cornea identified 1 case of corneal dystrophy within the stroke cohort and 3 cases within the control cohort (Fisher's exact test: .614), one participant from the stroke cohort had corneal scarring (Fisher's exact test: p=.458), and corneal arcus was present in 4 participants from the stroke cohort and 3 participants from the control cohort (Fisher's exact test: p=.433).

While no significant difference in the grading of anterior chamber angle was observed between groups (Mann-Whitney-U test: p=.334), anterior chamber angle was found to be narrow in two participants, both from the stroke cohort (Fisher's exact test: p=.205).

Posterior segment examination identified clinically significant cataract in 12 participants of the stroke cohort and 15 participants of the control cohort (Pearson chi-squared: χ^2=.048 df=1 p=.827). Of those participants in the stroke cohort 2 exhibited unilateral cataract, and 10 exhibited bilateral cataract, while all 15 participants exhibiting cataract within the control cohort exhibited bilateral cataract.

No optic nerve anomalies were identified within the stroke cohort while one participant within the control cohort was found to have disc drusen. Cupping was strongly correlated between the eyes of both cohorts (Spearman's rho: r=.952, N=48, p<.001), and no significant difference in optic nerve excavation was identified (Wilcoxon signed rank test: z=-1.363, p=.173) between eyes. Examination of the optic nerves found median cupping of 0.4 (range 0.1 to 0.6) for the right eye and 0.4 (range 0.2 to 0.6) for the left eye of the stroke cohort. Optic nerve excavation of the control group were found to have a median cupping of 0.3 (range 0.1 to 0.65) for the right eye and 0.3 (range 0.1 to 0.65) for the left eye. This difference was not found to be significant for either eye (Mann-Whitney U test: [right] p=.306; [left] p=.173).

Macular examination identified the presence of 5 cases of dry macular degeneration, and one participant with myelinated retinal nerve fibres amongst the stroke cohort, while the control cohort had 3 participants with macular degeneration and one participant with a macular hole. The presence of macular anomalies was not found to be significantly different between the stroke and control groups (Pearson chi-squared test: χ^2: 1.021, df=1, p=.312). One participant from the stroke cohort was observed to have a cholesterol embolus present in the retinal vasculature (**Figure 31**), no other vascular anomalies were observed in either cohort. Examination of the peripheral retina identified the presence of retinal degenerations in 3 participants of the stroke and 2 participants of the control group respectively (Fisher's Exact test: p=.649), Choroidal naevi were observed in 6 participants, two from the stroke and 4 from the control group (Fisher's Exact test: p=.674).

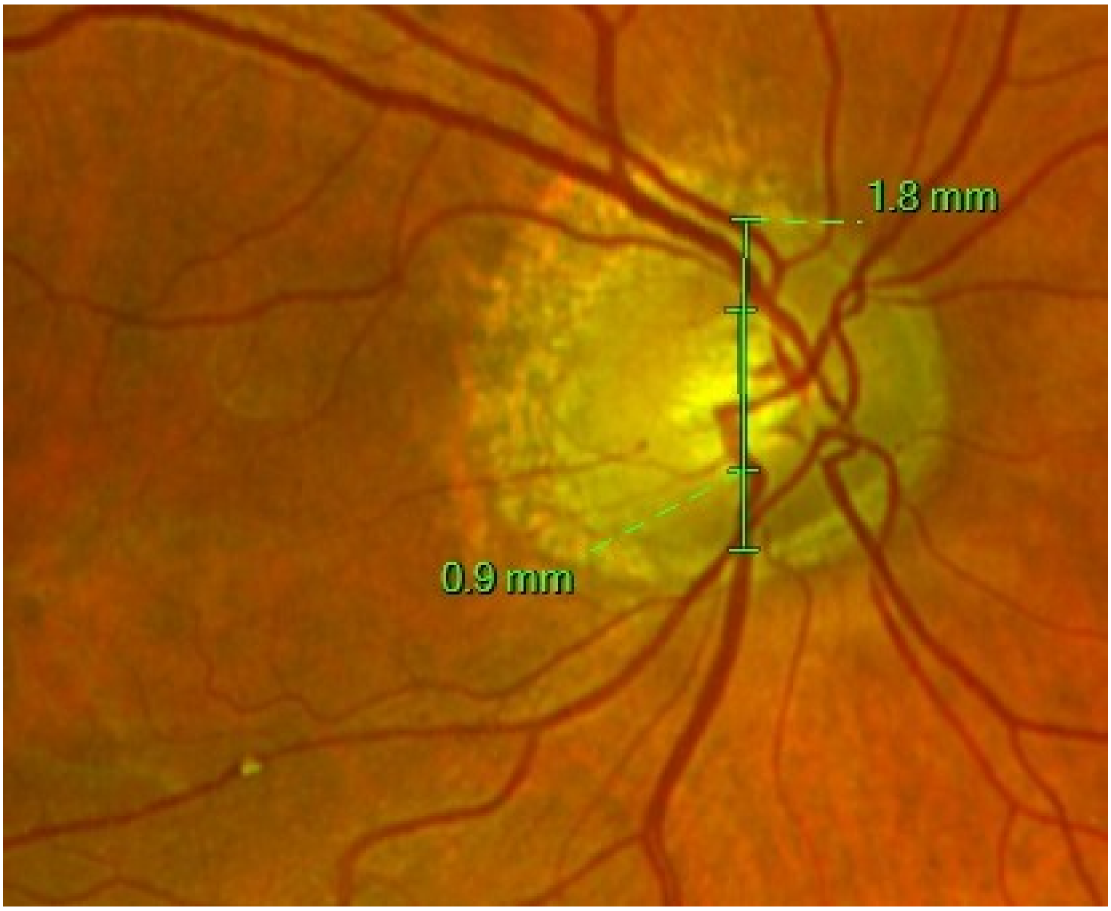


Figure 31. Cholesterol embolus in the right inferior-temporal vascular arcade. These embolism, also known as Hollenhorst plaques serve as biomarkers of carotid artery disease and have been used to identify greater morbidity and mortality from cardiovascular disease (Graff-Radford et al, 2015). These plaques frequently occur secondary to the embolisation of cholesterol from the carotid artery or more rarely the heart or other sources, these then travel through the ipsilateral vasculature frequently lodging in the bifurcation of retinal vessels, as can be seen here (Riese et al, 2021)

All participants were found to exhibit a normal range of intraocular pressure on applanation tonometry. The intraocular pressure measured was strongly correlated (Spearman's rho: r=.864, N=48, p<.001) between eyes, with no significant difference with median pressures (Wilcoxon signed rank test: z=-3.314, p<.001). Median pressure found to measure 14mmHg (range 8mmHg to 21mmHg) and 13mmHg (range 9mmHg to 18mmHg) for the right eyes, and 15mmHg (range 7mmHg to 22mmHg) and 14mmHg (range 9mmHg to 19mmHg) of the left eyes of the stroke and control groups respectively. No significant diff was found between cohorts for right (Mann-Whitney U test: p=.094) or left eyes (Mann-Whitney U test: p=.132).

Pupil diameters were found to be well correlated (r=.960 N=48 p<.001), with no significant difference in median diameter observed in either eye of the stroke or control cohort (Mann-Whitney U test: p=.307). A single participant within the stroke group was found to have anisocoria (Fisher's exact test: p=.447), and no cases of RAPD were observed.

Completion of the trial battery resulted in 5 participants from each cohort being recommended referral for further investigation (Fisher's exact test: p=1.000), for one participant in the stroke cohort, this was following the identification of the retinal vascular plaque, the remainder for assessment for suitability for cataract extraction.

5.3.2.2 Findings: Reference standard examination

In the course of the reference standard examination, detailed anterior segment assessment was undertaken on 42 participants, 18 from the stroke cohort and 24 from the control cohort, For the remainder, no record of anterior segment examination being undertaken had been made.

Ectropion was identified in two participants of the stroke cohort and one participant of the control cohort (Fisher's exact test: p=.587). On the lid margin, meibomian gland dysfunction was found in 5 participants from the stroke cohort and 3 from the control cohort (Fisher's exact test: p=.435), additionally two cases of anterior blepharitis were identified, one from each cohort. Conjunctival anomalies were rarely observed with two cases of pinguecula identified - one within each cohort.

In the course of corneal assessment three cases of corneal dystrophy were identified in the control cohort with no cases in the stroke cohort (Fisher's exact test: p=.247), in addition to this, two cases of corneal scarring were observed, one from each cohort, and two cases of corneal arcus were observed, again one from each cohort. Corneal staining was undertaken on 7 participants, 4 from the stroke cohort, 3 from the control cohort. Of these staining was only present on one participant from each group. Tear break up time was recorded against 1 participant from the stroke cohort, though no record of fluorescein staining was undertaken during this participant's reference standard examination, this case reported a reduced break up time of 9s bilaterally.

Anterior chamber angle was assessed on 44 participants, 20 from the stroke cohort and 24 from the control cohort; while no significant difference in median graded angles was observed between cohorts (Mann-Whitney U test: p=.213), a single participant from the stroke cohort was identified as having a narrow anterior chamber angle (Fisher's exact test: p=.455).

Posterior segment examination was undertaken on all participants. Assessment of the ocular media identified the presence of clinically significant cataract in 13 participants from both the stroke and control cohorts (Pearson chi-square test: χ^2=.397 df=1, p=.529). Of these two participants from the stroke cohort exhibited unilateral cataracts, the remaining 11 participants from the stroke cohort and the participants from the control cohort exhibited bilateral cataracts.

No anomalies of the optic nerve head were identified in either cohort. Optic nerve head cupping was found to be strongly correlated (Spearman's rho: r=.963 N=48, p<.001) between right and left eyes across both cohorts. Median optic nerve cupping was found to be 0.4 (range 0.2-0.6) in the right eye and 0.4 (range 0.2-0.6) in the left eye of both stroke and control cohorts, with no substantial difference in nerve excavation found between stroke and control cohorts for either the right (Mann-Whitney U: p=.441) or left (Mann-Whitney U test: p=.511) eyes.

Macular anomalies were identified in two participants from the stroke cohort and 4 participants from the control cohort (Fisher's exact test: p=.674). Within the stroke cohort one case of dry macular degeneration and one lamellar hole were reported, while the control group reported two participants with dry macular degeneration, 1 participant with macular scarring and a full macular hole. No vascular anomalies were recorded in the eyes of any participants.

Peripheral retinal degeneration was identified in 4 participants from the stroke cohort and 4 participants from the control cohort, additionally a single participant was found to have a choroidal nevus in one eye. Across both groups no difference in retinal anomalies was identified (Pearson's chi-squared: χ^2 =.088 df=1 p=.766).

Non contact tonometry was undertaken on all except one participant from the control group. The median recorded IOP was 13mmHg (range 7mmHg to 21.7mmHg) for the right eye and 14mmHg (range 8mmHg to 21mmHg) for the left eye of the stroke cohort, and 14.3mmHg (range 10mmHg to 21.3mmHg) and 15mmHg (range 10mmHg to 22.7mmHg) for the right and left eyes respectively. Strong correlation was observed between eyes across both groups (Spearman's rho: r=.854, N=46, p<.001). No substantial difference in median distributions were observed between stroke and control groups of either eye (right [Mann-Whitney U test: p=.223], left [Mann-Whitney U test: p=.250]).

Examination of pupil reflexes were undertaken on 38 participants (20 stroke cohort, 18 control cohort). Pupil diameters were not recorded for any participants within the College of Optometrists examination; a single participant from the control cohort was recorded as having anisocoria (Fisher's exact test: p=.474). Marcus gunn testing was undertaken on 28 of these, with a single case of RAPD being recorded in the control cohort.

Following completion of the reference standard examination, 4 participants from the stroke cohort and 5 participants from the control cohort were recommended referral for further investigation (Fisher's exact test: p=1.000), with all instances identifying the reason for referral as further assessment for suitability for cataract surgery.

5.3.3 Refractive findings

5.3.3.1 Findings: Trial battery examination

Objective retinoscopy refraction undertaken during the trial battery examination recorded mean sphere powers ranging from -9.75D to +4.88D, J0 from -0.94D to +3.17D, and J45 -1.15D to +1.62D in the right eye, and mean sphere powers ranging from -11.75D to +6.25D, J0 from -1.25D to +3.45D, and J45 from -1.48D to +0.75D in the left eye. A high degree of correlation was observed between left and right mean sphere (ICC:.982 95%CI .969-.990 $F[47,47]=56.359$, $p<.001$) and J0 of (ICC:.941 95%CI .895-.967 $F[47,47]=17.007$, $p<.001$) though poor correlation was obtained for J45 of (ICC:-3.081 95%CI -6.279- -1.288 $F[47,47]=.245$, $p=1.00$). No significant difference in the distribution of objective refraction results between cohorts was noted for the mean sphere, J0 or J45 powers of the right (Mann-Whitney U test: p=.494, p=.389, p=.245) or left eyes (Mann-Whitney U test: p=.534, p=.525, p=.476).

Subjective refraction during the trial battery found mean sphere powers ranging from -9.50D to +4.88D, J0 powers ranging from -1.00D to +2.74D, and J45 powers ranging from -1.22D to +1.62D in the right eye, and mean sphere powers of -11.23D to +5.25D, J0 ranging from -1.14D to +2.83D, and J45 powers ranging from -1.97D to +0.50D in the left eye. Subjective refraction was also found to have a high degree of correlation between left and right mean sphere (ICC:.985 95%CI .973-.992 $F[47,47]=66.223$, $p<.001$) and J0 of (ICC:.944 95%CI .900-.969 $F[47,47]=17.903$, $p<.001$) and poor correlation for J45 of (ICC:-2.286 95%CI -4.861- -.842 $F[47,47]=.304$, $p=1.00$). Again, no significant difference in the distribution of refractive findings between cohorts was observe for the mean sphere, J0 or J45 for the right (Mann-Whitney U test: p=.612, p=.313, p=.397) or left (Mann-Whitney U test: p=.413, p=.779, p=.121) eyes.

	Right			Left		
	Mean Sphere (D) & IQR(D)	**J0 (D) & IQR (D)**	**J45 (D) & IQR (D)**	**Mean Sphere (D) & IQR(D)**	**J0 (D) & IQR (D)**	**J45 (D) & IQR (D)**
Habitual correction	1.00 & 2.50	0.00 & 0.37	0.00 & 0.19	1.31 & 2.84	0.00 & 0.33	0.00 & 0.17
Retinoscopy	0.44 & 1.69	-0.09 & 0.37	0.00 & 0.13	0.56 & 1.69	0.00 & 0.33	0.00 & 0.16
Subjective refraction - trial examination	0.38 & 1.44	-0.12 & 0.37	0.00 & 0.29	0.25 & 1.59	-0.13 & 0.30	0.04 & 0.27
Subjective refraction - reference standard examination	0.25 & 1.44	-0.09 & 0.37	0.00 & 0.19	0.25 & 1.44	-0.02 & 0.35	0.00 & 0.24

Table 5-6. Summary of parameters & interquartile ranges of refractive measures presented in vector form measured for distance refractive requirements during the course of trial battery examination and reference standard examination.

Near reading addition was found to range from +0.00D to +2.75D (median +2.25D), with no uneven reading additions issued in either cohort. No significant difference in reading addition power was identified between cohorts (Mann-Whitney U test: p=.787).

Following completion of the trial battery refraction, 10 participants with a history of stroke, and 17 control participants were found to have a stable refraction, with 12 participants with a history of stroke and 9 controls requiring either an updated or replacement correction. These results were found to be independent of stroke history of stroke (Pearson Chi-Squared test: χ^2 (1, N=48)=1.923, p=.165), as well as gender (Pearson Chi-Squared test: χ^2 (1, N=48)=.085, p-.771).

5.3.3.2 Findings: Reference standard examination

During the course of the reference standard examination, objective refraction was not undertaken by any practitioner. Subjective examination found refractive powers ranging from -9.38D to +5.00D for the mean sphere, -2.63D to +3.63D for J0, and -1.17D to +1.48D for J45 in the right eye, and -10.75D to +5.00D for mean sphere, -1.25D to +2.95D for J0 and -1.97D to +0.62D in the J45 for the left eye. Once again a high degree of correlation between left and right mean sphere (ICC:.978 95%CI .961-.988 F[47,47]=44.685, p<.001), J0 (ICC:.921 95%CI .859-.955 F[47,47]=12.656, p<.001), and poor correlation for J45 (ICC:-2.701 95%CI -5.988- -1.012 F[47,47]=.283, p=1.00). As was found in the trial battery, no significant difference were observed in the results of the parameters of the right (Mann-Whitney U test: [mean sphere] p=.097, [J0] p=.807, [J45] p=.305) or left (Mann-Whitney U test: [mean sphere] p=.594, [J0] p=.067, [J45] p=0.082) eyes .

Near reading addition was found to range from +0.00D to +2.75D (median +2.25D), no significant difference was identified between stroke and control groups (Mann-Whitney U test: p=.441), no uneven reading additions were issued in either the stroke or control group following refraction in the College of Optometrists examination.

Upon completion of refraction in the College of Optometrists based examination, 13 participants with a history of stroke and 17 controls were found to have stable refractive findings to their habitual correction, while 9 participants from each cohort were found to require updated or replacement correction. Similar to the trial battery examination, refractive outcome was found to be independent of history of stroke (Pearson chi-squared test: χ^2 =.201, df=1, p=.654) and gender (Pearson chi-squared test: χ^2=1.422, df=1, p=.223).

5.3.4 Visual findings

Visual outcomes were assessed as part of both the trial battery examination (**Table 5-7**) as well as the reference standard examination (**Table 5-8**).

5.3.4.1 Findings: Trial battery examination

During the trial examination, good correlation was observed in the vision measured between eyes (ICC .935 95%CI .883-.963, F[47,47]=15.311, p<.001), with no significant difference found between the unaided visions of the right and left eyes (Wilcoxon signed rank test: z=-.257 , p=.797). No significant difference in unaided acuity was observed between cohorts for either right (Mann-Whitney U test: p = 0.590) or left eyes (Mann-Whitney U test: p=.195).

Similarly good correlation was observed in the findings of unaided near vision between eyes (ICC .880 95%CI .766-.939 F[47,47]=8.367, p<.001), once more no significant differences in acuity were found between eyes (paired-t test: t=-1.265, df=45, p=.212) and no difference was found between cohorts for the unaided near vision of both right (unpaired-t test: t=1.664, df=37.870, p=.104) and left eyes (unpaired-t test: t=.737, df=33.423, p=.466).

	Stroke cohort			Control cohort		
	Median	Range	IQR	Median	Range	IQR
Unaided distance vision - right eye	0.31	0.02 to 0.72	0.68	0.31	-0.10 to 1.20	0.57
Unaided distance vision - left eye	0.34	0.00 to 0.60	0.38	0.34	-0.10 to 1.20	0.51
Habitual distance vision - right eye	0.26	0.00 to 0.72	0.68	0.16	-0.10 to 0.42	0.24
Habitual distance vision - left eye	0.16	0.00 to 0.60	0.40	0.20	-0.10 to 0.42	0.29
Habitual near vision right eye	0.15	0.00 to 0.80	0.60	0.12	0.06 to 0.54	0.46
Habitual near vision - left eye	0.12	0.00 to 0.72	0.32	0.13	0.04 to 0.52	0.18
Visual acuity - right eye	0.14	-0.08 to 0.26	0.16	0.10	-0.10 to 0.36	0.31
Visual acuity - left eye	0.03	-0.08 to 0.22	0.18	0.10	-0.10 to 0.32	0.26
Near visual acuity - right eye	0.12	0.00 to 0.28	0.12	0.09	0.00 to 0.32	0.26
Near visual acuity - left eye	0.09	0.00 to 0.26	0.14	0.12	0.00 to 0.28	0.21

Table 5-7. Data of the median, range and interquartile range for vision (LogMAR) findings from the trial examination.

Habitual distance acuity between eyes was found to have moderate association (Spearman's rho: r=.579, N=48, p<.001), and no significant difference was found between eyes (Wilcoxon signed rank test: z=-.350, p=.726). No significant difference was found between cohorts for either the right (Mann-Whitney U test: p=.262) or left (Mann-Whitney U test: p=451) eyes. Near habitual acuity had strong inter-eye association (Spearman's rho: r .776, N=46, p<.001) with no significant difference between eyes (Wilcoxon signed rank test:z=-1.181, p=.237), and no difference observed in acuity between cohorts for either eye (Mann-Whitney U test: [right eye] p=.917, [left eye] p=.349).

	Stroke cohort			Control cohort		
	Median	Range	IQR	Median	Range	IQR
Habitual distance vision - right eye	+0.20	-0.10 to +0.70	0.38	+0.10	-0.08 to +0.30	0.24
Habitual distance vision - left eye	+0.20	-0.10 to +0.60	0.22	+0.06	0.00 to +0.24	0.17
Habitual near vision right eye	N6	N5 to N14	9	N6	N5 to N14	3
Habitual near vision - left eye	N6	N5 to N18	3	N5	N5 to N6	1
Visual acuity - right eye	+0.10	-0.08 to +0.50	0.20	+0.02	-0.10 to +0.20	0.26
Visual acuity - left eye	+0.10	-0.10 to +0.26	0.22	0.00	0.00 to +0.22	0.11
Near visual acuity - right eye	N5	N5 to N14	1	N5	N5 to N8	0.5
Near visual acuity - left eye	N5	N5 to N14	0	N5	N5 to N6	0

Table 5-8. Data of median acuity and range found during the course of the reference test. Note that parameters found during the course reference examination were measured using the near test charts scaled in accordance with the Royal College of Ophthalmologists near point chart.

Best corrected visual acuity was found to have moderate correlation between eyes (ICC [distance] .566 95%CI .225-.757 F[47,47]=2.302, p=.003, [near] .586 95%CI .252-.771 F[45,45]=2.415, p=.002), with no significant difference in means between eyes for distance (paired T-test: t=-.897, df=47, p=.354) and near (paired T-test: t=-1.299, df=45, p=.200). As found for previous measures, no differences in corrected acuity were observed between cohorts at distance (unpaired T-test: [right eyes] t=.089, df=46, p=.930, [left eyes] t=-2.037, df=46, p=.047) or near (unpaired T-test: [right eyes] t=-.259, df=46, p=.797, [left eyes] t=-.339, df=44, p=.737).

Amsler assessment was undertaken on all participants as part of the trial battery examination, no anomalies were identified for any participant. Field screening was undertaken on 46 (95.8%) participants following completion of the trial examination battery. Two participants from the stroke cohort were unable to complete the field assessment due to fatigue. Field defect was identified in 7 participants from the stroke cohort and 2 participants from the control cohort (Fisher's exact test: p=.056); detail of these fields can be seen on **Table 5-9**.

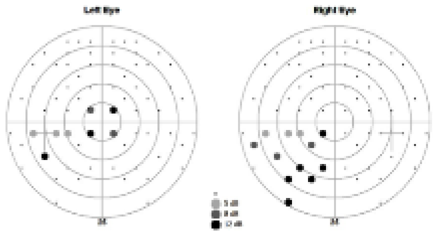
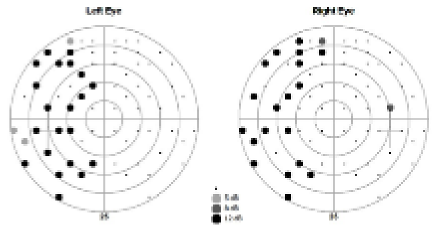
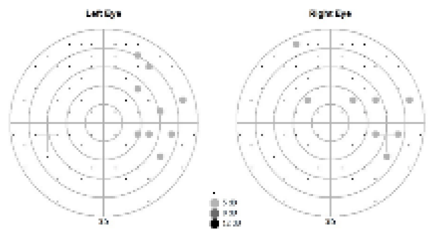
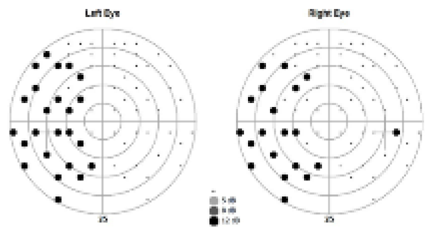
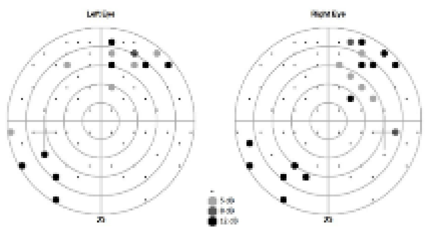
5.3.4.2 Findings: Reference standard examination

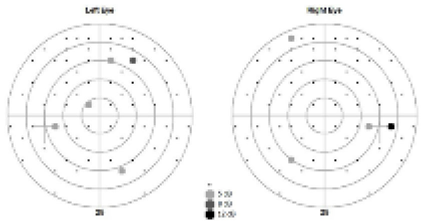
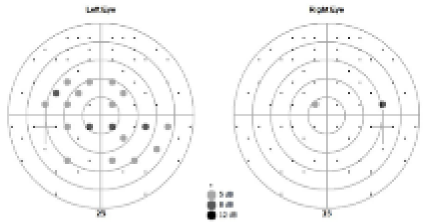
Acuity measured in the reference standard examination exhibited similar findings, habitual acuity was moderately correlated for distance (ICC .693 95%CI .442-.831, F[44,44]=3.261, p<.001) and near (Spearman's rho: r=.569 N=33, p<.001) vision measurements, with no significant differences between eyes at distance (paired T-test: t=-.565, df=44, p=.575) or near (Wilcoxon signed rank test: z=-1.775, p=.076). As was found in the measurements of acuity during the trial examination, no significant difference in acuity was obtained between cohorts for either eye at distance (unpaired T-test: [right] t=2.301, df=43, p=.048, [left] t=.503, df=43, p=.617) or near (Mann-Whitney U test: [right] p=.630, [left] p=.202).

Moderate correlation was found between the best corrected acuities of each eye at distance (Spearman's rho: r=.563, N=46 p<.001) and near (Spearman's rho: r=.459, N=44, p=.002); as found during the trial battery, no substantial difference was found in the best corrected visual acuity measured between eyes for either distance (Wilcoxon signed rank test: z=-.238, p=.812) or near (Wilcoxon signed rank test: z=-.225, p=.822) acuity. Review of the acuity measured between cohorts found no significant difference in either distance (Mann-Whitney U test: [right] p=.399, [left] p=.806) or near (Mann-Whitney U test: [right] p=.178, [left] p=.885) acuity between the stroke or control cohorts.

During the reference standard examination, clinicians undertook automated field screening on 25 participants (52%), 13 from the stroke cohort and 12 from the control cohort. Field defect was identified in 5 participants from the stroke cohort, while a defect was only present in 1 participant from the control cohort (Fisher's exact test: p=.097).

Table 5-9. Automated field plots of field loss identified in participants. Homonymous defects such as those seen with participants 8, 10 & 21 are typical defects observed post stroke **Figure 1**. Participant 22 exhibits an unusual "hourglass" type defect, which has been reported to emerge from lesions to the lateral geniculate nucleous (Luco et al, 1992; Donahue et al, 1995).

Participant	Field loss observed
Participant 7 (stroke cohort): Loss paracentral to fixaiton in both eyes.	
Participant 8 (stroke cohort): Left sided quadrantonopic field loss	
Participant 10 (stroke cohort): Left sided homonymous field loss with macular sparing	
Participant 15 (stroke cohort): Right sided homonymous relative scotoma.	
Participant 20 (stroke cohort): Extended blind spot and relative loss suggestive of early nasal step defect.	
Participant 21 (stroke cohort): Left sided homonymous field loss with macular sparing	
Participant 22 (stroke cohort): An unusual congruent "hourglass" type field defect.	

Participant 37 (control cohort): **Right eye: scattered points of relative loss** **Left eye: extended blind spot**	
Participant 48 (control cohort): **Right eye: expanded blind spot** **Left eye: central relative scotoma, consistent with left strabismic amblyopia present.**	

5.3.5 Binocular vision findings

Tests of the binocular vision system were undertaken for all participants within the trial examination and 43 (89.6%) of the reference standard examinations, a summary of frequency of tests can be seen on **Table 5-10**.

5.3.5.1 Findings: Trial battery examination

A summary of the binocular vision associated findings from the trial battery examination can be seen in **Table 5-11**. Within the trial battery examination, no significant difference in distribution was observed for distance cover test results between cohorts (Mann Whitney-U test: p=.508) or controlling for gender (Mann Whitney-U test: p=.172). Clinically significant heterophoria, falling out with the normal range of 1^{Δ} exophoria +/-1.96 standard deviations (Goss 1995), was observed in 4 participants, 2 from each cohort (Fisher's exact test: p=1.000). There was also no significant difference in the distribution of findings for near oculomotor assessment when controlling for gender (Mann Whitney-U test: p=.175) or cohort (Mann Whitney-U test: p=.474). Clinically significant near heterophoria falling out with 2.08^{Δ} exophoria +- 1.96 standard deviations (Freier and Pickwell 1983) was observed in two participants, one from each cohort (Fisher's exact test: p=1.000). Distance and near heterophoria were found to be moderately associated (Spearman's rho: r=.427, N=42, p=.005) with one another. Vertical oculomotor deviation was present in two male participants (Fisher's exact test: p=.490), 1 within each cohort (Fisher's exact test: p=1.000).

Near convergence range was found to not be substantially different between genders (Mann Whitney-U test: p=.285) or cohorts (Mann Whitney-U test: p=.203), with remote near points of convergence (>10cm) being found in 16 participants from the stroke cohort and 12 participants from the control cohort (Fisher's exact test: p=.347), no difference in gender was observed (Fisher's exact test: p=1.000). No significant correlation was observed between NPC and near heterophoria (Spearman's rho: r=-.047, N=41, p=.768).

	Trial battery examination	Reference standard examination
Distance cover test	48 (100%)	39 (81.3%)
Near cover test	48 (100%)	38 (79.1%)
Ocular Motility	48 (100%)	39 (81.3%)
Near point of convergence	43* (100%)	27 (56.3%)

Table 5-10. Frequency of binocular vision testing within trial battery and reference standard examinations. *near point of convergence testing was not undertaken on participants with strabismus in the trial battery examination. Within the reference standard examination, when strabismic were removed NPC testing was completed on 62.7% of participants.

Strabismus was present in 3 control participants and 1 stroke cohort participants (Fisher's exact test: p=.614), of those with strabismus three female (Fisher's exact test: p=.609). Incomitant deviations were observed within 3 participants from the stroke cohort, and no members of the control cohort (Fisher's exact test: p=.089), of these 2 were female (Fisher's exact test: p=1.000).

	Stroke cohort		Control cohort	
	Median	Range	Median	Range
Distance cover test	orthophoria	12^{Δ}esophoria-15^{Δ}exophoria	orthophoria	3^{Δ}esophoria-5^{Δ}exophoria
Near cover test	3^{Δ}exophoria	6^{Δ}esophoria-15^{Δ}exophoria	3^{Δ}exophoria	3^{Δ}esophoria-9^{Δ}exophoria
Near point of convergence	12cm	nose-25cm	11cm	nose-19cm

Table 5-11. Median oculomotor findings and range obtained during the trial battery examination. *where strabismus was present the degree of this was not counted in the measure of heterophoria.

Following completion of the binocular vision elements of the examination, 16 participants from the stroke cohort, and 18 participants from the control cohort were identified as having a binocular vision anomaly. No significant difference was observed between the rates of binocular anomalies identified between groups (Fisher's exact test: p=1.000) or genders (Fisher's exact test: p=1.000).

5.3.5.2 Findings: Reference standard examination

A summary of binocular vision associated findings from the reference standard examination can be seen in **Table 5-12**. Measures of aligning prism was not undertaken on any participants as part of the reference standard examination. No significant difference was observed for distance cover test results between cohorts (Mann Whitney-U test: p=.749) or gender (Mann Whitney-U test: p=.708). 7 participants were found to have distance heterophoria outside the normal range, 3 from the stroke cohort and 4 from the control cohort (Fisher’s exact test: p=1.000). No significant difference was also found for near oculomotor findings controlling for gender (Mann Whitney-U test: p=.583) and cohort (Mann Whitney-U test: p=.354). 5 participants were found to have near heterophoria exceeding the normal range, 1 from the stroke cohort and 4 from the control cohort (Fisher’s exact test: p=.357).

	Stroke cohort		Control cohort	
	Median	Range	Median	Range
Distance cover test	orthophoria	4^{Δ}esophoria-15^{Δ}exophoria	orthophoria	orthophoria-2^{Δ}exophoria
Near cover test	orthophoria	2^{Δ}esophoria-15^{Δ}exophoria	orthophoria	orthophoria-4^{Δ}exophoria
Near point of convergence	10cm	nose-25cm	9cm	nose-15cm

Table 5-12. Median oculomotor findings and range obtained during the reference standard examination. *where strabismus was present the degree of this was not counted in the measure of heterophoria.

The measures of distance and near cover test results were found to be strongly associated (Spearman’s rho: r=.597, N=26, p=.001). Vertical oculomotor deviation was present in two male participants (Fisher’s exact test: p=.488), with 1 within each cohort (Fisher’s exact test: p=1.000). Near convergence range was found to not be substantially different between genders (Mann Whitney-U test: p=.792) or cohorts (Mann Whitney-U test: p=.286), and near point of convergence was poorly correlated with near heterophoria (Spearman’s rho: r=.173, N=27, p=.387). Remote near points of convergence were found in 8 participants from the stroke cohort and 1 participant from the control cohort (Fisher’s exact test: p=.0.098), no difference in gender was observed (Fisher’s exact test: p=.683). Strabismus was identified in 4 control participants, no cases of strabismus were identified in the stroke cohort (Fisher’s exact test: p=.114), of those with strabismus three female (Fisher’s exact test: p=.609). Incomitant deviations were observed within 2 participants, one each from the stroke and control cohort (Fisher’s exact test: p=1.000), of these 1 was female (Fisher’s exact test: p=1.000). Following completion of the binocular vision elements of the examination, 10 participants from the stroke cohort and 4 participants from the control cohort were identified as having a binocular vision anomaly. This difference was found to be significant between groups (Fisher's exact test: p=.029) though it was not found to be the case between genders (Fisher's exact test: p=0.752).

5.3.6 Comparison of findings of trial battery and reference standard examination

A summary of the agreement found for key findings between the trial battery and reference standard can be seen in **Table 5-13**.

		k	p
Ocular Health	Anomaly of adnexa or ocular surface	-.015	.813
	Corneal anomaly	.649	<.001
	Anomaly of ocular media	.621	<.001
	Optic nerve anomaly	-	-
	Central retinal anomaly	.556	<.001
	Peripheral retinal anomaly	.009	.948
Refractive outcome	Change in ocular refraction required	.441	.002
Vision	Visual acuity range - right eye	.321	.023
	Visual acuity range - left eye	.355	.006
	Visual field anomaly	.500	<.001
Binocular vision	Significant heterophoria - distance	.534	<.001
	Significant heterophoria - near	.476	.002
	Remote near point of convergence	.169	.092
	Incomitant deviation	-	-
	Strabismus	.727	<.001
Referral	Need for onward referral	.672	<.001

Table 5-13. Summary of agreement (Cohen’s kappa) between the trial battery and reference standard examination for anomalies identified in the course of these examinations. It should be noted that across a number of areas agreement has likely been impacted by the absence of testing (eg absence of detailed anterior segment assessment undertaken in the reference standard assessment [**5.3.2.2**], differences in frequency of binocular vision tests [**Table 5-10**], and absence of field testing outlined by the test battery [**Table 5-2**]), as such caution should be exercised when interpreting these, as discrepancies may reflect differences in recording rather than true clinical disagreement.

5.3.6.1 Ocular Health findings

Between the trial examination and the reference standard test, poor correlation was observed when assessing adnexal & conjunctival anomalies; a summary of the differences observed between tests can be seen on **Table 5-14**. Examination of the tear film and ocular surface with the trial battery identified greater incidence of ocular surface issues than the reference standard. The presence of Meibomian gland dysfunction was found more frequently in the trial examination (McNemar test: p<.001), additionally the more frequent use of ocular surface staining with sodium fluorescein identified more cases of ocular surface anomalies including those of greater severity.

	Trial battery			Reference standard		
	Prevalence of anomaly - stroke cohort (%)	Prevalence of Anomaly - control cohort (%)	Relative risk stroke vs control	Prevalence of anomaly - stroke cohort (%)	Prevalence of Anomaly - control cohort (%)	Relative risk stroke vs control
Ectropion	9.1	3.8	2.58	9.1	3.8	2.58
Anterior blepharitis	4.5	7.7	0.58	5	4	1.25
Meibomian gland dysfunction	68.2	61.5	1.11	25	12	2.08
TBUT <10s	70	67.3	1.04	5	-	-
Pinguecula	13.6	7.7	1.76	4.8	4	1.2
Superficial epithelial staining	27.3	3.8	7.18	14.3	14.3	1
Corneal endothelial dystrophy	4.5	11.5	0.39	0	12.5	-
Corneal arcus	21.1	11.5	1.83	5.3	4	1.33
Corneal scar	4.5	0	-	5	0	-
Clinically significant cataract	54.6	57.7	0.94	59	50	1.18
Optic nerve anomalies	0	3.8	-	-	-	-
Dry age related macular degeneration	18.2	15.4	1.18	4.5	7.7	0.58
Macular hole	3.8	4.2	0.90	4.5	3.8	1.18
Macular scar	-	-	-	0	3.8	-
Peripheral retinal degeneration	18.1	14.4	1.25	22.7	15.4	1.47
Choroidal naevus	9.1	15.4	0.59	0	3.8	-
Anisocoria	4.8	0	-	0	5.6	-
Afferent pupillary defect	0	0	-	0	7.1	-
Elevated intraocular pressure	0	0	-	0	4	-

Table 5-14. Prevalence and relative risk of ocular anomalies from the stroke cohort compared to the control cohort identified in the trial battery and reference standard examinations.

To investigate further the factors influencing the presence of epithelial punctate staining a series of Kruskal-Wallis tests were undertaken. The presence of ectropion was observed to have an effect on the degree of staining observed in the right eye (Kruskal-Wallis H test: χ^2 =47.000, df=3, p<.001). Post hoc comparison found a mean rank difference between no staining and grade II in the presence of ectropion (Mann-Whitney U test: p<.001), no significant difference was found in the presence of ectropion between cases of no staining and grade I staining (Mann-Whitney U test: p=1.000), no staining and grade III staining (Mann-Whitney U test: p=1.000), grade I and grade II staining (Mann-Whitney U test: p=.057), grade I and grade III staining (Mann-Whitney U test: p=1.000) or grade II and grade III staining (Mann-Whitney U test: p=.500). No significant influence was found on the grade of corneal epithelial staining was found from tear film break up time (Kruskal-Wallis H test: χ^2 =7.465, df=3, p=.058), the presence of meibomian gland dysfunction (Kruskal-Wallis H test: χ^2 =5.016, df=3, p=.171), anterior blepharitis (Kruskal-Wallis H test: χ^2=.627, df=3, p=.890), or pinguecula (Kruskal-Wallis H test: χ^2 =1.355, df=3, p=.716).

For the left eye both the presence of ectropion (Kruskal-Wallis H test: χ^2 =34.467, df=3, p<.001) and reduced tear film break up time (Kruskal-Wallis H test: χ^2 =9.707, df=3, p=.008) had an effect on the presence of staining. Post hoc analysis found a mean rank difference between no staining and grade II staining in the presence of ectropion (Mann-Whitney U test: p=.011) and tear break up time (Mann-Whitney U test: p=.026), as well as no staining and grade I staining with tear break up time (Mann-Whitney U test: p=.014). No significant difference was observed for either variable for grade I and grade II staining (Mann-Whitney U test [ectropion]: p=.857, Mann-Whitney U test [fluorescein break up time]: p=.114). No significant influence on the degree of corneal epithelial staining was found in the presence of meibomian gland dysfunction (Kruskal-Wallis H test: χ^2 =2.793, df=3, p.247), anterior blepharitis (Kruskal-Wallis H test: χ^2 =.627, df=3, p=.731) or the presence of pinguecula (Kruskal-Wallis H test: χ^2 =1.355, df=3, p=.508).

The identification of the presence of corneal anomalies were found to have substantial agreement, with no significant difference found between examinations in the frequency of identification of corneal endothelial dystrophies (McNemar test: p=1.000, n=39), corneal arcus (McNemar test: p=.125, n=42), or scarring (McNemar test: p=1.000, n=42) noted.

No significant difference in the observation of narrow angles was observed (McNemar test: p=1.000, n=22), Anterior chamber angle grading was not significantly different for those assessed between the trial and reference standard examinations (Wilcoxon signed rank test: z=-.426, p=.670).

Substantial agreement was found for the presence of clinically significant cataract between examinations, while this was more frequently reported in the trial examination, this difference was not found to be significant (McNemar test: p=1.000, n=38).

The presence of optic nerve drusen in one participant was noted in the trial examination but not observed during the reference standard test, no other optic nerve anomalies were identified between groups. No significant difference in optic nerve cup to disc measurements were noted between the reference standard and trial examination for the right eye (Wilcoxon signed rank test: z-.564, p=.573) or left eye (Wilcoxon signed rank test: z=-1.312, p=.189). **Figure 32** outlines the difference plot (Bland and Altman, 1986; 1999) of optic nerve cupping between the trial and reference standard examination.

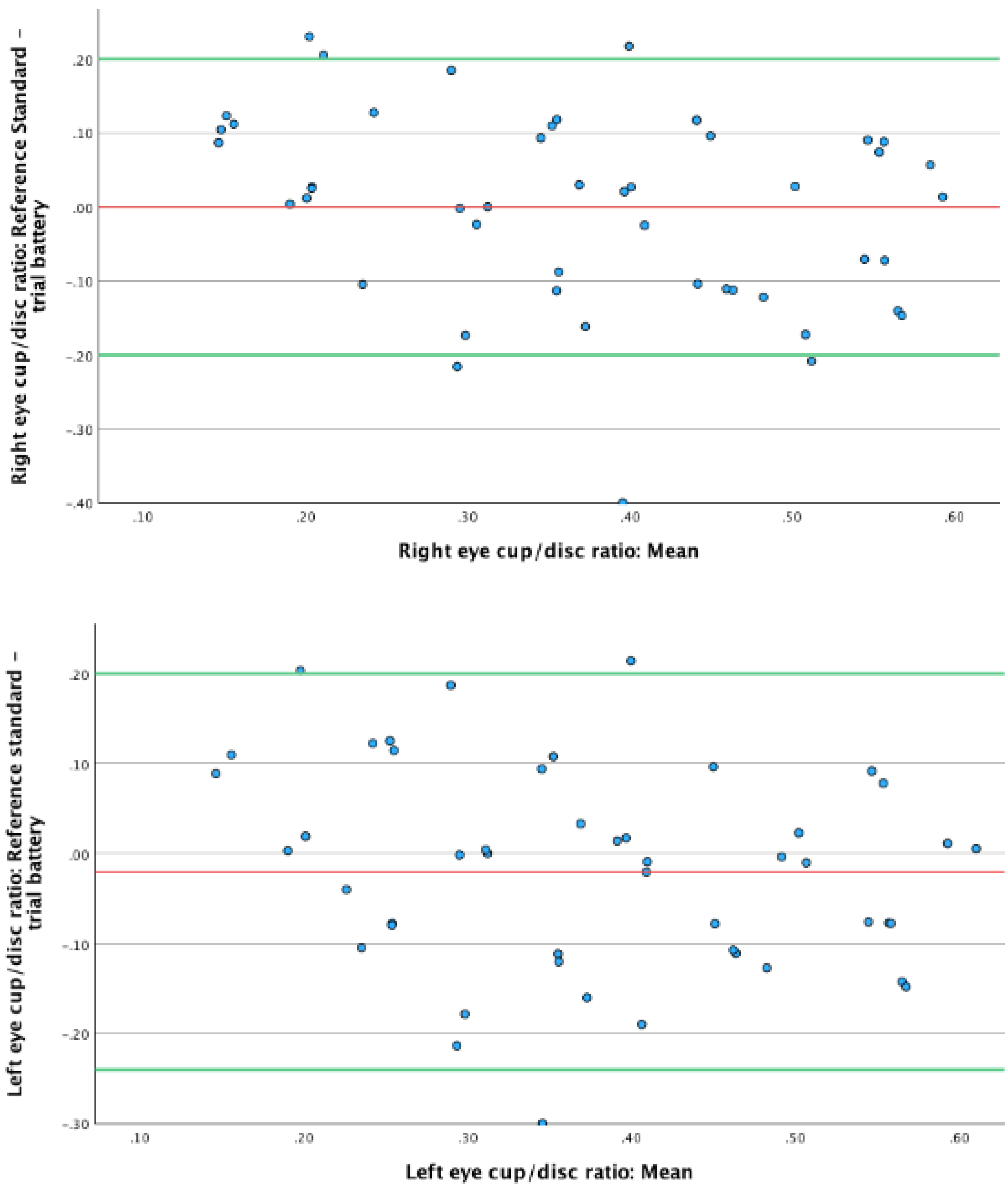


Figure 32. Difference plot of differences in vertical optic nerve cupping for right & left eyes recorded between the trial battery and reference standard examinations. For the right eye the mean difference was negligible (Median: 0), with 90% of differences in observed measured values ranging from -0.20 to 0.20, Similarly in the left eye a negligible difference (Mean:-0.02) was found with limits of agreement ranging from -0.24 to 0.20 (95%CI 0.004).

Assessment of the central retina exhibited moderate agreement between tests. While macular anomalies were more frequently identified during the trial examination, the difference in frequency was not found to be significant (McNemar test: p=.219). Similarly the identification of peripheral retinal anomalies exhibited poor agreement between examination protocols, though this was not found to be significant (McNemar test: p=.481). A single participant was observed to have elevated intraocular pressure during the reference standard test, though this was found to be within normal range during the trial examination. No significant difference in IOPs were observed between tests (Wilcoxon signed rank test: [right] z=-.893, p=.372, [left] z=-.008, p=.994).

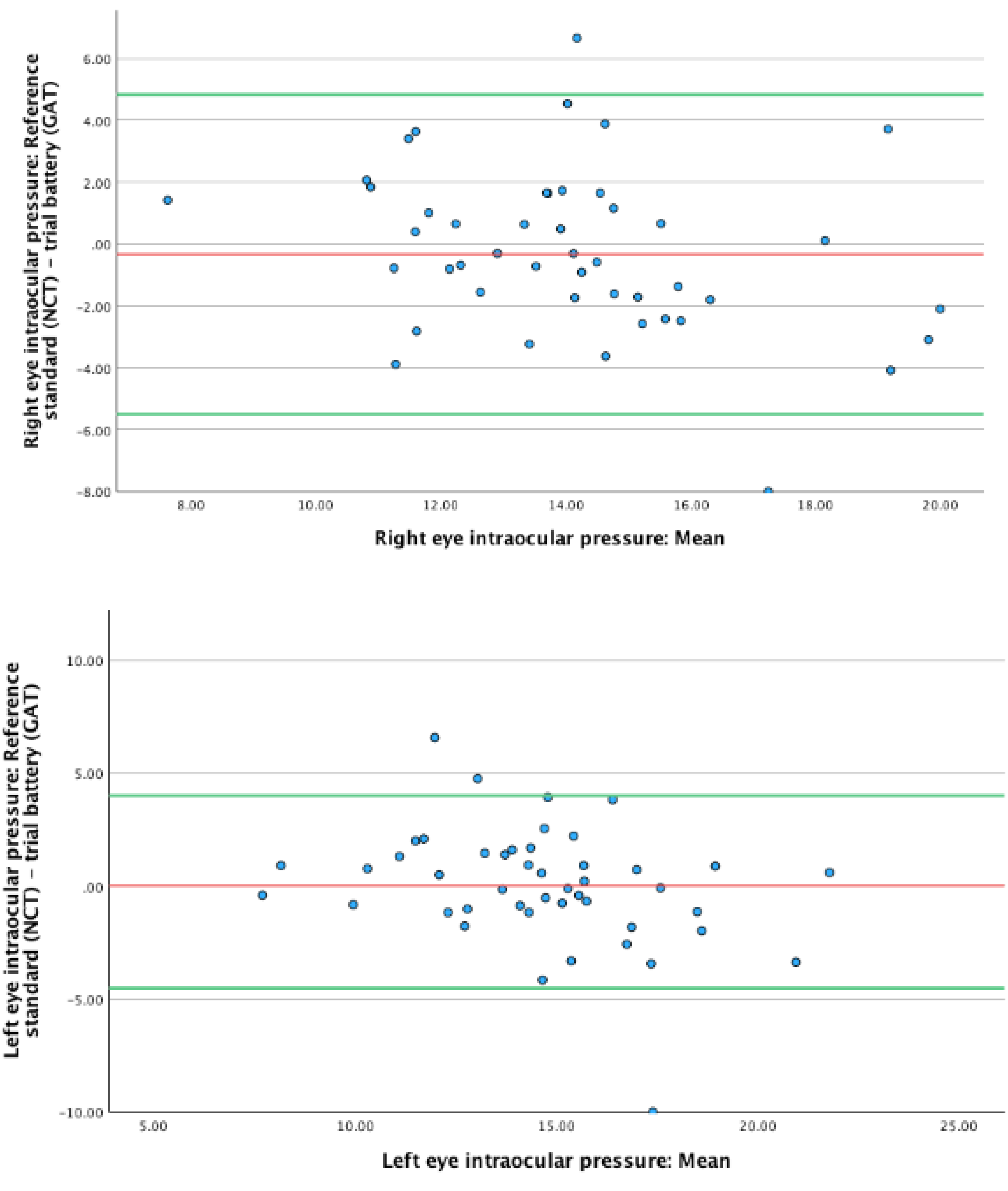


Figure 33. Difference plot of intraocular pressure measurements taken between the trial battery examination (by applanation tonometry) and reference standard examination (using non-contact tonometry). Applanation tonometry was found to provide a slightly lower measure of pressure (Mean: -0.337mmHg) compared to non-contact methods with limits of agreement of -5.50 to 4.83mmHg (95%CI 0.099). No significant difference was observed in the left eye, where pressure was again slightly lower (Median: 0) with 90% of the differences in observed measurement values falling between -4.55 and +4.00mmHg.

Figure 33 outlines the differences observed for the right eye between intraocular pressure measurements by applanation tonometry during the trial examination with non-contact tonometry measured during the reference standard assessment.

No significant difference in the rate of recommendation for onward referral for further investigation were identified between the trial and reference standard examinations (Wilcoxon signed rank test: z=.000, p=1.000), an overview of referrals can be found on **Table 5-15**.

Participant	Outcome Reference Standard Exam	Outcome: Trial battery	Comment
2	-	Referral (Routine)	Moderate unilateral cataract – extraction for improved vision. VA still within DVLA minimum requirements
4	Referral (Routine)	Referral (Routine)	Moderate bilateral cataract R>L.
7	-	Referral (Urgent)	Incidental observation of Hollenhorst plaque within retinal circulation. Risk factor for further neurological events. Onward referral imperative to reduce risk of further neurological injury.
15	Referral (Routine)	Referral (Routine)	Early lenticular opacities R&L but referred as coexistent macular pathology.
17	Referral (Routine)	Referral (Routine)	Moderate cataract impairing acuity
20	Referral (Routine)	-	Referred for unilateral cataract. Monocular pseudophakia, BVCA good bilaterally and anisometropia <1.00DS
28	Referral (Routine)	Referral (Routine)	Moderate lenticular opacities impacting on day-to-day vision – driver (vision >6/12)
30	Referral (Routine)	Referral (Routine)	Moderate cortical opacities L>R
32	-	Referral (Routine)	Moderate lenticular opacities with coexisting AMD, meeting DVLA requirements habitually – referred for improved acuity.
36	Referral (Routine)	Referral (Routine)	Moderate mixed cataracts – impaired acuity, meeting DVLA requirements
43	Referral (Routine)	-	Referred for Left cataract in reference standard. In trial battery exam minimal cataract observed, but notable geographic atrophy at macula
46	Referral (Routine)	Referral (Routine)	Moderate bilateral lenticular opacities

Table 5-15: Examination outcomes for participants referred following examinations. Similar outcomes were observed between examination outcomes. Three cases can be observed where one examination resulted in a referral while the other did not. Participants 2 and 43 were referred for cataract surgery for visual improvement. In both instances one eye had good acuity while the other had reduced acuity. In the latter case some discrepancy is observed as the clinician undertaking the trial battery opted against the decision to refer in the presence of advanced dry AMD. Participant 7's referral while serious, identifying the presence of an arteriolar emboli resulting in urgent onward referral, was ultimately incidental. It is possible that had the test been done on another day that no anomaly would have been observed.

5.3.6.2 Refractive findings

The findings of the subjective refraction undertaken in the trial battery assessment and the reference standard assessment exhibited good agreement. A high degree of agreement was observed for the results of the mean sphere (ICC .998 [95%CI .996-.999], $F[47,47]=424.454$, $p<.001$), J0(ICC .985 [95%CI .973-.992], $F[47,47]=66.184$, $p<.001$) and J45 (ICC .976 [95%CI .957-.987], $F[47,47]=41.588$, $p<.001$) of the right eyes. Similarly the results of subjective refraction of the left eyes exhibited good agreement between tests across mean sphere (ICC .998 [95%CI .996-.999], $F[47,47]=475.597$, $p<.001$), J0 (ICC .988 [95%CI .979-.993], $F[47,47]=84.432$, $p<.001$) and J45 (ICC .977 [95%CI .959-.987], $F[47,47]=43.736$, $p<.001$). **Figure 34** shows the difference plot for the mean sphere, J0 and J45 of both right and left eyes.

A high degree of correlation was observed in the findings of near addition (ICC .941 95%CI .895-.967, $F[47,47]=16.940$, $p<.001$) between examinations, with no significant difference in distribution of near addition power was identified (Wilcoxon signed rank test: $z=1.117$, $p=.264$).

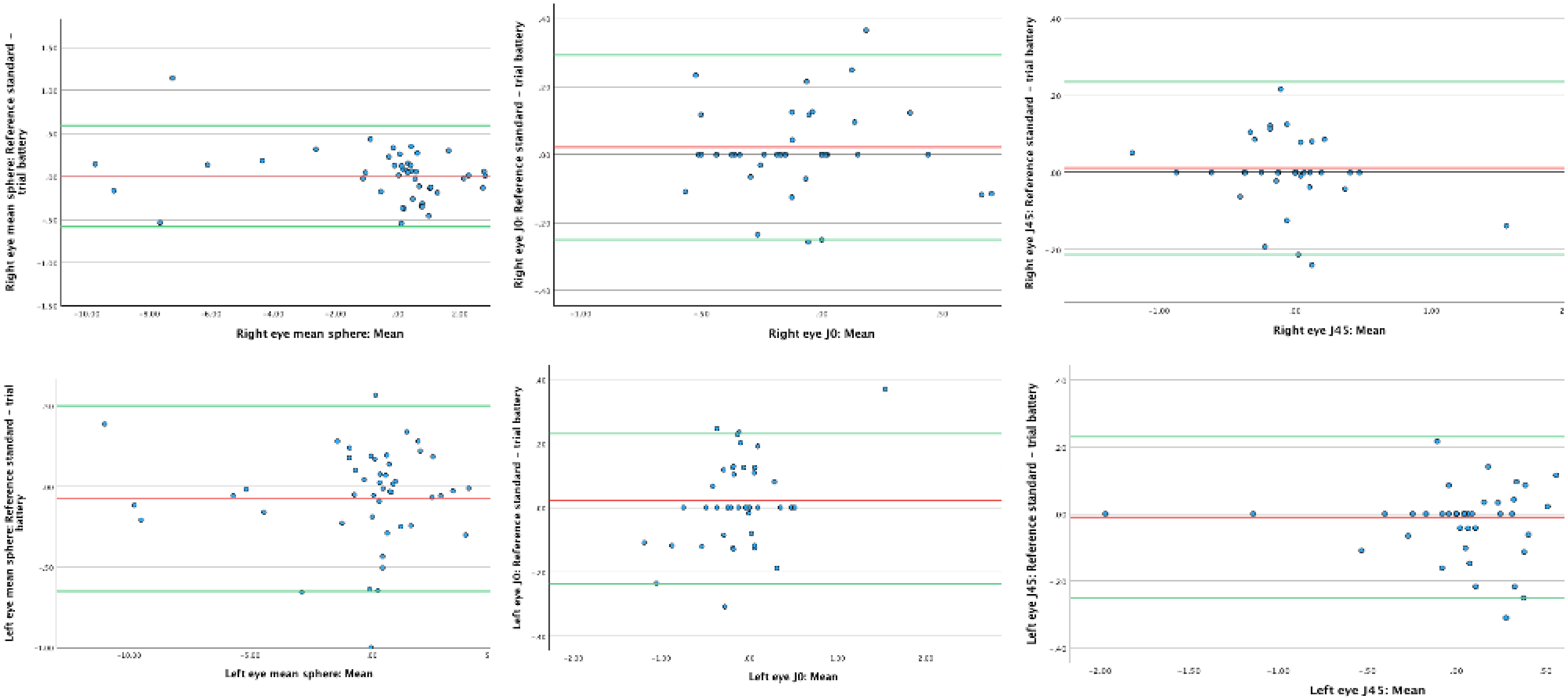


Figure 34. Difference plots of Mean sphere, J0 and J45 powers found for right and left eyes between the reference standard and trial battery examinations. In the right eye mean differences were low for mean sphere (-0.0026D) J0 (0.0223D) and J45 (0.0111D) with limits of agreement of -0.58D to +0.59D (95%CI 0.01D), -0.24D to +0.29D (95%CI 0.005D) and -0.24D to +0.21D (95%CI 0.004D) respectively. Similar agreement was found in the left eye with low difference of mean sphere (-0.073D), limits of agreement of -0.65D to +0.50D (95%CI 0.01D), J0 (0.02D) with limits of agreement of -0.24D to +0.28D (95%CI 0.0044D), and J45 (-0.01D) with limits of agreement of -0.25D to +0.23D (95%CI 0.0044D). Near addition was similar with low difference (-0.03D) between measures with limits of agreement between -0.46D and +0.39D (95%CI 0.007D)

A series of Friedman tests were undertaken to investigate the presence of differences between the results of the participant's habitual correction, the retinoscopy result, the result of refraction during the trial battery examination and the College of Optometrists examination for the mean sphere, J0 and J45 of both the right and left eyes.

Examination of the right eye mean spherical power identified a difference between refractive findings (Friedman test: χ^2=21.075, df=3, p<.001). As refractive results were not normally distributed, post hoc analysis was undertaken using the Wilcoxon signed rank test. Post hoc testing identified a significant difference between the results of the habitual correction and the findings of retinoscopy (Wilcoxon signed rank test: z=-3.803, p<.001), trial battery examination (Wilcoxon signed rank test: z=-4.129, p<.001), and the reference standard examination (Wilcoxon signed rank test: z=-3.444, p<.001). No significant differences were found between the results of retinoscopy and subjective refraction in the trial battery examination (Wilcoxon signed rank test: z=-1.345, p<.179), the subjective findings of the reference standard (Wilcoxon signed rank test: z=.951 p=.342), or the subjective findings of the trial battery and reference standard examination (Wilcoxon signed rank test: z=-.360, p=.719).

The analysis of J0 findings identified a difference between the different refractive outcomes (Friedman test: χ^2=13.782, df=3, p=.003). Further analysis identified differences between the habitual correction and the findings of retinoscopy (Wilcoxon signed rank test: z=-3.057, p=.002), refraction undertaken in both the trial battery (Wilcoxon signed rank test: z=-3.177, p=.001) and the reference standard examination (Wilcoxon signed rank test: z=-2.350, p=.019). No significant differences were observed between the findings of retinoscopy and refraction in the trial battery (Wilcoxon signed rank test: z=-.505, p=.614) or reference standard examination (Wilcoxon signed rank test: z=-1.256. p=.209), or between the reference standard and trial battery examination findings (Wilcoxon signed rank test: z=-1.050., p=.294).

The Friedman test for the right eye J45 found no significant differences in ranking (χ^2=.099, df=3, p=.992) across the four measures of refraction.

A difference between the refractive outcomes was observed between tests for the mean spherical power of the left eye (Friedman test: χ^2=16.779, df=3, p<.001). Differences were found to be significant between the habitual correction and the findings of retinoscopy (Wilcoxon signed rank test: z=-2.672, p=.008) and refraction undertaken in both the trial (Wilcoxon signed rank test: z=-2.956, p=.003) and reference standard examination (Wilcoxon signed rank test: z=-3.399, p<.001), as well as between the results of retinoscopy and refraction in both the trial battery (Wilcoxon signed rank test: z=-2.169, p=.030) and reference standard (Wilcoxon signed rank test: z=-3.065, p=.002) examinations. No significant differences were found between the results of the refraction from the reference standard and the trial battery examination (Wilcoxon signed rank test: z=-1.400., p=.162). The Friedman test found no identifiable difference in ranking for either J0 (Friedman test: χ^2=6.277, df=3, p=.099) or J45 (Friedman test: χ^2=1.172, df=3, p=.760) for the different refractive measures.

The difference between mean sphere, J0 and J45 for the trial examination and reference standard can be calculated, and the difference converted to an equivalent lens power difference (Miller, 2009). For the right eye, spherical differences within a range of +/-0.25D were found in 19 (86.4%) participants from the stroke cohort and 22 (84.6%) participants from the control cohort. Cylindrical differences under +/-0.25D were found in 17 (77.3%) participants of the stroke cohort and 20 (76.9%) participants of the control cohort (**Table 5-16**). Miller (Miller 2009) describes a mechanism for calculating an equivalent clinical lens from vector form to sphero-cylindrical form. This is described as the supplementary lens power to be used over the existing power to demonstrate the difference in refraction. Miller (2009) provides an example of a change from -0.50/+1.00x90 to -0.75/+1.00x83, once difference vectors are calculated and re-converted, the resultant "overrefraction" to demonstrate the difference is -0.25/+0.25x42. This has been reported as an equivalent axis change in some studies (Jorge et al. 2005).

This interpretation would be incorrect as the oblique cylinder orientation reported represents the axis required to transform the image from the original refraction to the image from the new refraction. In this instance the difference in cylinder axes were defined as the difference in axis between the trial battery and the reference standard. Cylinder axis accuracy is more complex to interpret as with increasing power of the cylinder variation in axis is more significant; and therefore, the tolerance of variation would be expected to decrease with increasing cylinder power. Consistency of cylinder axes were assessed against the tolerances for lens manufacture outlined in BS EN ISO 8980-1. A significant range in variation was found in cylinder axes for both eyes (right eye 0 to 45 degrees, left eye 0 to 72 degrees) with a mean difference of 4.54 (SD 10.29) and 7.86 (SD 18.30) for right and left eye respectively. Differences in cylinder axis fell within BS EN ISO 8980-1 tolerances for 17 (77.3%) participants from the stroke cohort and 23 (88.4%) participants of the control cohort.

	Right eye				Left eye			
	Sphere (%)	**Cylinder (%)**	**Axis* (%)**	**All Components (%)**	**Sphere (%)**	**Cylinder (%)**	**Axis* (%)**	**All Components (%)**
Stroke Cohort	86.3	77.3	77.3	63.6	90.9	54.5	77.2	45.5
Control Cohort	84.6	76.9	88.4	73.1	61.5	30.7	69.2	26.9

Table 5-16. Percentage of agreement (within +/-0.25D) of sphere and cylinder power, and agreement of axis within BS EN ISO 8980-1. All components indicating the percentage of cases where where sphere & cylinder were both in agreement and axis was within the range of tolerance between the reference standard and the trial battery examination.

Greater variability was observed in the left eye, with the sphere powers falling within +/-0.25D in 20 (90.9%) participants of the stroke cohort and 16 (61.5%) participants of the control cohort. This greater variability was observed in cylinder powers where 13 (54.5%) participants from the stroke cohort and 8 (30.7%) participants from the control cohort had differences in cylinder findings falling within the +/-

0.25D. Axis fell within BS EN ISO 8980-1 tolerances for 17 (77.2%) participants from the stroke cohort and 18 (69.2%) participants from the control cohort respectively.

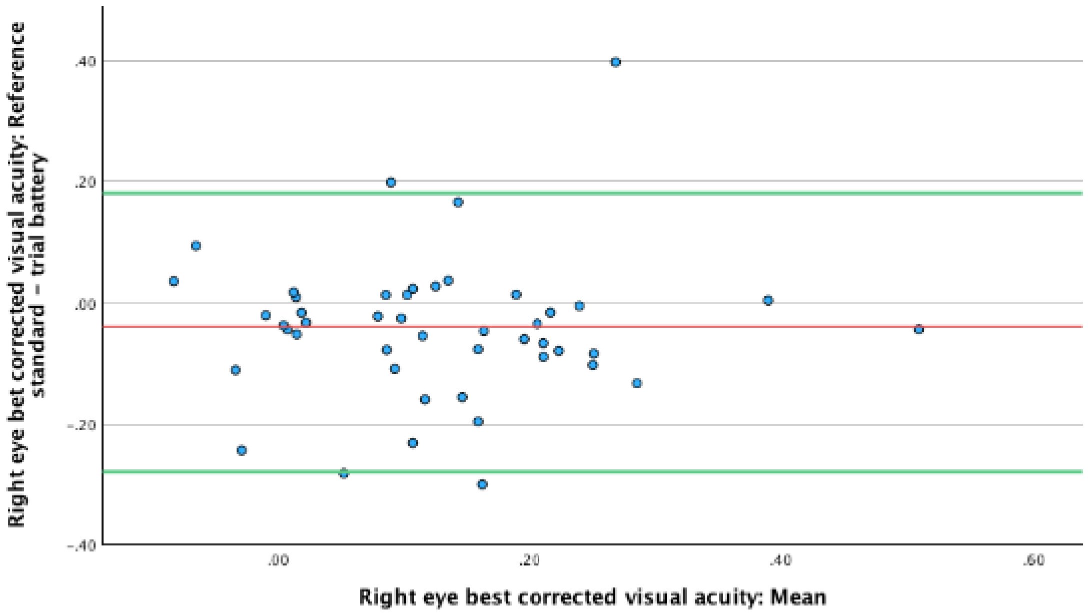
Refractive outcomes identified between the trial examination and the College of Optometrists examinations were in agreement for 22 participants with stable/unchanged refractive requirement and 13 participants requiring a new/updated correction. The differences in refractive outcomes between the College of Optometrists and trial battery examinations were not found to be significantly different (McNemar test: p=.581) with agreement of 0.729 (**κ**=.441 95%CI .186-.695, p=0.002).

5.3.6.3 Visual findings

To investigate the variance in acuity between examinations a series of Friedman tests were conducted. A difference in ranking was observed between the measures of habitual distance vision (measured during the trial battery examination), habitual distance vision (measured during the reference standard examination), corrected distance visual acuity (trial battery examination) and corrected distance visual acuity (reference standard examination), and unaided distance vision in the right eye (Friedman's test: χ^2=98.410, df=4, p<.001). Unsurprisingly, significant differences were found between uncorrected distance vision and habitual vision measured in the trial (Wilcoxon signed rank test: z=-4.434, p<.001), reference standard examinations (Wilcoxon signed rank test: z=-5.062, p<.001) and the best corrected visual acuity in both the trial (Wilcoxon signed rank test: z=-5.689, p<.001) and reference standard (Wilcoxon signed rank test: z=-5.445, p<.001) examinations. However it is notable that significant differences were observed in the findings of habitual acuity (Wilcoxon signed rank test: z=-3.377, p<.001), and best corrected acuity (Wilcoxon signed rank test: z=-3.305, p<.001) between examinations.

The same parameters were investigated for the left eye where a significant difference in median ranking was found (Friedman's test: χ^2 =79.794, df=4, p<.001). Post hoc assessment again found differences between uncorrected vision and habitual vision measured during the trial (Wilcoxon signed rank test: z=-4.373, p<.001), reference standard examinations (Wilcoxon signed rank test: z=-5.005, p<.001), as well as best corrected visual acuity measured in the trial (Wilcoxon signed rank test: z=-5.628, p<.001) and reference standard (Wilcoxon signed rank test: z=-5.526, p<.001). As was observed in the right eye, significant differences in acuity were observed between the measurements of habitual (Wilcoxon signed rank test: z=-2.208, p=.027) and best corrected acuity (Wilcoxon signed rank test: z=-2.530 p=.011) between the two examinations.

The measurements of best corrected visual acuity were found to have moderate correlation between tests for the right eye (ICC .681 [95%CI .423-.823], F[45,45]=3.132, p<.001). Difference plots for right and left eyes can be seen on **Figure 35**.



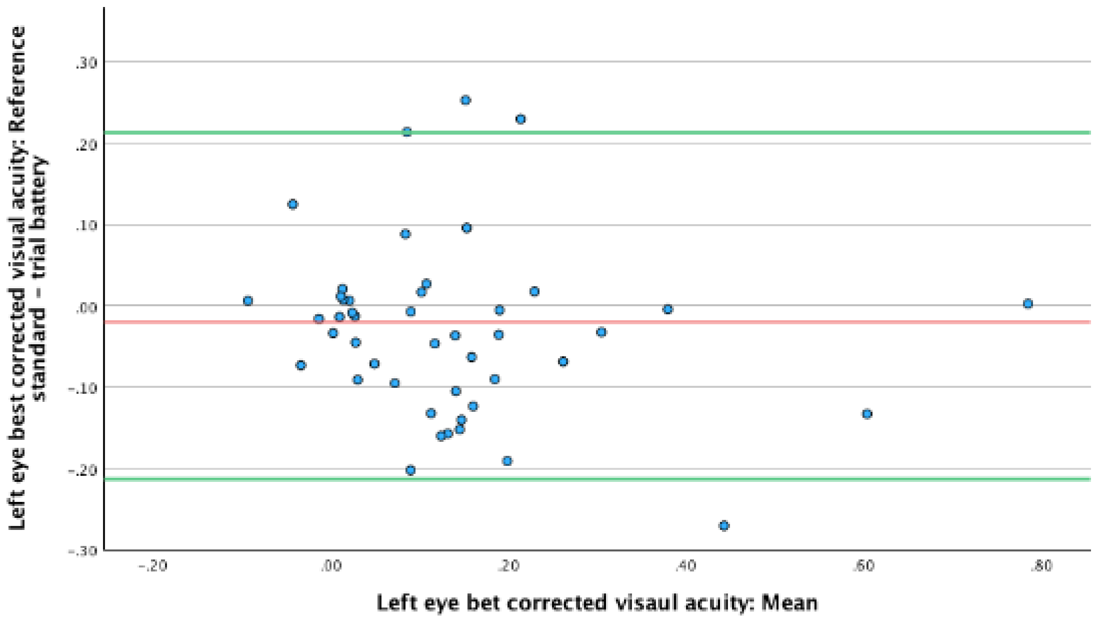


Figure 35. Difference plots of best corrected visual acuity (LogMAR) measured between the trial battery and reference standard examinations. The right eye found little difference (Median: -0.04 LogMAR) with 90% of the differences in measured values falling between -0.28 and +0.18 LogMAR. Similarly the left eye exhibited little difference (Median: -0.02 LogMAR) with 90% of observed differences in measured values falling between -0.213 and 0.213 LogMAR.

The International Classification of Disease 11th edition (World Health Organisation 2022) outlines a grading of vision into ranges of near normal, low vision and near-blindness. A clinical modification of this used more frequently in the United States (Centers for Disease Control and Prevention 2021) further subdivide this to ranges of normal vision, mild vision loss, moderate vision loss, severe vision loss, profound vision loss, near blindness and blindness (**Table 5-17**).

While it does not provide a linear scale of progression for measurement of impairment, the ICD-9-CM provides a convenient scale with which to investigate the factors affecting acuity. The best corrected visual acuity found for each eye during the trial examination were labelled in accordance with the appropriate classification.

Fair agreement in the ranges of vision measured were observed between the trial battery and reference standard examination for both right and left eyes. Despite not having been undertaken on all participants within the reference standard examination, the discretionary use of this investigation was observed to identify with moderate agreement the subjects exhibiting visual loss. By contrast the only peripheral vision test employed in the course of the trial battery, the Amsler test was observed to be insensitive to identifying defects of peripheral vision. It is notable that no anomalies were reported even in those subjects (of either cohort) with anomalies of the macula.

Ranges of vision		**VA Notation**	
ICD11	**ICD-9-CM**	**6m Snellen**	**LogMAR**
(Near-) Normal Vision	**Range of Normal Vision**	6/3.8	-0.2
		6/4.8	-0.1
		6/6	0
		6/7.5	+0.1
	Mild Vision Loss	6/9.5	0.2
		6/12	0.3
		6/15	0.4
		6/19	0.5
Low Vision	**Moderate Vision Loss**	6/24	0.6
		6/30	0.7
		6/38	0.8
		6/48	0.9
	Severe Vision Loss	6/60	+1.0
		6/75	1.1
		6/95	1.2
		6/120	1.3
	Profound Vision Loss	6/150	1.4
		6/190	1.5
		6/240	1.6
		6/300	1.7
(Near-) Blindness	**Near Blindness**	6/380	1.8
		6/480	1.9
		6/600	+2.0
	Blindness	No Light Perception	

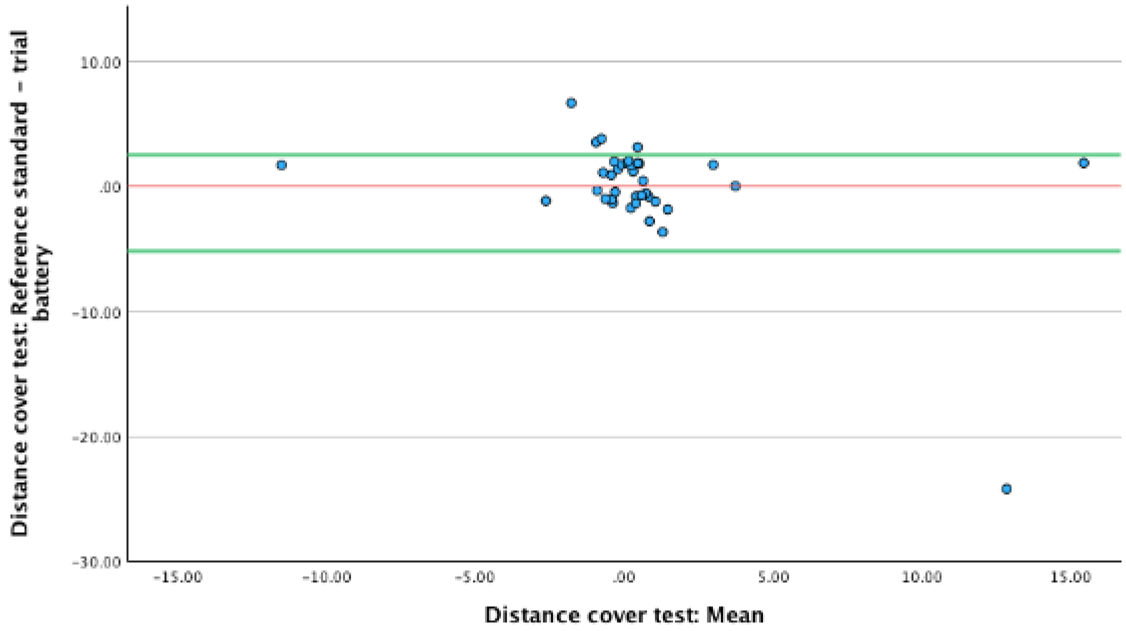
Table 5-17. Visual acuity ranges outlined by the International Classification of Diseases 11th edition (ICD11), and ICD-9-CM.

Exploratory investigation was undertaken to examine what ophthalmic factors may influence acuity in each eye within the trial battery examination. It was observed that the presence of meibomian gland dysfunction (Kruskal-Wallis H test: χ^2 =4.166, df=1, p=.041), and clinically significant cataract (Kruskal-Wallis H test: χ^2 =9.887, df=1, p=.002) influenced the range of acuity in the right eye. Further testing found a difference between normal range of vision and mild impairment for both the presence of meibomian gland dysfunction (Mann-Whitney U test: p=.041) and the presence of clinically significant cataract (Mann-Whitney U test: p=.002). No significant influence was observed on the range of vision from the degree of sodium fluorescein staining (Kruskal-Wallis test: χ^2 =.876, df=1, p=.349), corneal endothelial dystrophy (Kruskal-Wallis test: χ^2 =2.564, df=1, p=.109), ectropion (Kruskal-Wallis test: χ^2 =1.137, df=1, p=.286), pinguecula (Kruskal-Wallis test: χ^2 =.015, df=1, p=.904), corneal arcus (Kruskal-Wallis test: χ^2 =1.293, df=1, p=.255), corneal scarring (Kruskal-Wallis test: χ^2 =1.667, df=1, p=.197), age related macular degeneration (Kruskal-Wallis test: χ^2 =2.507, df=1, p=.113), macular hole (Kruskal-Wallis test: χ^2 =.600, df=1, p=.439), peripheral retinal degeneration, choroidal naevi (Kruskal-Wallis test: χ^2 =1.243, df=1, p=.265), or the refraction parameters of mean sphere (Kruskal-Wallis test: χ^2 =.045, df=1, p=.831), J0 (Kruskal-Wallis test: χ^2 =.849, df=1, p=.357), or J45 (Kruskal-Wallis test: χ^2 =.093, df=1, p=.760).

Acuity on the left eye was observed to be influenced by the refractive J45 finding (Kruskal-Wallis H test: χ^2 =8.055, df=2, p=0.18), Post hoc analysis found a difference between normal range and moderate vision loss with the J45 finding (Mann-Whitney U test: p=.009), no difference was found between normal range and mild vision loss (Mann-Whitney U test: p=.058) or mild vision loss and moderate vision loss (Mann-Whitney U test: p=.168). No significant differences were observed in the presence of sodium fluorescein staining (Kruskal-Wallis test: χ^2 =3.270, df=2, p=.195), corneal endothelial dystrophy (Kruskal-Wallis test: χ^2 =5.443, df=2, p=.066), corneal arcus (Kruskal-Wallis test: χ^2 =2.018, df=2, p=.365), corneal scarring (Kruskal-Wallis test: χ^2 =.714, df=2, p=.700), ectropion (Kruskal-Wallis test: χ^2 =5.222, df=2, p=.073), pinguecula (Kruskal-Wallis test: χ^2 =1.114, df=2, p=.573), meibomian gland dysfunction (Kruskal-Wallis test: χ^2 =.659, df=2, p=.719), clinically significant cataract (Kruskal-Wallis test: χ^2 =2.768, df=2, p=.251), age related macular degeneration (Kruskal-Wallis test: χ^2 =2.658, df=2, p=.265), macular hole (Kruskal-Wallis test: χ^2 =1.667, df=2, p=.435), peripheral retinal degeneration (Kruskal-Wallis test: χ^2 =1.114, df=2, p=.573), choroidal naevi (Kruskal-Wallis test: χ^2 =3.375, df=2, p=.185), or the refractive elements of mean sphere (Kruskal-Wallis test: χ^2 =2.969, df=2, p=.227) or J0 (Kruskal-Wallis test: χ^2 =.869, df=2, p=.648).

5.3.6.4 Binocular vision findings

Between examinations moderate agreement was observed in the detection of clinically significant heterophoria at both distance and near. Clinically significant heterophoria was defined as heterophoria that fell out with 2 standard deviations of the mean heterophoria, as reported by Goss (1995). While strong association was observed between distance and near cover test results within the trial examination and the reference standard examination, this was not observed when comparing the results between tests.



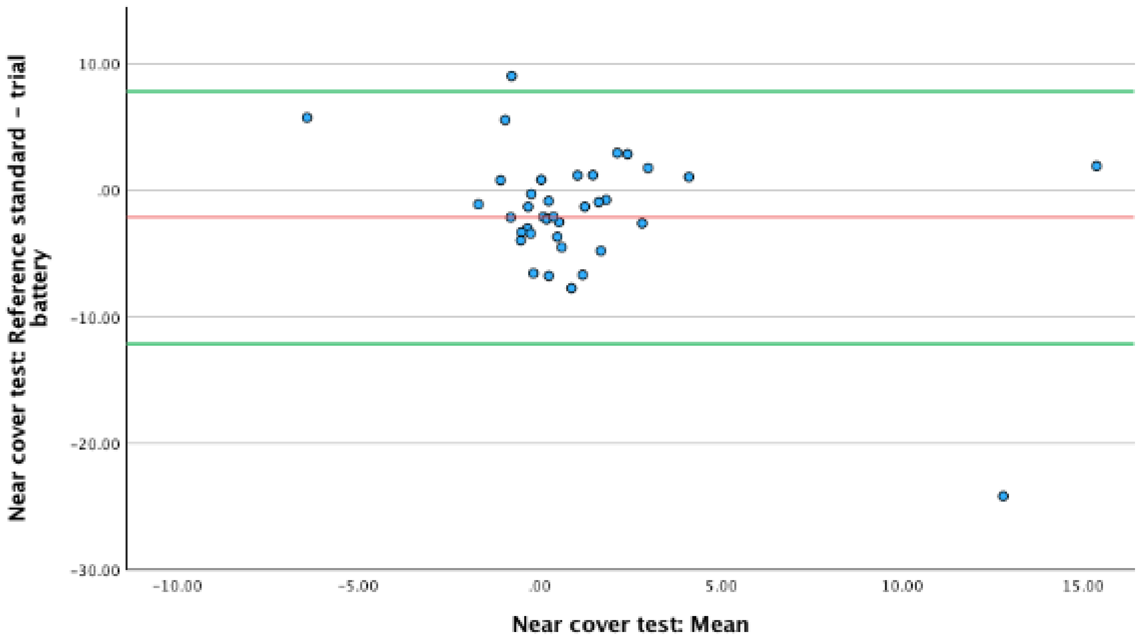


Figure 36. Difference plots of results of distance and near cover tests undertaken between examinations. low median difference (-2.00cm), however significant range was found with 90% of observed differences in measures falling between -5.20cm and +2.5cm. While at near a low mean difference was present (-2.19), significant variability was found with limits of agreement ranging from -12.16 to +7.78 (95%CI 0.23).

Fair association was observed between findings (Spearman's rho: r=.404, N=37, p=.013), and no significant difference in median ranking (Wilcoxon signed rank test: z=-.426, p=.670). The difference plot of distance cover test findings can be observed in **Figure 36**. By contrast poor association was observed between the results of near cover testing (Spearman's rho: r=.114, N=37, p=.502), with significant median difference in results (Wilcoxon signed rank test: z=-2.833, p=.005).

Significant agreement was observed between the reference standard and trial battery examination when assessing for the presence of strabismus, while no differences were observed in the detection of vertical ocular deviation (McNemar test: p=1.000), or the presence of incomitant deviations (McNemar test: p=1.000). Poor agreement was observed in the ability to detect remote near points of convergence. Where testing was undertaken, notable variability was observed of convergence range measured, though no difference in median measurement was observed between examinations (Wilcoxon signed rank test: z=-1.479, p=.139).

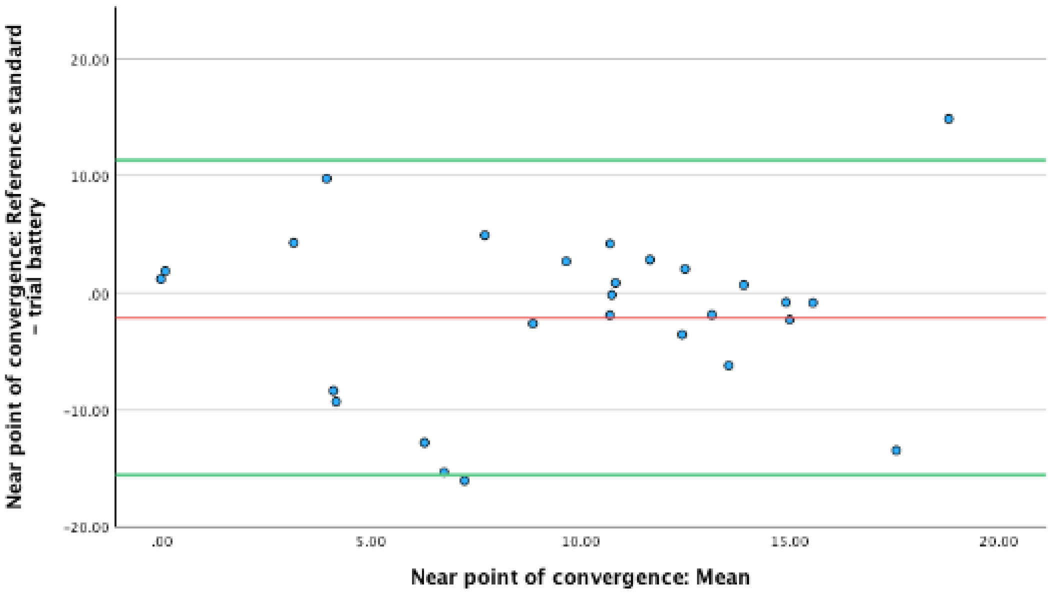


Figure 37. Difference plot of recorded near point of convergence between trial battery and reference standard examinations. Mean difference measured -2.15cm, with limits of agreement of -15.60cm to +11.30cm (95%CI 0.44cm).

Where testing of convergence range was undertaken, a remote near point was more frequently observed in the trial examination than the reference standard examination (McNemar test: p=.012). As was found with the results of near cover testing, the results of near point of convergence testing exhibited significant variability, a difference plot of these can be observed on **Figure 37**.

While the reference standard examination, anomalies of binocular vision – defined as the presence of strabismus, incomitant eye movements, a remote near point of convergence, or heterophoria exceeding the mean ±1.96 standard deviations – were observed in 10 participants from the stroke cohort and 4 from the control cohort. By contrast the trial battery examination identified binocular vision anomalies in 16 participants from the stroke cohort and 18 participants from the control cohort. These differences were found to be significant (McNemar test: p<.001).

5.4 Discussion

In this study we have investigated the results of the trial examination battery derived from the Delphi study undertaken in **Chapter 3** to examine patients with a history of stroke and compare this with the results of a typical examination undertaken in community optometry practice.

The health questionnaire exhibited a disappointing response rate across both cohorts. While low response rates to questionnaires have been reported upon (Booker et al. 2021; Price et al. 2022; Shiyab et al. 2023) caution is needed when interpreting the results. While the survey was supplied to subjects in large font with the opportunity to discuss questions with the author, the length and personal nature of the questions may have raised concerns with respondents, reducing their willingness to complete this task. As highlighted in other studies (Rowe et al. 2009; Rowe 2010b; Stalin et al. 2024a; Stalin et al. 2024b) the assessment of vision following stroke appears to have been variable amongst respondents, with significant inconsistencies observed between levels of care.

When considering the findings of the trial battery and reference standard examinations several areas under test found agreement, notably refraction, visual acuity, corneal anomalies, peripheral vision anomalies, intraocular pressure and the presence of media anomalies as well as optic nerve and central retinal findings were found to have fair to moderate agreement. However, some areas of discrepancy were found between the tests, particularly centring on anomalies of the anterior segment and ocular surface, defects in of peripheral vision, peripheral retina testing and the detection of anomalies of binocular vision.

Rutner et al (2006) undertook a retrospective analysis of selected records for visually symptomatic patients that had presented to their clinics with a history of traumatic brain injury or cerebrovascular accident, comparing the findings of their review of records with published data (Suchoff et al. 1999; Brewitt and Sistani 2001; Brown et al. 2002; Brown et al. 2003). While the parameters of recruitment and analysis of data were different, some agreement can be found between the results of Rutner et al’s (2006) cerebrovascular accident cohort and this study’s stroke cohort. This study provides the first prospective investigation of the prevalence of ocular disease within a sample of participants with a history of stroke and compares this to an age matched control cohort. Eyelid function is innervated via three different pathways, the orbicularis oculi is innervated by the facial nerve (CNVII), the levator palpebrae superioris via the oculomotor nerve (CNIII) and Muller’s muscle by the sympathetic nerve fibres. Following neurological insult, these pathways have the potential to be impacted, resulting in issues of eyelid function. Like Rutner et al (2006), this study found an increased incidence of lid anomalies and superficial fluorescein staining in stroke survivors. Unlike Rutner et al (2006), no cases of ptosis were observed, instead ectropion, the outward turning of the lower eyelid was observed with greater frequency within the stroke cohort (2/24 stroke and 1/26 control subjects). This study observed that this factor had the greatest association with the presence of superficial corneal staining, with the presence of other lid anomalies such as blepharitis or meibomian gland dysfunction not associated with its presence.

While the presence of an anomaly of the anterior segment does not in itself give rise to dry eye disease, the influence of anomalies of the anterior segment on the development of dry eye disorders has been described extensively in the (Schaumberg et al. 2011; Tomlinson et al. 2011; Bron et al. 2017). The 2017 Dry Eye Workshop (DEWS II) reports outlined the key influencing factors (Stapleton et al. 2017), as well as a diagnostic approach for the diagnosis of dry eye disease (Wolffsohn et al. 2017). Significant range in the prevalence of lid margin disease has been reported ranging from 3.5% to 68%, with an estimated pooled prevalence of 35.8% (Schaumberg et al. 2011; Hassanzadeh et al. 2021). The prevalence of lid margin disease found in this study varied significantly between clinicians, with the trial study finding prevalence towards the upper limit of the literature, while the reference standard test found lid margin disease towards the lower end of the range. Examination of the external eye can be undertaken by several methods, this is most frequently done using a slit lamp biomicroscope, though where a patient is unable to position themselves at the instrument alternative methods such as loupes, burton lamp, handheld slit lamp or even the direct ophthalmoscope may be used. The examination of the ocular surface for anomalies is not limited to the use of topical dyes such as sodium fluorescein, though these facilitate the observation of corneal surface disruption. While diagnostic assessment of the anterior segment was undertaken in all trial battery examinations, consisting of ocular surface and tear film assessment with sodium fluorescein staining, no tear film assessment was undertaken in the majority of participants undergoing the reference standard. Additionally, in neither test were tear film osmolarity undertaken or a standardised dry eye questionnaire used to assess symptomatology. The increased presence of clinically significant staining however highlights the importance of ocular surface assessment within this group.

While it may be expected that the detection rate of differences in tear film integrity would be identified between clinicians, it is unclear why such differences in the prevalence of lid margin disease is present between tests. It is possible that other factors may have played into clinical attention during testing. While examination of the anterior eye is a core component of the eye examination, this needn’t necessarily include assessment of the integrity of the tear film. In many practices the provision of dedicated dry eye care is more frequently being undertaken as a private service separate to routine sight testing. This approach was the one undertaken at the practice acting as the research venue. It may be that the absence of symptoms, and presence of a dedicated private dry eye service provision may have led clinicians to not consider undertaking a dedicated ocular surface assessment on subjects more frequently.

The selection of clinical tests is guided by the symptoms reported during the course of the initial case history interview (Du Toit 2015). The case history undertaken during examination may have suffered from issues around communication. Several biases can influence the approach clinicians take when conducting a clinical interview. At the initial stages of the interview, insufficient questioning may have occurred to elicit all the relevant information, especially where the presenting information was unrelated to ocular surface issues. It is not unusual for clinicians to focus on presenting issues, at the expense of potential supplementary findings, and curtailing the diagnostic process once the apparent primary diagnosis is identified. This can be compounded by the perception of the potential impact that secondary anomalies may have, playing down ‘routine’ pathology, such as ocular surface issues due to their perceived low morbidity. To counter this, examinations should begin with open questioning to establish the reason(s) for visit, eliciting the core information from the patient and providing a space for the patient to identify what else may be troubling them. This can be compounded during the course of the examination, where if the clinician has prejudged a condition to be present, their findings may be unduly influenced by their perception of the expected anomaly (Baker et al. 2005; Davis and Murray 2016). Many clinicians raise concern over undertaking an approach to testing that encourages open questioning however, citing the perceived potential loss of examination time and impact upon clinic scheduling. It was suggested by Pointer (2014) however that the risk of loquacious patients disrupting a clinic’s examination time or appointment schedule was unlikely.

While corneal sensitivity has been found to reduce with age (Nosch et al. 2023), the presence of an unstable tear film has been associated with relative corneal hypersensitivity (Tagawa et al. 2019) with it being suggested from animal modelling that this is due to increased sensitisation of the trigeminal nucleus (Tei et al. 2022). Loss of nerve fibres on confocal microscopy has been associated with loss of sensation across a number of conditions (Rosenberg et al. 2000; Erie et al. 2005; Hamrah et al. 2010; Labbé et al. 2012; Bouheraoua et al. 2015; Bitirgen et al. 2017). Khan et al (2017; Khan et al. 2022) undertook confocal microscopy examination of patients post stroke, finding a loss of nerve density. While the relationship between structure/function remains inconsistent, and variation exists with inter-observer repeatability (Patel and McGhee 2013) the loss of corneal nerve density reported post stroke may have resulted in reduced symptoms reported to examiners, explaining in part the absence of further investigation of ocular surface anomalies undertaken on participants during the reference standard examination.

Anomalies of the crystalline lens increase in incidence with age (Klein et al., 2008). Typically these anomalies result in a change in the internal structure of the lens, resulting in a loss of transparency and clouding within the lens, a phenomenon known as cataracts. Within the aged population the estimated prevalence of cataract is around 54.38% (Hashemi et al. 2020), with increasing risk of these causing visual impairment with increasing age (Reidy et al. 1998). Both trial battery and reference standard were consistent in the identification of clinically significant cataract, with findings commensurate with Hashemi et al (2020). Treatment for clinically significant cataract is undertaken by surgical removal of the crystalline lens and implantation of a man-made intraocular lens. Surgery for cataract removal is the most common elective surgical procedure undertaken in the UK (The Royal College of Ophthalmologists 2018), with approximately 330,000 procedures undertaken in England annually. The decision to undertake cataract surgery depends upon a number of factors, the main factor being the effect that the cataract has upon the patient's quality of life. Patients should be provided with an understanding of their prognosis, including the risk of further visual deterioration when considering whether surgery would be suitable for them. The presence of cataracts in both eyes will be expected to have a greater impact than where their presence is unilateral with greater deterioration in vision through loss of contrast, acuity and binocular summation (Pardhan and Elliott 1991; Pardhan 1993; AGIS Investigators 2000). During the course of this study no significant difference in the decision for onward referral was found.

While the use of dilation for the routine posterior segment examination has become normal practice in some areas, it does not represent the standard of care recommended by the College of Optometrists. While some degree of concern may arise over the possibility of missed pathology, the absence of widespread sequelae of undetected peripheral retinal disease given the frequency of routine testing without dilation should give clinicians some degree of confidence that this risk is low (Varner 2014). While controversy remains (Michaud and Forcier 2014), it has been argued that - in the absence of known pathology, or significant symptoms - that routine dilation may be excessive, resulting in increased costs of routine care, with limited benefits to patients (Batchelder et al. 1997; Augsburger 2005). An alternative that has been proposed is that widefield retinal imaging be used as an alternative to dilated fundus examination in first line diagnostics (Midena et al. 2022), several imaging systems are available, some of which incorporate mult-modal imaging such as fundus autofluoresence or OCT. These instruments have fields of view ranging from 105 degrees to over 200 degrees of retina (Patel et al. 2020). Such systems can facilitate prompt examination, without the need for the inconvenience of dilation.

However not all agree that widefield imaging can be used as a substitute for examination. These instruments are limited by their field of view, most of which are unable to view ora to ora in a single image and rely on composite imaging based on multiple images and the use of algorithms to modify the image quality. Additionally some systems generate pseudo-colour interpretations, complicating interpretation compared to true colour images (Kato et al. 2019; Ulfik-Dembska et al. 2021).

While not identified as part of the trial battery developed in **Chapter 3**, the results of this study using dilation within the trial battery mirror many of these points. While a significant difference in the prevalence of peripheral retinal anomalies was found to be greater in the trial battery group, the results identified did not alter the immediate clinical management in the majority of participants exhibiting these anomalies. Similarly, while the presence of dilation altered the classification of some of the macular anomalies identified, no change in clinical management resulted from the results of dilated assessment. The increased detection of retinal naevi warrants highlighting, as the dilated fundus examination resulted in an increased detection rate compared to the reference standard examination. The College of Optometrists recommends assessment of pigmented lesions using the Oxford University developed

MOLES system for examining and grading suspicious lesions (Roelofs et al. 2020), which indicates the necessity for onward referral for suspicious lesions exhibiting a grade of 3 or greater, while benign lesions should undergo imaging and annual review. While no participant that completed the study was found to have signs indicative of possible progression to malignancy, the impact of this finding was that these participants require more frequent follow-up to monitor the low risk to conversion of the nevus to melanoma.

The assessment of pupil reflexes to light is used to examine the integrity of the visual pathway, with the follow-up swinging flashlight test being used to assess the relative integrity of the afferent pathway. Anomalies of the pupil reflexes can be indicative of damage to the optic nerve, oculomotor nerve, the presence of brainstem lesions or as a response to some types of medication (Crippa et al. 2007; Richa and Yazbek 2010; Wilhelm 2011; Ciuffreda et al. 2017). While pupil testing was not universally employed within the reference standard examination, where this was undertaken the detection of pupil anomalies was inconsistent with the findings of the trial battery. This is perhaps unsurprising, as previous assessments of reliability of pupil assessment have found only moderate reliability between graders of pupil size, shape and reactivity (Olson et al. 2016). Automated pupillometry has been suggested as an improvement to conventional clinical testing due to its improved interrater reliability, with the potential to improve detection of anomalies of pupil function (Couret et al. 2016; Lussier et al. 2019), and aid in the management of conditions associated with neurological deterioration post-stroke (Marshall et al. 2019). Automated pupillometry devices are however rare in clinical practice, with conventional flashlight-based testing remaining the method of choice. The adoption of smartphone technology to facilitate visual field assessment has opened the possibility of using this technology for other areas of eyecare, notably the pupillary assessment. This approach to pupil assessment has been found to have fair accuracy compared to conventional testing and dedicated infrared pupillometry (Piaggio et al. 2021; McGrath et al. 2022; Bruegger et al. 2023). An alternative approach that has been investigated is the use of technology already in routine clinical practice to facilitate pupil assessment. Chopra et al (2020) investigated the possibility of objective pupillometry using OCT. This study had good test-retest reliability but was found to be inferior to a commercially available pupillometer. The findings of pupil examination in this study mirror those of Rutner et al (2006) which found low incidence of pupil reflex anomalies in the cerebrovascular accident group. It has been proposed that in patients whose strokes have resulted in more mild neurological deficits that defects of pupil function may be subtle, associated with dysregulation of autonomic control; affecting the change of pupil responses back to baseline post testing, rather than the direct, consensual or afferent response typically observed for during clinical pupil assessment (Peinkhofer et al. 2018).

Where uncorrected, refractive error can have a major impact upon wellbeing and quality of life (Coleman et al. 2006; Kandel et al. 2017). The assessment of refractive error is typically undertaken during the sight test. Testing of sight in the UK is regulated by the Opticians act (1989) and primarily undertaken by optometrists within a primary eye care setting. An accurate non-cycloplegic subjective refraction is an important clinical measure, and the benchmark against which alternative refractive approaches are measured (MacKenzie 2008). Issues of refraction have been found to be the leading cause of patient dissatisfaction with primary eye care providers (Freeman and Evans 2010; Bist et al. 2021; Beesley et al. 2022). It is important that accurate measurement of refraction is attained, especially in the presence of ocular pathology, where greater variability in measurements may be found (Leinonen et al. 2006), or indeed where refractive changes may indicate the presence of ocular or systemic pathology (Pesudovs and Elliott 2003; Kaštelan et al. 2018). It is important therefore for practitioners to be able to accurately undertake refraction and issue an acceptable, comfortable prescription that enables the patient to meet their visual needs, as this is often what the outcome of the care provided to them is judged upon.

The results of subjective refraction undertaken as part of the trial battery and reference standard examination were not found to significantly differ between tests, with a low mean difference between tests. A review of literature (Goss and Grosvenor 1996) reported that typically 95% agreement was present between practitioners within +/-0.50D and 80% within +/-0.25D for sphere power, equivalent sphere power and cylinder power. In this study, variation in astigmatic components were found to be like previous investigations that have been undertaken of inter-rater reliability of refraction (Bullimore et al. 1998; MacKenzie 2008; Shah et al. 2009c), while slightly greater variation of spherical error found with 95% limits of agreement for both eyes exceeding the +/-0.50 range suggested by the literature. Additionally, no significant difference in this reliability was observed between participants with a history of stroke or controls.

A number of factors may give rise to the greater degree of variation found. Most studies utilise a younger mean cohort than this study (Bullimore et al. 1998; MacKenzie 2008; Shah et al. 2009c; Mukash et al. 2021; Mathebula and Rubin 2022; Kozlov et al. 2024), with increasing age, the prevalence of clinically significant ocular pathology is likely to be greater, increasing the variability of refractive findings (Leinonen et al. 2006). Where higher refractive powers are present, variations in the vertex distance between the eye and trial frame may have resulted in altered refractive outcomes. Additionally, the presence of reduced acuity secondary to amblyopia can make determination of an end point challenging when conducting refraction.

While all testing undertaken in the course of the trial battery were undertaken using letter by letter scoring, it is unclear whether this was the case for all reference standard examinations. Assessment of visual acuity was found to have a fair degree of consistency between the test battery and the reference standard examination. While the reliability measured in this study appears to be similar to that reported by other studies of acuity in photopic conditions (Chaikitmongkol et al. 2018; Sánchez-González et al. 2021). However, if letter-by-letter scoring was not uniformly adopted in the reference standard examinations, this may have introduced a reduction in instrument precision, limiting the confidence that can be placed in the comparison of results.

The association of reduction in vision with the presence of cataract was not unexpected, given that impairment of visual acuity is a well reported sequelae of this condition (NICE 2022). The association to refractive error in the left eye is perhaps surprising, though it should be noted that in all cases where strabismus was observed this was found to affect the left eye. Closer examination of the findings of the participants with strabismus identifies that 3 of the four exhibited significant astigmatic refractive error, it is likely that the presence of reduced acuity secondary to amblyopia in these cases may have given rise to these findings, as well as the refractive variability observed.

The presence of peripheral vision loss can be substantial following brain injury. Given the wide distribution of visual signals, and the significant portion of the brain involved with visual processing, damage to the visual pathway or centres can give rise to substantial visual loss. This has the potential to cause significant impact on a patients' day to day activities and quality of life, impacting reading, household tasks, mobility, and driving. While no strong evidence exists for functional treatments of peripheral vision loss, several adaptive and compensatory mechanisms have been suggested (Pollock et al. 2019).

In addition to field loss, a phenomenon that may occur post stroke is that of visuospatial neglect. This phenomenon results in the affected individual not having awareness of loss of sensitivity of the field of vision. The prevalence has been proposed to range from 20 to 80% dependent upon the lesion location, stage of recovery, and nature of test used (Ten Brink et al. 2017; Esposito et al. 2021; Bosma et al. 2023; Durfee and Hillis 2023). A major limitation of the test battery is the absence of any assessment of visuospatial neglect. Visuospatial neglect can be readily screened using a variety of simple paper-based tools (Cermak and Hausser 1989; Kersel 1993; Agrell et al. 1997; Plummer et al. 2003; Lindell et al. 2007; Hanna et al. 2017) or digital applications (Pallavicini et al. 2015; Cipresso et al. 2018; Quinn et al. 2018) designed for clinical use. Although no participants in the present study were formally identified as exhibiting symptoms of visuospatial neglect, the omission of such assessment reduces the use of the battery. Consequently, individuals with unrecognised neglect may be deprived of appropriate onward referral for formal diagnostic evaluation and rehabilitation (Bartolomeo 2021; Durfee and Hillis 2023).

The use of clinician discretion in the decision to employ automated perimetry was found to be sensitive in the identification of peripheral vision loss for the majority of patients where this was present. Indeed, only a single participant went on to be found to have a field defect on field testing following the trial examination that had not been identified during the course of the reference standard assessment. It should however be noted that the originally derived trial battery examination (**Chapter 3**) had limited assessment of the central visual field by Amsler test, but did not incorporate automated field testing into its protocol. Given the absence of anomalies identified (even in the cases of macular anomalies) the absence of field assessment would have resulted in none of the episodes of field loss being detected.

This has resulted in the identification of a blind spot in the test battery, that can be improved upon, through the incorporation of automated field testing.

By contrast binocular vision testing, while a key clinical area within optometry, is frequently viewed as an area of uncertainty for many clinicians (Harvey and Franklin 2005). The reduced use of binocular vision testing was significant as this resulted in a difference of the findings in the binocular vision system.

Examination of ocular alignment by the cover test differed significantly in the results at the nearpoint, with the trial battery examination finding a greater degree of exophoria and more receded near point of convergence than the reference standard. Significant variability was observed between the results of these procedures in both tests, with the potential to alter the clinical management indicated. Interrater reliability of near cover test results has been undertaken to examine variability between experienced optometrists (Anderson et al., 2010; Johns et al., 2004; Rainey et al., 1998b), and between optometry students and experienced optometrists (Fogt et al. 2000; Hrynchak et al. 2010). The degree of variability observed in this study was greater than reported elsewhere. Previous reports had been undertaken on a range of participants, typically students to 65 years of age which would make this a younger cohort than that reviewed here. While these observed differences may in part reflect age related neurological changes, an alternative cause may be the presence of a Hawthorne effect. It is possible that optometrists when conducting the reference standard assessment were more attentive to the procedures assessing binocular vision anomalies, particularly those reporting a history of cerebrovascular accident. By contrast, this may have been less pronounced when assessing binocular vision in participants without a history of stroke, potentially resulting in an under-reporting of anomalies in control subjects. It has been reported that with progressing age that ocular saccade activity, latency and velocity decrease (Klein et al. 2000; Dowiasch et al. 2015). With the decrease of these movements, it may be that the accurate detection of movements was impaired resulting in increased variation. Another factor that may have influenced this could have been the technique utilised by examining optometrists. While all participants undergoing the trial battery underwent a cover test with a prism bar to neutralise movements, this is rarely employed during routine practice. Many optometrists instead use an estimated cover test in the course of routine testing, which was the case during the trial battery examination for all participants where cover test was undertaken. With experience many optometrists build familiarity with the size and speed of fixation/refixation after the removal of an occluder and are able to make an estimate of the degree of variation present. While Ludvigh (1949) indicated that an experience examiner would not be expected to identify $<2^{\Delta}$ of movement reliably, studies on the repeatability of the estimated cover test method have been mixed (Calvin et al., 1996; Rainey et al., 1998b), so it is challenging to confirm the impact that the use of this approach may have had.

While target type has been found to be independent of measured near point of convergence in presbyopes (Siderov et al. 2001), the normal range frequently reported is dominated by younger participants (Goss 1995; Scheiman et al. 2003). While it is established that convergence range reduces with age (Siderov et al. 2001), limited normative data for convergence range has been measured for older adult populations. While no association was found between the degree of heterophoria and near point of convergence across either test, the trial battery identified the presence of a higher rate of receded near point of convergence than the reference standard test. Though this may be the result of a classification of a near point of convergence anomaly existing in the presence of a breakpoint of less than 10cm (Scheiman and Wick 2014; Axelsson et al. 2019), likely is unduly stringent in this demographic.

While the Opticians Act (1989) sets out the legal responsibilities for optometrists—including the requirement to examine both the internal and external structures of the eye—the Act allows for a degree of professional discretion in how these examinations are conducted. In practice, this means that no universally applied "standard sight test" exists, and the scope of an individual examination may vary depending on the optometrist’s clinical judgment. This variation in procedures was most stark in the assessment of ocular surface anomalies and binocular vision care, which had influence upon the difference in findings observed. The Opticians Act (1989) requires an optometrist to undertake an examination of the internal and external surface of the eye and associated structures in its immediate vicinity for the purpose of detecting signs of injury, disease or abnormality in the eye or elsewhere. In the course of the reference standard examination, 4 participants were not recorded as having received an examination of the anterior segment, potentially compromising the level of care received. It is not clear whether this is the result of no examination having occurred, or whether an examination was undertaken, but findings not recorded (Shah et al. 2009a). In the absence of symptoms indicative of ocular surface disease, it would be reasonable for an optometrist to undertake a basic assessment of the ocular surface and not undertake a dedicated ocular surface examination in the course of a routine test (Smith et al. 2008; Graham et al. 2009; Downie et al. 2016).

During this study exploratory testing of variance was undertaken to investigate the factors associated with reduced acuity and corneal punctate staining. As reported a number of factors were found to be significant upon investigation with post-hoc testing. While the decision not to use a correction factor increases the risk of a Type I error within this study, post hoc testing was undertaken in an exploratory fashion, to investigate factors in an unplanned fashion. As recommended by Armstrong (2014) no correction was undertaken as the results of these investigations should be considered as findings of interest that may be further investigated in future work.

This study is limited by several factors. The cohort of participants with a history of stroke had in the main experienced milder long-term sequelae secondary to their neurological episode(s). While these participants may be typical of the general patient that may present to a primary care practice after having had a stroke, the results of this test may not be generalisable to those with more severe long-term impact. As a study run from a primary eye care practice, there is a risk that participants may present due to being more visually symptomatic, with those potential participants without visual symptoms being less inclined to participate. The recruitment of this study coincided with research done by the College of Optometrists (2023a) which identified that 50% of people indicated that the cost of living crisis would have an impact on their seeking eyecare, while 22% had admitted to postponing or cancelling a sight test appointment in the previous year, this mirrors similar research by the Association of Optometrists (2022) the previous year. It is possible that undertaking the research in a commercial setting may have unsettled potential participants, who may have difficulty recognising the research study as separate from the commercial activity of the business. Convenience of location was likely a factor, while the practice has onsite parking and is close to local bus routes, it sits out with the centre of Southampton. The relative inaccessibility of attending this site may have served to put off potential participants from taking part due to difficulty in reaching this location. While the majority of stroke participants (n=20) were recruited externally this was not the case for the control group, most of whom (n=22) were existing clients of the practice, having responded to recruitment materials onsite. As such this group was more likely to routinely attend eye care services, and is likely a major factor in the differences between cohorts in terms of habitual eye care provision.

While comparable in participant number to similar primary eye care practice-based research (Beasley and Davies 2012; Beasley and Davies 2013a), this study exhibited a modest sample size. This limited sample size reduces the generalisability of findings due to the risk of Type II errors. While sample sizes are sufficient to assess that no major within-subject differences are present, the sample size is insufficient to be assured of the absence of erroneous negative findings in between subject and between cohort evaluation. While a target of 59 subjects was set based upon Viechtbauer et al. (2015) this work's sampling calculation was around identification of errors of procedure that may occur within pilot studies. An evaluation of this protocol with a larger sample of participants may enable more robust examination of data and potentially identify data where differences may have been too subtle to identify in the current cohort. To adequately power this study to ensure identification of a medium effect size (f=0.25) a sample of 252 would be needed for examination of differences between multiple groups, and 92 for comparison between two groups (d=0.5).

This study has compared the findings of the newly developed sight test battery with those obtained through a conventional sight test undertaken in community practice. Some variability was observed, particularly in terms of the procedures employed. While core components such as refraction and posterior segment examination were consistently undertaken, procedures to assess binocular vision were not routinely completed, and anterior segment examination details were frequently absent. Though this may, in part, reflect limitations of clinical record keeping (Shah et al. 2009a), this constrains the ability to compare and fully analyse the outcomes of these two testing approaches, further limiting the statistical power noted previously. Despite these limitations, this study found that while conventional sight tests demonstrated good sensitivity in the detection and management of refractive errors, visual anomalies, and posterior segment pathology, but was more limited in the detection ocular surface anomalies across both subject groups. Greater incidence of lid anomalies and superficial punctate keratopathy was observed among stroke survivors. Furthermore, dilated examination revealed a higher frequency of peripheral retinal anomalies, however within the context of this study, these findings had limited influence on the overall care delivered. In the course of this study, while masking was present between the results of the trial battery and reference standard examination, all testing of the trial battery was undertaken by the author, while all reference standard testing was undertaken by other optometrists. This introduces the risk of examiner bias and fails to control for inter-examiner variability, further raising the risk of Hawthorne effect. Future work would benefit from randomisation of examiners to reduce these risks. The structured approach of the trial battery also revealed greater variability in near point binocular vision anomalies, surprisingly within control subjects, though as highlighted previously this may have been the result of examiner bias when examining known stroke survivors.

While this study has found little difference between the refractive and ocular health findings of the test battery and the results of routine sight testing, significant limitations are present in the appraisal of field loss and visuospatial neglect. Clinicians should be aware of the potential for greater incidence of ocular surface and near point binocular vision anomalies when testing patients with a history of stroke.

These findings have previously been presented as a poster:

Maciver M. Wolffsohn J.S., & Logan N. (2024, Sept) *A clinical evaluation of a diagnostic examination battery for assessing vision in stroke survivors.* Poster presented at the 6th Interdisciplinary Postgraduate Research Conference, Aston University. Birmingham

Chapter 6 Binocular vision characteristics in stroke survivors: A cross-sectional investigation

6.1 Introduction

In the physiological visual system, when fixating upon real-world stimuli, a three dimensional percept is created by integration of the two dimensional retinal images. These images are brought together in the process of sensory fusion, with errors of ocular coordination corrected for by motor fusional reflexes (Stidwill and Fletcher 2011). Where in alignment the visual system derives disparity information from each retinal images' location in relation to the corresponding retinal points of each eye to derive a relative depth. This system is mediated by several cortical areas, with direct nervous innervation of the extraocular muscles originating from the brainstem, with cortical control for different eye movements deriving from frontal, occipital, parietal, and temporal lobes as well as other centres (Liversedge et al. 2013; Ventura et al. 2014). Given the diverse range of cortical regions involved in oculomotor control, binocular viewing and feedback and spatial awareness, it is not unexpected that following a cerebrovascular accident the binocular visual system would be impacted.

The prevalence of binocular vision anomalies post stroke has been explored in a number of works. Ciuffreda et al (2007) undertook a retrospective review of clinic records of 60 patients that presented to their clinic following a cerebrovascular accident. These records were reviewed and diagnoses classified by "conventional clinical standards". Cranial nerve anomalies were observed in 10% of records reviewed, while 36.7% presented with strabismus. In a series of prospective trials, the Vision In Stroke group found higher incidence of oculomotor anomalies, with 54% exhibiting deficits of ocular motility (Rowe 2011a), but lower incidence of strabismus with 19% exhibiting anomalies of ocular alignment (Rowe 2010a). While frequently transient, gross anomalies of eye movements were found to be particularly common presenting in around 23% of stroke survivors (Pedersen and Troost 1981; Rowe et al. 2013b), with smooth pursuit anomalies present in around 4% of subjects, and saccade anomalies in under 3%. The disruption of binocular systems, loss of vision and the presence of field loss and visual neglect have all been found to impact on reading ability, with saccadic accuracy (especially in dextroversion), and impaired function of the frontal eye fields in the presence of homonymous defects (Zihl 1995; Leff et al. 2000; Zihl 2010; Rowe et al. 2011; Stein 2022).

While much of the literature focuses on the gross defects observed following acute stroke, there has been limited work undertaken to investigate the clinical binocular visual status of stroke survivors. This is compounded by a paucity of data on the changes in expected binocular visual measures in older populations, with many authoritative texts reporting normals for pre-presbyopic subjects.

6.2 Methods

Following completion of the refractive elements of the trial battery outlined in **Chapter 5** participants undertook binocular vision testing as part of this study.

A summary of the procedures undertaken in the binocular vision examination can be seen in **Table 6-1**. An overview of these procedures can be found in **Chapter 4**. While masking was in place to the findings of the reference standard examination conducted in **Chapter 5**, the examiner was not masked to the results of the trial battery findings or from the subjects. The results of the cover test at distance and near were drawn from the findings of the trial battery examination. All binocular vision testing was undertaken in free space with the appropriate optimal refractive correction in place.

Tests of ocular alignment	Distance cover test (prism neutralisation) Near cover test (prism neutralisation) Distance Maddox Rod examination Near Thorington Method
Tests of eye movement	Ocular motility (Physiological X) NSUCO Pursuits NSUCO Saccades
Tests of sensory status	Worth 4 spot (Distance) Aligning prism (Distance)* Aligning prism (Near - NV100)* Fixation disparity (Saladin Card)* Aligning prism (Saladin card)* Forced duction curve (Saladin card)* TNO test for stereoscopic vision Stereo Fly Test
Tests of ocular vergence	Near point of convergence (break/recovery) Negative relative vergence - distance Positive relative vergence - distance Negative relative vergence - near Positive relative vergence - near
Tests of fixation disparity	Aligning prism (Distance) Aligning prism (Near - NV100) Fixation disparity (Saladin card) Aligning prism (Saladin card) Forced duction curve (Saladin card)

Table 6-1. Overview of diagnostic tests undertaken with participants within this study. All procedures were undertaken with appropriate distance correction in place. While such a study would frequently include tests of ocular accommodation, all participants within this study were presbyopic, negating the utility of tests of ocular accommodation. * Tests associated with fixation disparity parameters are undertaken in binocular conditions, with loss of sensory fusion being evident by the loss of a monocular target (Scheiman and Wick 2013). It should be noted however that loss of a monocular target may result from other factors such as retinal rivalry and that these tests should not be used in isolation for this purpose.

The aim of this study is to investigate the presence of differences in binocular function between participants with a history of stroke, and a control cohort. A secondary aim was to investigate the impact of field loss upon binocular visual function following stroke.

Test procedure	Average	Variance	Source
Distance cover test (prism neutralisation)	Mean -1.1$^{\Delta}$	SD 2.0$^{\Delta}$	Yekta et al., 2017
Near cover test (prism neutralisation)	Mean -5.0$^{\Delta}$	SD 4.7$^{\Delta}$	Yekta et al, 2017
Distance Maddox Rod examination	Mean -0.2$^{\Delta}$	SD 1.1$^{\Delta}$	Mathebula et al., 2002
Near Thorington Method	Mean -1.0$^{\Delta}$	SD 4.0$^{\Delta}$	Lyon et al., 2005

Table 6-2. Summary of published averages of heterophoria assessment by cover test, Maddox rod & modified Thorington methods in a presbyopic population. Negative values represent exo-deviations

There are limited published normal ranges of the typical parameters of binocular vision tests in older populations. **Table 6-2** provides a summary of the normal range of measures of heterophoria found by the tests employed by this study. **Table 6-3** provides an overview of the expected findings of ocular motility testing employed in this study.

Test procedure	Average	Variance	Source
Ocular motility (Physiological X)	Smooth, accurate & Fully Extensive	-	Carlson & Kurtz, 2004
NSUCO Pursuits (minimal expected)	Ability 5 Accuracy 5 Head movement 4 Body movement 5	-	Maples, 1995
NSUCO Saccades (minimal expected)	Ability 5 Accuracy 4 Head movement 4 Body movement 5	-	Maples, 1995

Table 6-3. Summary of published ocular motility normal data by physiological ocular motility testing and NSUCO oculomotor test. Scoring for the NSUCO saccade and pursuit subtests can be found in **Table 4-2** and **Table 4-3** respectively.

A fair amount of literature has been published on the sensory and stereoscopic measures within older populations, these are summarised in **Table 6-4**. However, testing of ocular convergence and divergence ranges suffers from a lack of research within the presbyopic population, with most measures found in the literature being derived from pre-presbyopic adult, or more frequently child populations (Wajuihian 2019). **Table 6-5** outlines the normal vergence ranges most frequently encountered within the ophthalmic literature, while **Table 6-6** summarises fixation disparity data. Notably, these are mainly derived from pre-presbyopic populations.

Test procedure	Average	Variance	Source
Worth 4 spot (Distance)	Binocular Fusion	-	Carlson & Kurtz, 2004
TNO test for stereoscopic vision	Mean 248 seconds of arc	SD 171.2 seconds of arc	Lee & Koo, 2005
Stereo Fly Test	Mean 94 seconds of arc	SD 60.4 seconds of arc	Lee & Koo, 2005

Table 6-4. Summary of published normals of sensory fusion and stereopsis by TNO & Titmus type stereo fly test in a presbyopic population.

Statistical analysis was undertaken using the commercially available software SPSS (IBM SPSS Statistics for Macintosh, Version 29.0.1.0 Armonk, NY: IBM Corp). The data was analysed to investigate prospective differences between stroke subjects with visual field defects, stroke subjects without visual field defects, control subjects with visual field defects and control subjects without visual field defects. Participants from **Chapter 5** proceeded to undergo this study following completion of the trial battery assessment. The examiner in this study was unmasked to the status of participants. Due to the uneven cohort size, testing of differences between these groups was undertaken using a one-way analysis of ranks (Kruskal-Wallis H test). All quantitative data was assessed for normality using the Shapiro-Wilk test, and analysis was also undertaken between stroke and control cohorts using appropriate testing methods. A significance level of α=0.05 was used throughout. Where post-hoc testing was indicated, a Bonferroni correction was used to reduce the risk of Type I errors, this resulted in a reduced significance value of $\alpha = 0.05/6 = 0.0083$.

Test procedure	Average	Variance	Source
Near point of convergence	Mean 13.06cm	SD 5.06cm	Ostadimoghaddam et al., 2017
Distance negative relative vergence (blur)	-	-	-
Distance negative relative vergence (break)	Mean 7$^{\Delta}$	SD 3$^{\Delta}$	Morgan, 1944
Distance negative relative vergence (recovery)	Mean 4$^{\Delta}$	SD 2$^{\Delta}$	Morgan, 1944
Distance positive relative vergence (blur)	Mean 9$^{\Delta}$	SD 4$^{\Delta}$	Morgan, 1944
Distance positive relative vergence (break)	Mean 19$^{\Delta}$	SD 8$^{\Delta}$	Morgan, 1944
Distance positive relative vergence (recovery)	Mean 10$^{\Delta}$	SD 4$^{\Delta}$	Morgan, 1944
Near negative relative vergence (blur)	Mean 13$^{\Delta}$	SD 4$^{\Delta}$	Morgan, 1944
Near negative relative vergence (break)	Mean 21$^{\Delta}$	SD 4$^{\Delta}$	Morgan, 1944
Near negative relative vergence (recovery)	Mean 11$^{\Delta}$	SD 5$^{\Delta}$	Morgan, 1944
Near positive relative vergence (blur)	Mean 17$^{\Delta}$	SD 5$^{\Delta}$	Morgan, 1944
Near positive relative vergence (break)	Mean 21$^{\Delta}$	SD 6$^{\Delta}$	Morgan, 1944
Near positive relative vergence (recovery)	Mean 11$^{\Delta}$	SD 7$^{\Delta}$	Morgan, 1944

Table 6-5. Summary of published normal ranges of near point of convergence and fusional ranges. Morgan (1944) reported on the results of testing on a range of pre-presbyopic subjects, this data has been reproduced in a number of prominent optometry texts such as Goss (1995), Scheiman and Wick (2013), and Evans (2022)

Ethical approval was obtained for this study from the Health and Life Sciences Ethics Committee of Aston University (#HLS21005) and this study was conducted in accordance with the requirements of the Declaration of Helsinki (2001). All participants provided written consent in advance of undertaking this study.

Test procedure	Average	Variance	Source
Aligning prism (Distance)	-	-	-
Aligning prism (Near - NV100)	Mean -0.086$^{\Delta}$	SD 0.503$^{\Delta}$	Alanazi et al., 2009
Fixation disparity (Saladin card)	Mean -1.9$^{\Delta}$	SD 2.7$^{\Delta}$	Corbett & Maples, 2004
Aligning prism (Saladin card)	Mean -0.096$^{\Delta}$	SD 0.49$^{\Delta}$	Alanazi et al, 2009
Forced duction curve (Saladin card)	-	-	-

Table 6-6. Summary of published normal ranges for Aligning prism using the distance and near testing of Aligning prism using instruments based on the Mallett principle and fixation disparity metrics on the Saladin card. While Ogle (1967) reported on the frequency of forced duction curve types (see **Figure 27**), no data has been published on the findings of fixation disparity curve types using the Saladin card. Negative represents exo-deviations.

6.3 Results

6.3.1 Ocular alignment

Binocular vision testing was undertaken on all participants who completed the investigation undertaken in **Chapter 5**, consisting of 22 participants with a history of stroke and 26 control participants. Most participants exhibited some degree of binocularity, with no cases of intractable diplopia present in either cohort. Sensory suppression was observed in 3 participants from the stroke cohort and 5 participants from the control cohort (Fisher's exact test: p=.706). Of these, 1 participant from the stroke and 3 participants from the control cohort exhibited strabismus (Fisher's exact test: p=.614).

Incomitant eye movements were observed in 3 participants from the stroke cohort, and no participants from the control cohort (Fisher's exact test: p=.089). Of these 3, two had restrictions of abduction of the right eye, and the other exhibited limited abduction of the left eye, with no retraction of the eye on adduction for any participants.

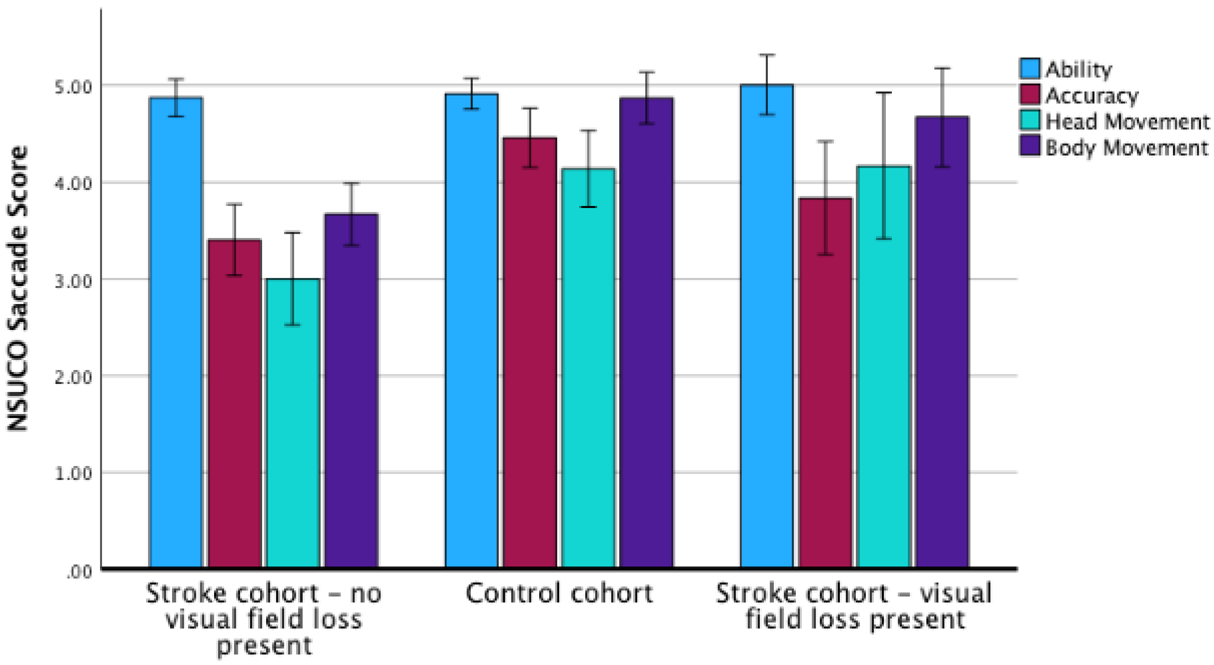


Figure 38. NSUCO Saccade scores observed between cohorts. While most subjects were able to complete the task successfully, subjects from the stroke cohort exhibited greater incidence of saccadic dysmetria than controls. Surprisingly, greater degrees of compensatory head and body movement were observed in stroke subjects without defects than those with defects. Error bars represent 95% CI.

Examination of oculomotor movements using the NSUCO test (Maples 1995) was completed on all participants of the stroke cohort and 22 participants of the control cohort (Fisher's exact test: .239). A summary of saccade scores by cohort can be seen in **Figure 38**. While no significant difference between cohorts was observed on the ability to complete saccadic testing (Kruskal-Wallis H test: χ^2=1.079, df=2, p=.053), differences were observed in saccade accuracy (Kruskal-Wallis H test: $\chi^2$2=11.012, df=2, p=.004), head movement (Kruskal-Wallis H test: χ^2=8.773, df=2, p=.012) and body movement (Kruskal-Wallis H test: χ^2=21.171, df=2, p<.001). Poorer performance was observed in stroke subjects without field defects in both saccadic accuracy (Mann-Whitney U test: p=.002) and the presence of body movement (Mann-Whitney U test: p=<.001), whilst post-hoc assessment of body movement found no significant differences between the different cohorts. Examination of ocular saccades found no significant differences in the ability to complete the necessary cycles between stroke and control groups (Mann-Whitney U test: p=.677). Accuracy of saccadic movements were found to be worse in the stroke cohort (Mann-Whitney U test: p<.001), with increased head (Mann-Whitney U test: p=.026) and body movement (Mann-Whitney U test: p<.001) evident when compared to the control cohort. No differences of saccade ability (Mann-Whitney U test: p=.478), accuracy (Mann-Whitney U test: p=.971), the presence of head movement (Mann-Whitney U test: p=.393) or body movement (Mann-Whitney U test: p=.946) were observed between genders.

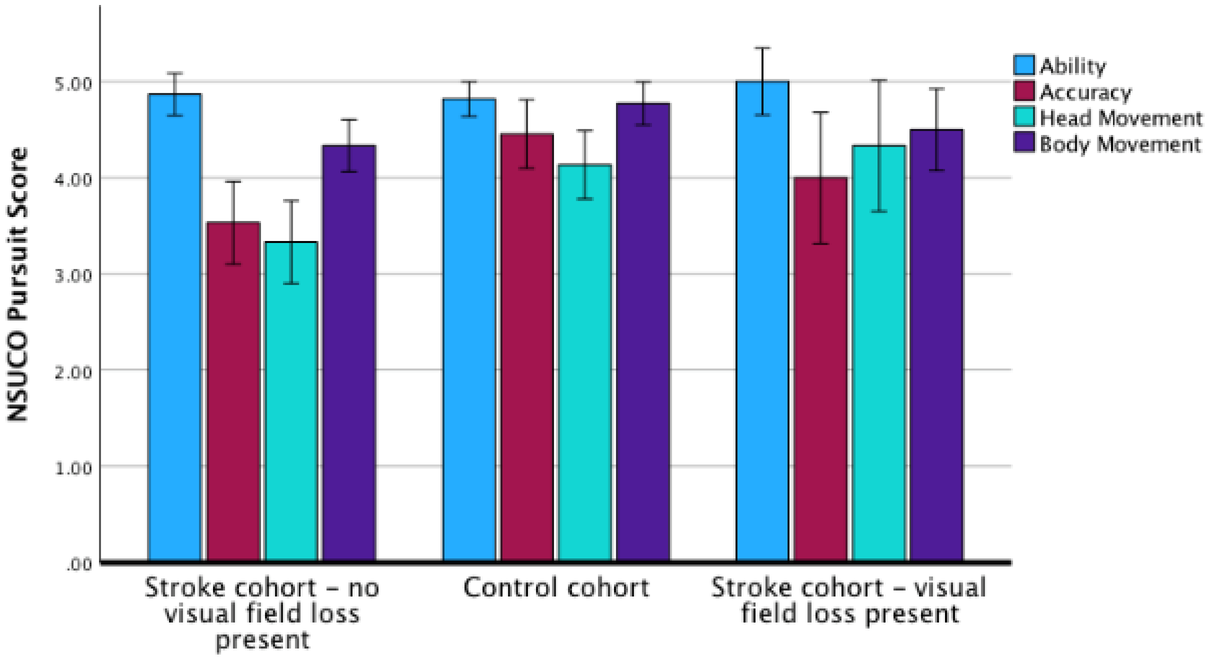


Figure 39. NSUCO pursuit scores observed between cohorts. Similar to the findings of the saccade subtest (**Figure 38**), good completion rates were observed across all cohorts, with greater degrees of refixation and compensatory head movements observed within the stroke subjects without field loss than those with loss and controls.

Assessment of pursuit movements found no significant difference in the ability (Kruskal-Wallis H test: χ^2=2.552, df=2, p=.279), accuracy of completion (Kruskal-Wallis H test: χ^2=5.448, df=2, p=.066), or body movement (Kruskal-Wallis H test: χ^2=5.719, df=2, p=.057) between cohorts when considering the presence of field loss. A summary of Pursuit scores can be seen in **Figure 39**.

While difference was found on head movement (Kruskal-Wallis H test: χ^2=6.014, df=2, p=.047), post hoc testing between groups did not reach significance. Assessment between stroke and control cohorts found no significant difference in subject's ability (Mann-Whitney U test: p=.677) to complete the task, but again accuracy (Mann-Whitney U test: p=.110) was found to be reduced in the stroke cohort. While no significant head movement was present (Mann-Whitney U test: p=.156) between cohorts, body movement was observed more frequently within the stroke cohort (Mann-Whitney U test: p=.011). No difference was observed between the performance of the different genders for ability (Mann-Whitney U test: p=.773) or accuracy (Mann-Whitney U test: p=.605) of pursuits, or the presence of head (Mann-Whitney U test: p=.122) or body movement (Mann-Whitney U test: p=.623) during testing.

No significant differences in distance cover test results were observed between cohorts (Kruskal-Wallis H test: χ^2=.192, df=3, p=.979), similarly no difference was observed between stroke and control subjects (Mann-Whitney U test: p=.094) or gender (Mann-Whitney U test: p=.462).

Similarly assessment of distance heterophoria using the Maddox rod found no significant difference between cohorts for either vertical (Kruskal-Wallis H test: χ^2=5.872, df=3, p=.118) or horizontal deviations (Kruskal-Wallis H test: χ^2=5.138, df=3, p=.162), and no difference was observed between stroke and control subjects for horizontal (Mann-Whitney U test: p=.983) deviations measured, vertical deviations measured (Mann-Whitney U test: p=.736), or indeed between genders (Mann-Whitney U test: p=.709).

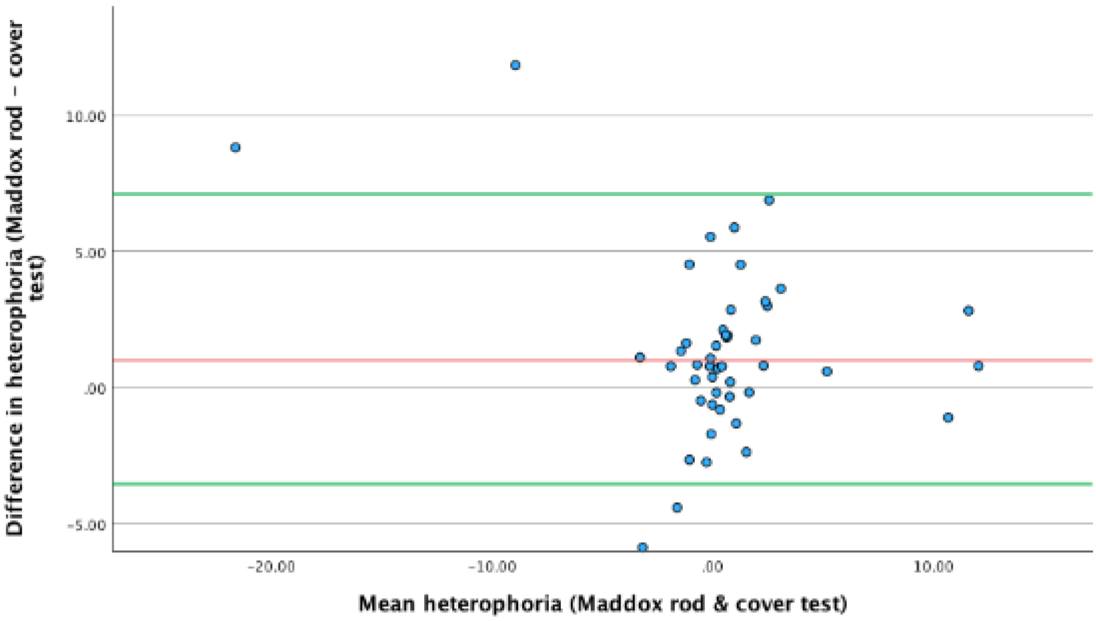


Figure 40. Difference plot of findings between the distance Maddox rod and distance prism cover test results. Maddox rod obtained measures that were relatively more esophoric than the cover test (median difference +1.00$^{\Delta}$) with 90% of observed measurements falling between -3.55$^{\Delta}$ and 7.10$^{\Delta}$. Minus represents relative exophoria.

When assessing the degree of heterophoria present in distance viewing, significant differences were observed between the different techniques used to measure horizontal heterophoria (Friedman test: χ^2=72.989, df=3, p<.001) but not for vertical measures (Friedman test: χ^2=.474, df=3, p=.925). Moderate association was found between the measurements of heterophoria using the prism cover test and the Maddox rod (Spearman's rho: r=.426, N=48, p=.003). While no significant difference in median measures was found in the difference between the techniques for measures of vertical ocular deviations (Wilcoxon signed rank test: z=-.085, p=.932). The Maddox rod was found to be relatively more esophoric than the cover test (Wilcoxon signed rank test: z=-2.585, p=.010). A difference plot (Bland

and Altman, 1986; 1999) of the findings of the Maddox rod test and prism cover test at distance can be seen in **Figure 40**. At near, greater exophoria was observed using the Thorington method compared to the cover test to assess horizontal heterophoria (Wilcoxon signed rank test: z=-3.593, p<.001), though no significant difference was observed between vertical measures (Wilcoxon signed rank test: z=-.412, p=.680).

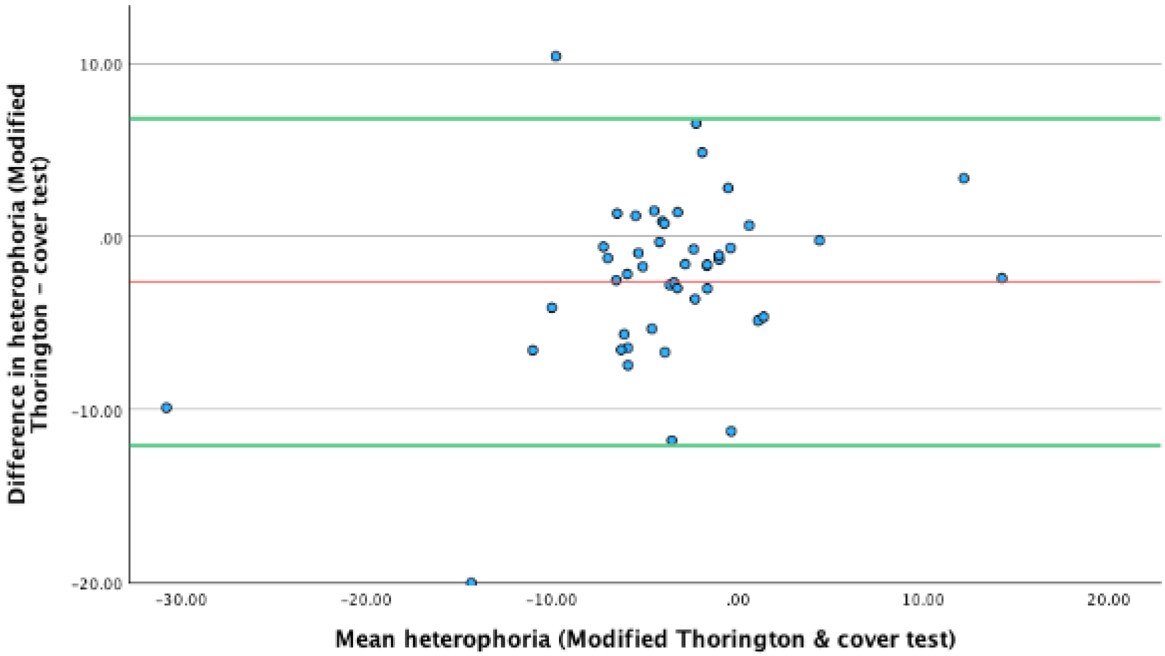


Figure 41. Difference plot of near heterophoria measured using the Thorington method and prism cover test. The Thorington's method exhibited greater degrees of exophoria than the cover test (mean -2.64$^{\Delta}$), with limits of agreement ranging from -12.07$^{\Delta}$ to +6.80$^{\Delta}$ (95%CI 0.09$^{\Delta}$). Minus represents relative exophoria.

Greater degrees of exophoria were observed at near compared to distance viewing, this was observed using both prism cover test (Wilcoxon signed rank test: z=-4.455, p<.001) and Maddox rod based (Wilcoxon signed rank test: -5.807, p<.001) methods. When assessing the degree of heterophoria present in near viewing using the cover test, no significant difference was observed between cohorts (Kruskal-Wallis H test: χ^2=.352, df=3, p=.950), this was similar between stroke and control groups (Mann-Whitney U test: p=.880), and between genders (Mann-Whitney U test: p=.103). Similarly assessment using the Thorington method found no significant difference between cohorts (Kruskal-Wallis H test: x^2=4.967, df=3, p=.174), genders (Mann-Whitney U test: p=.909) or between stroke and control subjects (Mann-Whitney U test: p=.194).

Moderate association was found between the measurements of heterophoria using the prism cover test and Thorington's method (Spearman's rho: r=.552, N=47, p=<.001). Similar to the comparison of cover test and Maddox rod at distance, Thorington's method was found to elicit greater degrees of exophoria at near than the cover test (Wilcoxon signed rank test: z=-3.593, p<.001), a difference plot can be seen in **Figure 41**. While significant differences in findings between methods were observed for horizontal deviations at near, no difference in vertical findings were observed (Wilcoxon signed rank test: $z=-.412$, $p=.680$).

6.3.2 Vergence

6.3.2.1 Distance Fusional Reserves

Vergence measurements were completed in 39 participants. A summary of vergence data can be observed in **Table 6-7**. When undertaking testing of divergence ranges in distance viewing, 23 participants did not describe a blur point, but instead reported the image going from clear to diplopic without blur; this was not found to differ between cohorts (Fisher's exact test: p=.528). A similar finding was observed when undertaking convergence ranges in 14 participants (Fisher's exact test: .772). The blur point was less frequently observed by participants during divergence testing than convergence testing (McNemar test: p=.035).

		Heterophoria (cover test)	Heterophoria (Maddox rod)	NRV Blur	NRV Break	NRV Recovery	PRV Blur	PRV Break	PRV Recovery
Stroke Cohort	**Distance**	-0.09±4.48	1.05±3.05	1.00±.82	6.50±2.52	4.00±2.83	6.50±3.00	12.50±3.41	8.00±2.82
	Near	-2.71±4.61	-4.19±3.10	8.50±6.61	14.00±5.88	10.50±6.60	9.50±4.12	14.00±5.89	10.00±5.88
Control Cohort	**Distance**	-0.19±6.03	0.87±5.41	3.33±1.15	8.00±2.00	4.00±2.00	4.00±2.00	15.33±5.03	7.33±1.15
	Near	-2.34±6.83	-5.92±9.59	10.66±6.11	16.66±4.16	12.00±5.29	8.66±4.16	18.33±7.63	5.33±5.03

Table 6-7. Means and standard deviations for heterophoria by prism cover test, Maddox rod-based methods (Maddox rod at distance and modified Thorington test at near) and fusional reserve data in prism diopters ($^{\Delta}$). Negative numbers represent exo- deviations, while positive numbers represent eso- deviations. NRV negative relative vergence, PRV positive relative vergence.

No significant differences were observed between cohorts for the degree of prism required to elicit blur (Kruskal-Wallis H test: χ^2=3.453, df=2, p=.178), break (Kruskal-Wallis H test: χ^2=3.147, df=2, p=.207), or recovery of single vision (Kruskal-Wallis H test: χ^2=3.479, df2, p=.176). When comparing stroke and control subjects directly no significant differences in divergence ranges were found, with the stroke cohort exhibiting a lower amount of prism required to elicit blur (unpaired T-test: t=-1.389, df=14, p=.186) and break to diplopia (unpaired T-test: t=-.983, df=37, p=.332) than the control cohort with similar points of recovery of fusion (unpaired T-test: t=.510, df=37, p=.613). Where present, while the degree of prism that elicited blur was lower than the prism to bring about recovery, this difference was not found to be significant (paired T-test: t=-1.754, df=15, p=.100). No significant differences were observed between genders for prism required to bring about blur (unpaired T-test: t=.000, df=14, p=1.000), diplopia (unpaired T-test: t=.266, df=37, p=.792) or recovery (unpaired T-test: t=1.173, df=37, p=248) of single vision.

No significant difference was observed for blur (Kruskal-Wallis H test: χ^2=1.707, df=2, p=.426), break (Kruskal-Wallis H test: χ^2=1.689, df=2, p=.430) or recovery (Kruskal-Wallis H test: χ^2=1.711, df=2, p=.425) of convergence ranges between cohorts. Comparing stroke and control subjects no significant difference in degree of convergence induced by prism to elicit blur (unpaired T-test: t=.871, df=23, p=.393), bring about a break to diplopia (unpaired T-test: t=-.510, df=37, p=.613) or the prism power that re-established fusion (unpaired T-test: t=-.028, df=37, p=.978) was found. Where present the prism power that elicited blur was found to be lower than that to recover fusion (paired T-test: t=-3.302, df=24, p=.003). While convergence ranges were found to be slightly lower in female subjects for blur (unpaired T-test: t=1.792, df=23, p=.086) and break (unpaired T-test: t=1.722, df=37, p=.094), they were significantly lower in prism required to re-establish binocular viewing (unpaired T-test: t=2.209, df=37, p=.033).

When testing for near divergence ranges, 12 participants did not experience blur with any prism before diplopia occurred (Fisher's exact test: p=.085), while for convergence no blur point was reported by 23 participants (Fisher's exact test: p=.081), participants who did not experience blur during divergence were not significantly more likely to observe it during convergence (McNemar test: p=.774).

6.3.2.2 Near Fusional Reserves

Similar to the findings of distance vergence ranges, no significant differences between cohorts were observed for the measure of blur (Kruskal-Wallis H test: χ^2=3.305, df=2, p=.192), break (Kruskal-Wallis H test: χ^2=2.463 df=2, p=.292) or recovery (Kruskal-Wallis H test: χ^2=3.170, df=2, p=.205) when assessing near divergence ranges. This was consistent when considering stroke and control subjects, with no significant difference observed for break point (unpaired T-test: t=-.937, df=37, p=.355), or prism to re-establish fusion (unpaired T-test: t=.666, df=37, p=.510). While no significance was observed in the difference between cohorts for the degree of prism that elicited blur (unpaired T-test: t=.116, df=18, p=.909) Levene's test indicated unequal variances (F=8.056, p=.007), further non-parametric investigation failed to identify any difference between cohorts (Mann-Whitney U test: p=.943). Where blur was experienced, similar to distance viewing, the degree of prism that brought about blur was found to be lower than that required to re-establish fusion after diplopia had been elicited (paired T-test: t=-3.513, p=.002). No significant differences were observed between genders in the prism required to elicit blur (unpaired T-test: t=-.730, df=25, p=.472), break (unpaired T-test: t=.082, df=37, p=.935), or recovery (unpaired T-test: t=1.062, df=37, p=.295) of binocularity

While convergence ranges at near varied, once more no significant differences were observed between cohorts for the prism required to elicit blur (Kruskal-Wallis H test: χ^2=5.562, df=2, p=.062), bring about diplopia (Kruskal-Wallis H test: χ^2=1.928, df=2, p=.381) or recover from diplopia (Kruskal-Wallis H test: χ^2=1.760, df=2, p=.415). The stroke cohort exhibited (where present) greater degrees of prism required to elicit blur (unpaired T-test: t=-.689, df=21, p=.498) and to re-establish binocular viewing (unpaired T-test: t=1.279, df=37, p=.209), while the control cohort required greater degrees of prism to bring about diplopia (unpaired T-test: t=-.831, df=37, p=.411), though these were not significant. No significant differences were observed between genders for the prism required to elicit blur (unpaired T-test: t=.946, df=21, p=.355), break to diplopia (unpaired T-test: t=.415, df=37, p=.680) or recovery (unpaired T-test: t=1.093, df=37, p=.680) of binocularity. As with previous testing, the degree of prism required to re-establish binocular vision was greater than that which brought about blur, though this was not found to be significant (paired T-test: t=-1.382, df=22, p=.181).

Where observed moderate association was found between the near divergent and convergent blur (Spearman's rho: r=.482, N=18, p=.043) and break points (Spearman's rho: r=.408, N=39, p=.010), No significant difference was observed between the degree of prismatic lens that elicited (where present) the blur (paired T-test: t=.475, df=17, p=.641) or break down of binocular vision to diplopia (paired T-test: t=.811, df=38, p=.422).

6.3.2.3 Fusional Stamina

No significant difference was observed between cohorts for fusional stamina measured at distance (Kruskal-Wallis H test: χ^2=1.547, df=2, p=.462) or near (Kruskal-Wallis H test: χ^2=.920, df=2, p=.631), where esophoric subjects were removed no significant differences were observed in fusional stamina between cohorts at distance (Kruskal-Wallis H test: χ^2=3.540, df=2, p=.170) or near (Kruskal-Wallis H test: χ^2=3.540, df=2, p=.170). Similarly, no significant differences in fusional stamina were observed more generally between stroke survivors and controls at distance (Mann-Whitney U test: p=.418) or near (unpaired T-test: t=.761, df=38, p=.451). A summary of fusional stamina measures can be found on **Table 6-8:** Fusional stamina between stroke and control cohorts.

Fusional Stamina		**All subjects (n=39)**	
		Mean values (SD)	95% CI
Stroke cohort	Distance	0.40$^{\Delta}$ (4.11$^{\Delta}$)	-1.52$^{\Delta}$- 2.32$^{\Delta}$
	Near	-0.80$^{\Delta}$ (3.87$^{\Delta}$)	-2.61$^{\Delta}$- 1.01$^{\Delta}$
Control cohort	Distance	1.77$^{\Delta}$ (3.63$^{\Delta}$)	0.16$^{\Delta}$- 3.38$^{\Delta}$
	Near	-1.22$^{\Delta}$ (3.75$^{\Delta}$)	-2.87$^{\Delta}$- 0.42$^{\Delta}$

Table 6-8: Fusional stamina between stroke and control cohorts.

6.3.2.4 Near Point of Convergence

Like vergence ranges, near point of convergence ranges exhibited no significant difference between cohorts for push-up (Kruskal-Wallis H test: χ^2=.371, df=2, p=.831) or pull down (Kruskal-Wallis H test: χ^2=.304, df=2, p=.859) methods of convergence testing.

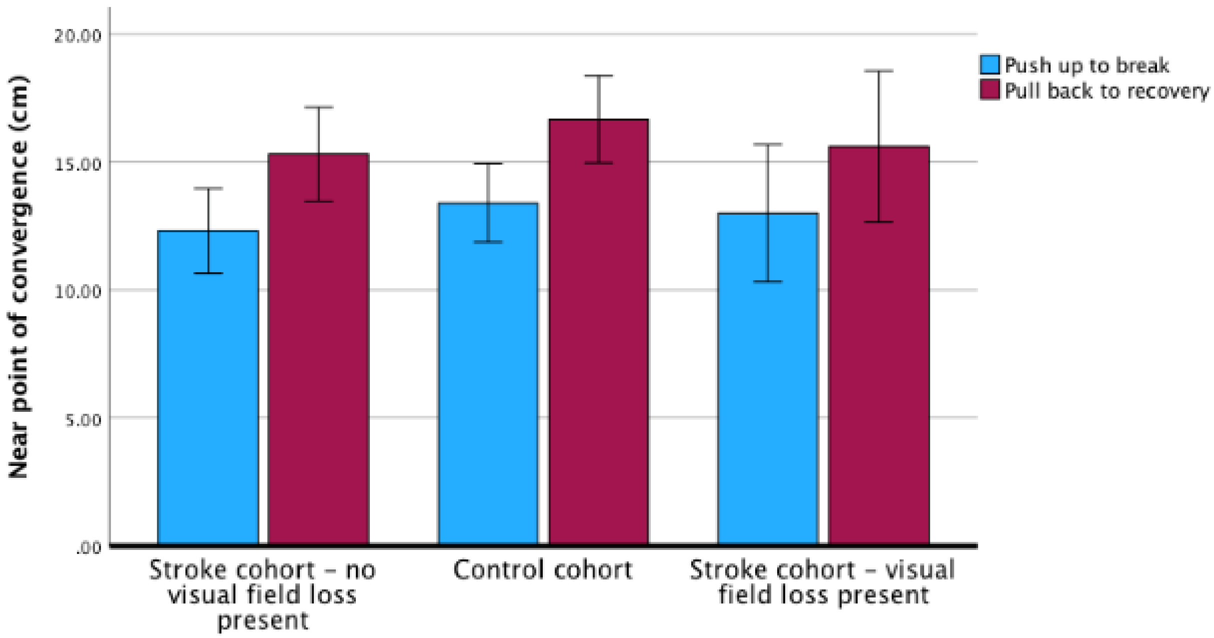


Figure 42. Results of near point of convergence break and recovery measures for stroke and control participants. Error bars represent 95% confidence intervals.

Within the group of stroke subjects, the near point of convergence by push up method was found to break to diplopia at 12.1cm (SD +/-5.34cm), while control cohort were found to have a more proximal breakpoint of 10.05cm (SD +/-6.54cm), these differences were not found to be significant (unpaired T-test: t=1.112, df=40, p=.273) and no differences were observed between genders (unpaired T-test: t=-.038, df=40, p=.970). A summary of findings can be seen on **Figure 42**. Strong association was observed between the measures found for near point of convergence by push up, and the recovery by the pull down method (Spearman's rho: r=.838, N=33, p<.001).

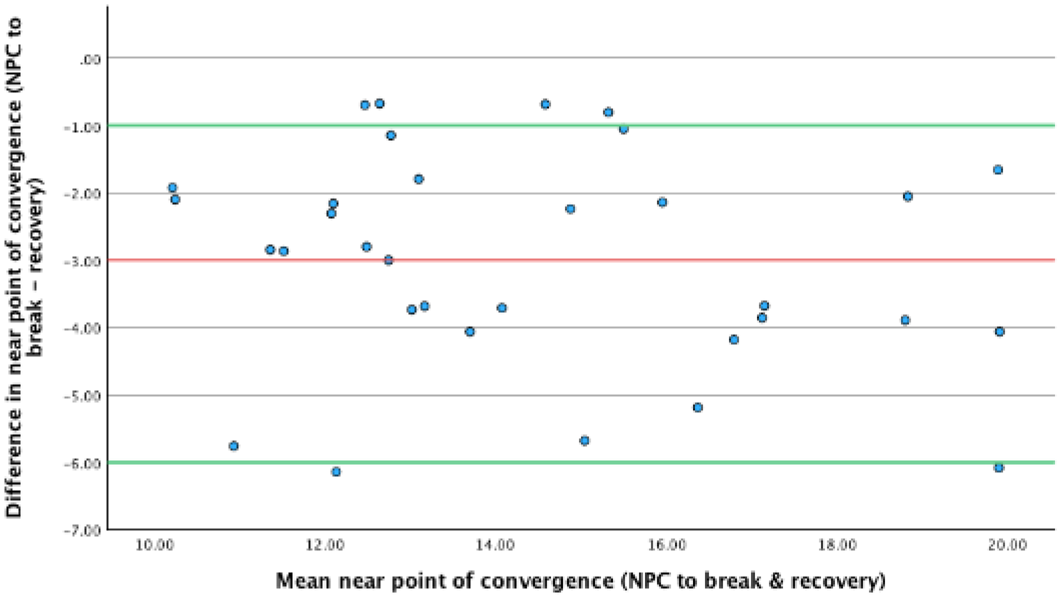


Figure 43. Difference plot of near point of convergence break and recovery points. Recovery of vergence was more remote than the break point (median difference -3.00cm), with 90% of observed differences in measures falling between -6.00cm and -1.00cm.

The near point where vergence was reestablished by the pull down method was found to be lower in both cohorts (Friedman test: χ^2=33, df=1, p<.001) with a mean difference -3.06cm, occurring at 15.39cm (SD +/-2.30cm) in the stroke cohort and 16.67cm (SD +/-3.97) in the control cohort. No significant difference was found to occur between stroke subjects and control subjects (Unpaired t test: t=-1.100, df=21.544, p=.283), or between genders (unpaired T-test: t=1.779, df=31, p=.085). A difference plot of the near point of convergence break and recovery can be seen in **Figure 43**.

Near point of convergence break was found to have moderate correlation with the break point of positive relative vergence for near (Spearman's rho: r=-.402, N=38, p=.012), no association was observed between positive relative vergence findings and the near point of convergence recovery. Near point of convergence break and recovery points were found to have moderate association with both the break (Spearman's rho: r-.584, N=38, p<.001 and Spearman's rho: r=-.467, N=30, p=.009 respectively) and recovery (Spearman's rho: r=-.570, N=38, p<.001 and Spearman's rho: -.459, N=30, p=.011 respectively) point of negative relative vergence.

6.3.3 Stereopsis

Stereopsis was successfully measured in 12 participants from the stroke cohort, and 13 participants from the control cohort using the TNO test for stereoscopic vision, with the remaining participants unable to identify any stereoscopic target (Fisher's exact test: p=.780). For those participants able to achieve a degree of stereopsis, no significant difference was observed between cohorts (Kruskal-Wallis H test: χ^2=5.519, df=2, p=.063). Mean stereoacuity achieved was found to be 160 seconds of arc (SD ±123.52) for participants with a history of stroke, and 150 seconds of arc (SD ± 79.37) in control subjects. No significant differences were observed between stroke and control subjects (Mann-Whitney U test: p=852) or between genders (Mann-Whitney U test: p=205).

Using the Stereo Fly Test, a greater number of the stroke cohort were able to achieve a measure of stereoacuity (McNemar test: p=.008), stereopsis was measured in 17 subjects with a history of stroke and 16 control subjects (Fisher's exact test: p=.106). No significant differences were observed between cohorts (Kruskal-Wallis H test: χ^2=.241, df=2, p=.886), with mean measures of stereopsis of 60.83 seconds of arc (SD ± 25.03) in stroke subjects and 79.23 seconds of arc (SD ± 35.93) in control subjects. Again, no significant difference was observed between subjects (Stroke subjects: 50 seconds of arc, IQR 50, Control subjects: 60 seconds of arc, IQR 50; Mann-Whitney U test: p=.731), or gender (Mann-Whitney U test: p=503).

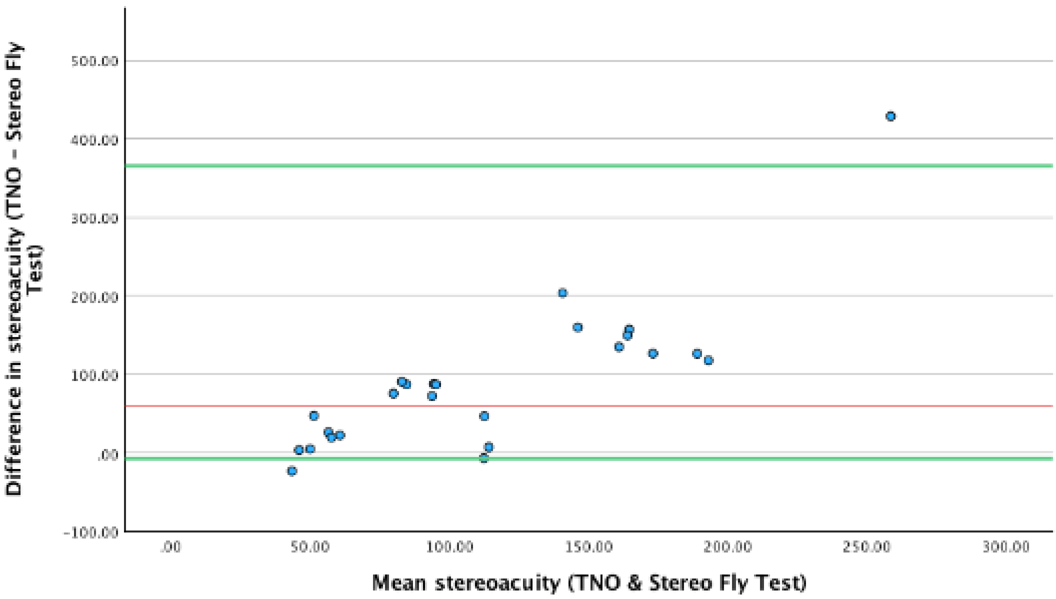


Figure 44. Difference plot of the findings of the TNO test for stereoscopic vision and the Stereo Fly Test. The TNO test exhibited greater stereoacuity scores than the Stereo Fly Test (median 60 seconds of arc), with 90% of observed differences in measurements falling between -7 seconds of arc and +365 seconds of arc.

The findings of the TNO test and Titmus fly test of stereopsis were found to have moderate correlation (Spearman's rho: r=.567, N=25, p=.003), though where participants were able to see both the TNO, and the Titmus fly test, the stereoacuity elicited by the Titmus fly test was found to be significantly lower than that found using the TNO Test (Wilcoxon sign ranked test: z=-4.259, p<.001), a difference plot of the stereoacuity measured by TNO and the Stereo Fly test can be seen on **Figure 44**.

6.3.4 Fixation Disparity Analysis

Aligning prism as measured on the distance fixation disparity test, was achieved in 19 participants of the stroke cohort and 20 participants of the control cohort. While a greater range of prism required to bring about alignment were observed within the stroke cohort (Median: 0.00^{Δ} IQR: 1.25^{Δ}) than the control (Median: 0.00^{Δ} IQR: $.50^{\Delta}$), no difference was observed between cohorts (Kruskal-Wallis H test:

χ^2=.268, df=2, p=.875). This was also the case when considering the stroke and control subjects (Mann-Whitney U test: p=.759) or gender (Mann-Whitney U test: p=512).

Cohort	Type I curve	Type II curve	Type III curve	Type IV curve
Stroke subject - no field loss	3	1	5	3
Stroke subject - field loss	5	0	0	1
Control subject - no field loss	10	2	2	1

Table 6-9. Distribution of curve types obtained using the Saladin card for the stroke cohorts with and without the presence of visual field loss and control cohorts without field loss. No forced duction curve could be plotted for the two control subjects with field loss due to insufficient data.

A single participant was observed within the control cohort to require vertical prism correction, while 3 participants were observed to require vertical correction within the control cohort (Fisher's exact test: p=.320). Less variation of aligning prism was observed in near viewing with the near vision test unit, with Median (0.00$^{\Delta}$) and Interquartile range (1.00$^{\Delta}$) being similar across the cohort groups (Kruskal-Wallis H test: χ^2=.642, df=2, p=.726) and between stroke and control subjects (Mann-Whitney U test: p=.668) and between genders (Mann-Whitney U test: p=840). Of the three participants from the control cohort found to require vertical aligning prism at distance, only two of these were found to require prismatic correction to bring about alignment at near, no difference was observed in the stroke cohort (Fisher's exact test: p=.587).

Forced duction curves were plotted for 18 participants from the stroke cohort and 15 participants from the control cohort (Fisher's exact test: p=.118), a summary of the profile of the forced duction curves as described by Ogle et al (1967) can be seen on **Table 6-9**.

While no differences were observed between cohorts (Kruskal-Wallis H test: χ^2=2.235, df=2, p=.327), fixation disparity as measured by the Saladin card was found to be more exophoric in stroke subjects though this was not significant (Mann-Whitney U test: p=.443) and no difference was observed between genders (Mann-Whitney U test: p=.888). By contrast, a greater degree of exo-slip was found in control subjects when assessing for Aligning prism (Mann-Whitney U test: p=.439), though this was not found to be significant between cohorts (Kruskal-Wallis H test: χ^2=.859, df=2, p.651), or between genders (Mann-Whitney U test: p=.735). A summary of these findings can be found in **Table 6-10**.

	Stroke		Control	
	Median	**Interquartile range**	**Median**	**Interquartile range**
Forced duction curve - Fixation Disparity	-1.50	2.00	0.00	1.50
Forced duction curve - Aligning prism	-1.00	4.00	-2.00	3.00
Sheedy's criterion	0.00	2.00	0.00	1.00
Near vision test unit - Aligning prism	0.00	1.00	0.00	1.00

Table 6-10. Summary of forced duction & near Mallett unit findings of fixation disparity and aligning prism in prism diopters ($^{\Delta}$). Exo-deviations are denoted as negative.

Moderate association was found between the measurements of Aligning prism found on the near vision test unit and Saladin card (Spearman's rho: r=.415, N=31, p=0.020), however the Saladin card was found to measure greater degrees of exo-slip compared to the aligning prism found with the near vision test unit (Wilcoxon signed rank test: z=-2.299, p=.021), a difference plot can be seen on **Figure 45**.

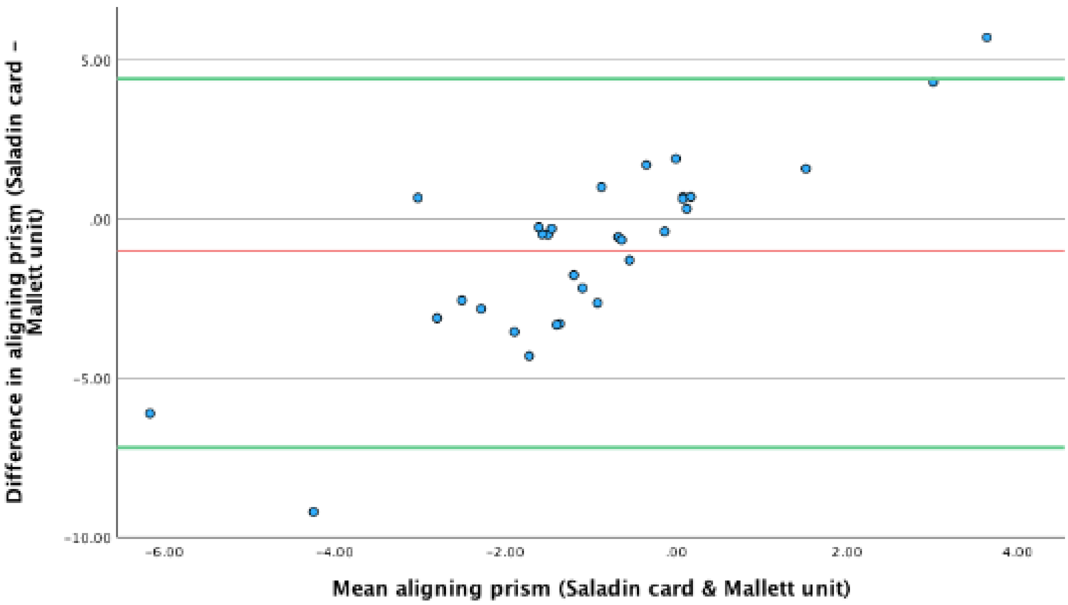


Figure 45. Difference plot of aligning prism measured between the Saladin card and the near vision test unit. Greater degrees of exo-slip were observed with the Saladin card compared to the near vision test unit (median -1.00$^{\Delta}$), with 90% of observed differences falling between -7.20$^{\Delta}$ and +4.40$^{\Delta}$.

A strong association was found between the measurement of fixation disparity as measured on the Saladin card and the measurement of aligning prism on the near vision test unit (Spearman's rho: r=.635, N=36, p<.001). Fixation disparity was found to exhibit slightly greater degrees of exo-slip than Aligning prism found on the near vision test unit (mean -0.16D), and lower variation than that found between the near vision unit and the Saladin card's Aligning prism measurement, difference plot can be seen on **Figure 46**.

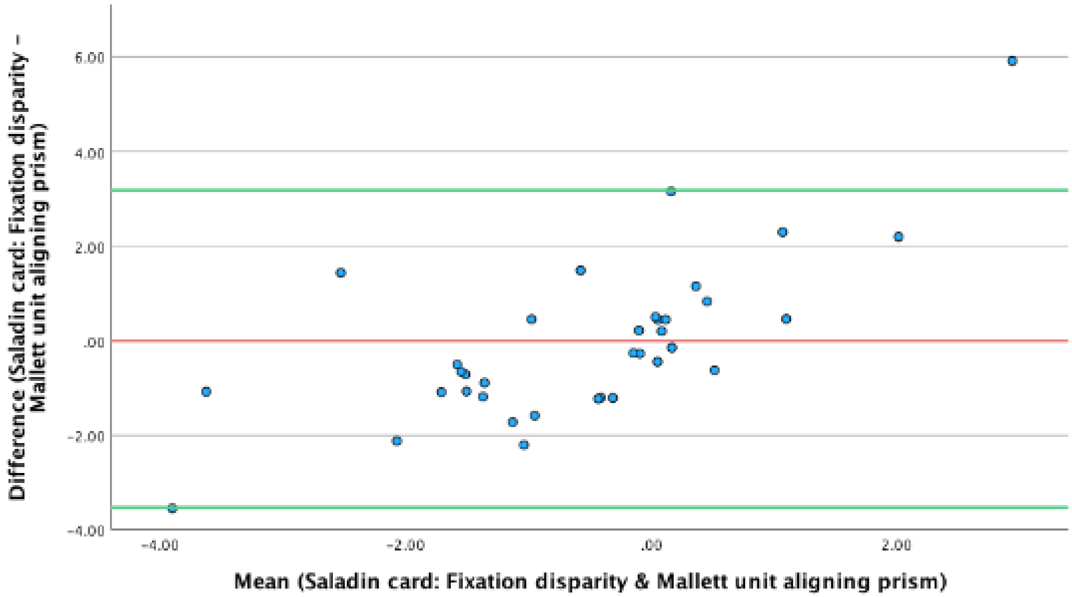


Figure 46. Difference plot of fixation disparity measured by the Saladin card and Aligning prism measured by the near vision test unit. Greater agreement was observed between these measures than aligning prism measures, with a median difference of 0.00Δ and 90% of observed differences falling between -2.30Δ and +3.18Δ.

6.4 Discussion

While an important aspect of optometric practice, the provision of binocular vision and orthoptic care suffers from a weak evidence base to support many elements of contemporary practice (Barrett, 2014). Indeed, most elements of normative data describing the parameters of normal binocular vision are derived from child or young adult populations (Jiménez et al. 2004; Wajuihian 2019), and rarely from presbyopic populations (Freier and Pickwell 1983; Palomo Álvarez et al. 2006). This study is the first prospective study to investigate the oculomotor, vergence and fixation disparity of the visual system of stroke survivors in detail with an age matched control. Given the typical occurrence of stroke is in later life, this study had an older mean age than many published works in binocular vision.

While the prevalence of oculomotor anomalies present in the stroke cohort in this study is comparable to previously reported figures (Ciuffreda et al. 2007; Rowe 2010a), a greater prevalence of oculomotor deficits were observed in the stroke cohort than previously reported in the literature. Both saccade and pursuit eye movements are initiated and mediated by multiple cortical centres that have the potential to be damaged following stroke (Ventura et al. 2014). Given the range of cortical regions involved in this regulation and coordination, it is unsurprising that differences were noted between stroke and control cohorts. While the presence of field defects was observed to be associated with poorer saccade and pursuit performance than controls, it was unexpected that greater deficits would be observed in those stroke survivors without field loss. The presence of field defects have previously been reported to interfere with the planning and execution of saccades, especially in rightward eye movements, impeding accurate refixation and potentially interfering with reading ability (Leff et al. 2000; Zihl 2010; Rowe et al. 2011; Howard et al. 2022). The use of observational tests to assess eye movements has been controversial due to their subjective nature and repeatability (Vinuela-Navarro 2018). Due to the small movements being undertaken, concerns have been raised that only significant deficits of ocular motility are observed, with subtle signs missed. Given the subjective nature of these tests, significant concerns are present over both their repeatability and inter-clinician consistency. While the NSUCO test reports high interrater reliability and test-retest repeatability (Maples and Ficklin 1988; Maples 1995), it exhibits an age specified test ceiling of 17 years, and few independent studies have been undertaken to assess its validity, none of which have been used to examine the target demographic of this study. While anomalies of saccadic and pursuit eye movements were observed and recorded quantitatively, a limitation in this study was the lack of qualitative characterization of the deficits observed, with dysmetria not classified as deficits of overshoot (hypermetric) or undershooting (hypometric), while pursuit movement deficits were not classified specifically by direction.

Examination of the eye frequently incorporates assessment of heterophoria to investigate binocular vision anomalies. While a poor indicator of compensation (Jenkins et al. 1989), the size of heterophoric deviation is useful in aiding in the classification of anomalies detected. Oculomotor measures found in this study were similar to previously published measures, though a greater spread was observed. Like published results, Maddox rod assessment of heterophoria exhibited relatively more esophoric posture compared to the prism neutralised cover test at distance viewing, conversely at near the Maddox rod based methods exhibited relatively more exophoria than the equivalent prism neutralised cover test results.

The Maddox rod (and similar dissociative tests) operate by creating complete dissociation through the unusual visual environment created. While the deviation may be greater than that observed by cover test, except for identification of subtle vertical deviations is of limited use in clinical prescribing (Evans 2005), and subject to fair variability (Schroeder et al. 1996). The non-accommodative nature may explain in part the greater degrees of exophoria observed compared to the cover test. In the absence of an accommodative stimulus at near, the convergence response expected with the near triad is unlikely to be initiated, resulting in lower accommodative-convergence and subsequently greater degrees of exophoria at near viewing.

Inadequate convergence at near has been associated with a range of near vision difficulties, especially in younger subjects (Borsting et al. 2003; Scheiman et al. 2008; Ghadban et al. 2015; Scheiman et al. 2020; Darko-Takyi et al. 2022). Where poor convergence is present, ocular coordination at near is expected to be impaired, resulting in possible symptoms of asthenopia, near diplopia and possibly affecting quality of life. Ostadimoghaddan et al, (2017) undertook an investigation into the normal near point of convergence with increasing age, finding a steady increase in the proximal near point before binocular fixation was lost. This study found a similar near point of convergence to this work, surprisingly without significant difference between the different cohorts. Similarly, while vergence ranges were found to be lower than previously published ranges, no significant difference was observed between cohorts.

In a clinical intervention study Schow et al (2016) undertook orthoptic therapy on stroke patients with binocular vision anomalies, recording their progress over 40 vision therapy sessions conducted over a four-month period. While these subjects will have been included within this study due to the presence of symptoms of binocular vision dysfunction, the baseline characteristics reported are similar to those observed in this study, exhibiting reduced vergence ranges compared to published normals. Unfortunately, no control group was present within this study, so while this work reports the improvement of binocular parameters, it is unclear whether the subject's symptoms may have been attributable solely to these measures. The results of this section are limited, fusional vergence testing is a challenging test to investigate and assess normative data upon, as variability exists between test-retest values, as well differences in instructions, instrumentation (Antona et al. 2008; Lança and Rowe 2019), and potential fatigue due order of testing (Rosenfield et al. 1995; Koslowe et al. 2010; Askarizadeh et al. 2022). While the latter two points should have limited impact upon this study as all subjects underwent binocular testing in consistent order with the same instructions, the former does impact upon the confidence of measures, something that would be improved with larger sample size.

While loss of stereoacuity has been previously reported post stroke, with an estimated 1 in 5 reported to be stereo blind (Ross 1983), it has been reported that injury to the right hemisphere gives rise to anomalies of global and local stereopsis (Ross 1983). Separate assessment of stereo disparity using augmented reality identified similar levels of stereoscopic vision as in healthy subjects (Höhler et al. 2021), similarly this study found no significant differences between the stereoacuity of participants from the stroke or control cohorts in either test.

While insensitivity to stereoscopic targets was frequent across both cohorts, where stereopsis was present, improved sensitivity was found using the Stereo Fly Test compared to the TNO Test. As was observed in **Figure 44** stronger agreement was observed at lower test measures while the disparity was increased at higher measures of stereoacuity. Previous studies investigating the difference between the TNO test and other tests of stereoacuity using polarised filters found similar results (Simons 1981; Antona et al. 2015; Vancleef et al. 2017), with disparity increasing with increased stereoscopic threshold estimates. While better stereoacuity was observed on the Stereo Fly Test, two factors should be considered. While the TNO test is a global stereopsis test requiring the integration, identification and perception of corresponding points within complex imaging, the Stereo Fly test is a test of local stereopsis, requiring matching of image simple image features without issues of correspondence.

Although the loss of stereopsis would be expected to negatively impact the ability to perform activities of daily living (Dhital et al. 2010; Mehta and Baig 2025), there remains some debate regarding the functional significance of reduced stereoacuity (Fielder and London 1996; Kuang et al. 2005). Studies have shown that stereoacuity declines with increasing age (Lee and Koo 2005), with a substantial proportion of older adults demonstrating impaired stereoacuity, and up to 30% exhibiting no measurable stereopsis (Wright and London 1992). Notably, a reduction in stereoacuity to worse than 85 seconds of arc has been associated with an increased risk of falls (Mehta et al. 2022). While the present study did not find a significant difference in stereoacuity between stroke survivors and control participants, the high prevalence of impaired stereopsis observed emphasises the importance of stereopsis assessment in clinical care, particularly when managing older populations.

There is some debate to the nature of stereopsis with some schools of thought suggesting that two separate systems of stereo processing occur. This suggests that processing of global and local stereopsis occur using separate pathways, citing cases where local stereopsis survives in the absence of global stereo perception (Rose and Price 1995; Momeni-Moghaddam et al. 2014; Chopin et al. 2021). This view is challenged by studies that have found transfer of improvement in global stereopsis following training and exposure to local stereoscopic cues, suggesting a single mechanism with two interacting stages (Chopin et al., 2021; Gantz & Bedell, 2010). A recently proposed model (Ding and Levi 2021) suggests that stereopsis arises because of simultaneous spatial frequency selective pathways for luminance and secondary pathways for disparity. This model proposes that correspondence is checked across these two pathways, beginning with lower spatial frequencies where disparity is likely to be more easily detected, before filtering at successively higher frequencies, using this matching to support disparity detection at higher spatial frequencies.

The Wirt circle type target used within the Stereo Fly Test suffers from the presence of monocular cues to the presence of disparity. Without the use of the polarised filter, the stereoscopic target within the Wirt circle has a blurred appearance, that with filters in place, appears to have disparity in the presence of normal stereopsis. In the presence of monocular viewing however, the circle will appear to alter its position to the left or right depending upon the eye affected, enabling detection of the stereoscopic target correctly down to around 70 seconds of arc (Holmes and Fawcett 2005; Chopin et al. 2019).

This is less of a concern with global tests of stereopsis, where a static-like random dot pattern is observed. Where stereopsis is present, viewing global targets results in the detection of disparity as an emergent percept, while generally no cues to monocular viewing are present. It should be noted however, that binocular cues have been similarly reported in the design of the TNO test when rotated (Charman and Jennings 1995), something that is not typically done in clinical practice. The TNO test has been reported to have poorer test-retest reliability than the Wirt circles used in the Stereo Fly test, with the Stereo Fly test exhibiting coefficient of repeatability of +/-12 seconds of arc, compared to +/-54 seconds of arc for the TNO test (Antona et al. 2015). While this may factor into the findings above, it cannot explain the consistency with which the findings of the Stereo Fly Test identified better stereoacuity. It is possible that the increased cognitive complexity of the task led to the difficulty in identifying the appropriate target, as compared to the visually simple forced choice of a Wirt circle target. It is more likely however that as Yamada et al (2008) found in their work, that while good agreement can be observed in similar tests using polarised filters and red-green anaglyphs to around 600 seconds of arc, for lower levels of stereopsis the anaglyph based tests were inferior in performance to the polarised tests of global stereopsis. It is possible that differences in image contrast as a result of the disparate retinal images caused by the anaglyphs may result in voluntary suppression of one of the images (Bogdanovich et al. 1986; Garnham and Sloper 2006; Varón et al. 2014; Zhang et al. 2021) artificially lowering the stereoacuity measured.

While a number of studies have investigated the consistency of the Saladin card (Corbett and Maples 2004; Ngan et al. 2005; Frantz et al. 2011), no published studies exist using this instrument in presbyopic subjects. Compared to the previously published work in this age group (Wick 1986) this study found a similar distribution of forced duction curve patterns within the control cohort, but identified a greater incidence of type III and IV curves within the stroke cohort. Despite the vergence ranges reported above, Type III curves are believed to indicate the presence of exophoric deviations at risk of break to diplopia (Ogle et al. 1967; Stidwill and Fletcher 2011), requiring prismatic correction. Type IV curves have been associated with symptoms of binocular instability in pre-presbyopic subjects (Ogle et al. 1967), Though due to the absence of accommodation Wick (1986) proposed that subjects with type IV curves needn't necessarily experience such symptoms as inappropriate accommodative-convergence is unlikely to interfere with the convergence reflex in presbyopia.

Subjects in this study exhibited a tendency towards exo-slip at distance and greater exo-slip at near, while greater than Karania & Evans (2006), this is similar to Pickwell et al (1991) and likely due to the greater proportion of older subjects in the latter study, similar to the demographics of this study. An unusual finding of this study was the observation that the measure of Aligning prism using the near vision test unit had better association with the fixation disparity measure of the Saladin card than the Aligning prism test of this instrument.

This difference is likely explained by the instrument design. The Saladin card presents a series of fixation disparity targets that exhibit peripheral fusion, but no detail within the foveal fusion area to lock the images, resulting in the observation of greater degrees of fixation disparity (Brownlee and Goss 1988) and less stability in results found (Wildsoet and Cameron 1985). By contrast the Mallett unit exhibits both foveal and peripheral fusion elements, reducing these effects (Karania and Evans 2006).

With the diverse range of areas controlling eye movements, it would be expected that damage secondary to cerebrovascular accidents would result in notable binocular deficits. While differences in performance were observed across cohorts in pursuit and saccade eye movements, the finding of no significant differences across the other main binocular measures is unexpected. It may be that this lack of difference may be the result of cortical re-organisation to compensate for possible loss due to the injury (Dilks et al. 2007; Grefkes and Ward 2014; Housman 2020; Tscherpel et al. 2020; Namgung et al. 2024), resulting in near normal performance. In this study subjects with a history of stroke tended to have mild symptoms, so it is possible that less extensive initial damage was present, diluting any impact in coordination. It may also be the case that the impact of these brain injuries disproportionately impacts dynamic ocular movement, explaining differences in oculomotor function, but consistent results in testing reliant upon optical changes at primary gaze.

While a number of case reports for management of binocular vision anomalies in stroke survivors have been published (Smaakjær et al. 2018; Axelsson et al. 2019), to date the evidence base for interventions of this nature is spartan (Pollock et al. 2011; Hill et al. 2015; Hanna and Rowe 2017; Hanna et al. 2017b; Rowe et al. 2018). While a range of procedures for eye movement, vergence, binocular vision and perceptual rehabilitation have been proposed (Chang et al., 2016; Scheiman, 2011; Suter & Harvey, 2011), these are largely based upon case studies & small case series with no randomised trials to date. This challenge is not limited to rehabilitation of these anomalies post brain injury but as indicated earlier, the management of a large range of binocular anomalies (Barrett 2014). This study raises further questions, as contrary to what might be expected. No significant difference in binocular vision profile was observed between cohorts. Further investigation is warranted to confirm whether this pattern holds across a larger cohort.

This study has some limitations. The small sample size recruited does impact upon the power that may be attributed to this study. Post hoc power analysis indicates that the one way analysis of ranks for the sample size recruited with a medium effect size would elicit a power of 0.30, increasing to 0.66 for large effect size. Similarly for the comparison between stroke and control cohorts to identify a medium effect size would exhibit a power of 0.51 and for large effects 0.86. With the exception of the latter assessment, these fall short of the ideal of 0.8 (Araujo and Frøyland 2007; Prajapati et al. 2010). While the next logical approach would be to review differences found with respect to their relative confidence intervals, the absence of difference between cohorts would make this approach redundant. As such while with some degree of confidence it may be proposed that no large differences in binocular vision profile can be observed between stroke survivors and controls, this cannot be said for low or moderate differences, and limited confidence may be placed in the results between cohorts without this potentially being erroneous (Type II error).

This is further confounded as the repeatability of some binocular vision tests may limit the ability to determine subtle differences between stroke and control subjects. The measurements taken may have been influenced by their administration. The testing protocol employed to assess fixation disparity did not follow that recommended by Karania and Evans (2006), but instead followed a more traditional approach (Elliott 2013). This change may have influenced the results found, in particular the absence of questioning around movement of the nonius markers may have adversely influenced findings – potentially under recording this important sign of binocular instability. In terms of vergence testing, the results of this measure may have been impacted by the order of testing used which measured divergent vergence ranges initially, followed by convergence ranges irrespective of the phoria present (Carlson and Kurtz 2004; Benjamin 2006). As identified by Rosenfield (1995), this can give rise to undesired vergence adaption, adversely influencing results.

Additionally the stroke subjects recruited into this study generally exhibited mild symptoms and may not represent the true presenting profile of stroke survivors with binocular vision deficits that may be observed to exhibit more severe symptoms suggestive of these anomalies. The self-selecting nature of the sample also introduces potential bias, as individuals who chose to participate may not be representative of the broader stroke population. Furthermore, the control group was small, raising concerns about whether it accurately reflects normal population variability in binocular function. Another limitation was the absence of investigation into specific symptoms associated with binocular vision dysfunctions, or use of instruments to achieve the same (Alvarez et al. 2012; Laukkanen et al. 2016; Laukkanen et al. 2017; Trbovich et al. 2019; Theadom et al. 2021), which would enable investigation into the parameters that may have greater association with symptoms of binocular vision anomalies.

Due to the absence of masking, there is the potential for observer bias, unconsciously impacting the end points of testing depending upon the cohort of the subject. In terms of generalisability, while this study relied on testing in free space, using trial frame, and free lenses, prisms and filters to undertake measurements, internationally examinations are more frequently undertaken with phoropter. While for many of the tests undertaken no significant difference may be expected, for some tests such as fusional reserves, greater ranges would typically be expected (Antona et al. 2008). Future investigation should look to undertake investigation with a larger, less homogenous trial group and consider investigation using instrumentation more widely employed internationally within optometric practice.

These findings have previously been presented as a poster:

Maciver M. Wolffsohn J.S., & Logan N. (2024, Sept) *The binocular vision profile of stroke survivors: An investigation.* Poster presented at the British Congress of Optometry and Vision Science (BCOVS). London

Chapter 7 The influence of stroke, both with and without associated visual field loss on pattern glare and reading fluency.

7.1 Introduction

Stroke survivors often experience a range of perceptual anomalies that may impact their quality of life and inhibit their recovery. While ophthalmic sequelae such as visual field loss, strabismus and gaze palsies are widely reported (Ciuffreda et al., 2007; Hepworth et al., 2016; Rowe, 2010, 2013; Rowe et al., 2019; Rutner et al., 2006; Suchoff et al., 2008), a range of perceptual anomalies frequently encountered in practice receive less attention.

Visual stress describes a perceptual phenomenon where susceptible individuals experience discomfort and perceptual distortions when viewing moderate to high spatial frequency patterns such as stripes or text. Frequently this results in symptoms of headaches, eye strain, blurred or doubled vision, and difficulty focusing, which may interfere with reading and other visual tasks (Wilkins 2002; Evans and Stevenson 2008; Evans and Allen 2016; Wilkins et al. 2022; Wilkins and Evans 2022). Coloured overlays and precision tinted lenses have been used to reduce these symptoms, reducing the trigger of discomfort in these individuals. The use of coloured overlays have been reported to be beneficial in reading difficulties (Evans et al. 1995; Scott et al. 2002; Wilkins 2002; Ray et al. 2005; Stein 2014; Evans and Allen 2016; Stein 2019) and a number of neurological conditions (Wilkins et al. 2007; Fernandez and Wilkins 2008; Beasley and Davies 2012; Beasley and Davies 2013b; Wilkins et al. 2022).

Previous investigation by other authors (Beasley and Davies 2012; Beasley and Davies 2013b) has highlighted the increased presence of symptoms associated with pattern glare within stroke survivors and the impact of coloured overlays in mitigating these symptoms. Further work by these authors (Beasley and Davies 2013a) investigated the impact of coloured overlays upon the reading speed and error rate of stroke survivors compared to an age matched control cohort.

Symptoms associated with visual stress	Symptoms associated with anomalies of binocular vision
Words appear to move	Words appear to move or jump at near vision
Words appear to merge	Asthenopia
Patterns or shadows in text	Blurred vision
Text seems to stand out in 3-D above page	Visual discomfort/fatigue
Words or letters fade or darken	Reading difficulties
Discomfort with artificial lighting or flicker	Sensitivity to light
Symptoms of headaches when reading	headache

Table 7-1. Symptoms of visual stress and symptoms associated with binocular vision anomalies (adapted from Evans et al, 2017 and García-Muñoz et al, 2014).

Investigation can be challenging however as many subjects following stroke may report visual hypersensitivity symptoms similar to those associated with pattern glare or may report photophobia more generally (Digre and Brennan 2012; Wu and Hallett 2017; Thielen et al. 2023; Thielen et al. 2024). These symptoms can give rise to difficulty in day-to-day activities such as driving, work, sports or even general mobility. The presence of symptoms of visual stress has been attributed to a range of causes, though no definitive cause has been identified.

Anomalies of binocular vision have been reported to occur following cerebrovascular accident (Ciuffreda et al., 2007; Hepworth et al., 2016; Pedersen & Troost, 1981; Rowe, 2010, 2011; Rowe et al., 2013b; Rowe et al., 2019; Suchoff et al., 2008). A significant overlap occurs between the symptoms of many binocular vision anomalies, and those of visual stress (**Table 7-1**). The importance of binocular vision testing is frequently highlighted in the literature, with appropriate management of anomalies observed frequently resolving symptoms of visual stress without the need for overlay assessment (Scott et al. 2002; Wilkins 2002; Evans 2005; Scheiman and Wick 2013).

Investigations into the binocular function of children who benefit from coloured filters have been observed to exhibit reductions in accommodation, vergence, poorer stereopsis and more likely to report binocular instability on fixation disparity testing (Evans et al. 1996; Scott et al. 2002). While these may give rise to the symptoms associated with visual stress their presence are poor indicators of those who are likely to benefit from overlays, suggesting that other factors are more likely to give rise to these symptoms (Evans et al. 1996; Monger et al. 2015).

Following neurological episodes such as traumatic brain injury, concussion or stroke, it is not uncommon for individuals to exhibit difficulties in acuity, reduced accommodation and eye movement performance, notable degrees of exophoria and in some instances the adoption of anomalous body postures (Padula. W.V. 1988; Padula and Argyris 1996; Townsend et al. 1999; Ciuffreda et al. 2007; Zihl 2010; Padula et al. 2017). These findings have been described by some as post-trauma vision syndrome (Padula 1988; Padula and Argyris 1996; Padula et al. 2017). Investigation in this domain has centred on electrophysiological studies. While limited in size, many of these studies found deficits in the wave patterns of visually evoked potentials (Padula et al. 1994; Freed and Hellerstein 1997; Dupuis et al. 2000; Gaetz et al. 2000; Lavoie et al. 2004; Bolduc-Teasdale et al. 2019; Harris and Myers 2023) suggesting a deficit in the transmission of information along the visual pathway, particularly those pathways associated with 'ambient' visual processing, such as the magnocellular pathway (Padula et al. 2017).

The magnocellular pathway describes an afferent visual pathway that transmits transient, temporally sensitive information primarily from the retinal periphery to the occipital lobe. Another theory proposes that the symptoms experienced by those with visual stress arise due to an impairment in this pathway (Stein 2001; Stein 2014; Stein 2019). The retinal magnocellular cells project via the thalamus to the magno-cells of the dorsal pathway, and potentially interlinking with cells in the auditory, somatosensory, proprioceptive and motor systems. It has been proposed that disruption to this pathway results in poor visual search, inaccurate saccadic movements and poor oculomotor control (Stein 2001; Stein 2014; Stein 2019). This view is controversial as while investigations into spatial sensitivity in susceptible individuals is consistent with this theory, investigations into contrast sensitivity is not (Skottun 2000).

This theory proposes that where used, coloured filters (especially those that block short wavelength light) enhance magnocellular function by reducing the inhibitory effect of short wavelength sensitive cones (Stein et al. 2000a; Ray et al. 2005). This however has been disputed both experimentally (Kuba et al. 2001; Stein 2014) and by investigations that have found low prevalence of findings associated with magnocellular dysfunction in individuals with visual stress (Evans et al. 1994; Evans et al. 1995).

The most widely accepted theory for the origin of visual stress attributes the anomaly to a response to cortical hyperexcitability, with excessive sensory stimulation resulting in a reduction in inhibitory action which results in inappropriate neuronal response (Bargary et al. 2015; Wilkins and Evans 2022). The typical stimulus that has been found to trigger such effects has been found to be greatest for mid-range spatial frequencies of around 3 cycles/degree (Fernandez and Wilkins 2008; Juricevic et al. 2010) In this theory lines of printed text, may approximate the pattern of a mid-spatial frequency grating, giving rise to overstimulation within the visual cortex and giving rise to the symptoms of visual stress. However electrophysiological studies suggest that the response may be diffuse and not localised, with potentially multiple mechanisms may underlie these symptoms (Radhakrishnan et al. 2005; El Shakankiry and Kader 2012; Chang 2013; Tempesta et al. 2021).

The use of coloured overlays and lenses have become widespread for reducing the symptoms associated with pattern glare and visual stress though it is not without controversy. While precision in lens colour is widely recommended (Wilkins et al. 1994; Wilkins 2002; Wilkins et al. 2005; Cardona et al. 2010; Evans and Allen 2016), some authors suggest that the use of a blue or yellow filter should be sufficient (Stein et al. 2000b; Stein 2014). Debate continues on the mechanism and efficacy of coloured filters, primarily due to the limit of high-quality evidence (Evans and Allen 2016; Griffiths et al. 2016).

Loss of peripheral vision is a common occurrence following stroke, with reports of 20-57% of stroke survivors exhibiting field loss (Townend et al. 2007; Rowe et al. 2013a; Pollock et al. 2019), with the prevalence of visuospatial neglect occurring in up to 80% of stroke survivors (Ten Brink et al. 2017; Esposito et al. 2021; Bosma et al. 2023; Durfee and Hillis 2023). A sizable portion of those with field loss both with and without neglect after stroke go on to develop difficulties in reading, even where language function remains intact (Berhmann et al. 2002; Schuett 2009; Zihl 2010). The loss of peripheral vision has been reported to inhibit visual exploration and saccadic movements, resulting in greater number of small refixation eye movements, longer fixation durations and a greater number of errors in reading (Zihl 1995; Leff et al. 2000; Schuett 2009; Niehorster et al. 2013; Elfeky et al. 2021). A number of studies using masking in normal readers have suggested the main driver of these difficulties to be visual, though the evidence is mixed (Schuett et al. 2008).

Since the work of Beasley & Davies (2012) no further investigation has been undertaken to investigate issues of pattern glare in stroke survivors. While Beasley & Davies (2013b) reported upon the improvement in symptoms of visual stress in a stroke survivor with field loss, their research was limited to a single case with the relationship between pattern glare, visual stress and field loss post stroke unexplored. Furthermore, there has been no investigation on how the use of coloured overlays impacts on the reading of stroke survivors with field loss.

Stroke survivors frequently report visual discomfort and sensitivity to glare and patterned stimuli, impacting their quality of life (Beasley and Davies 2012; Wilkins et al. 2022). Investigation into the impact of field loss on pattern glare, reading speed, and the effect of coloured overlays could provide valuable insights into effective management strategies for visual stress symptoms in stroke survivors both with and without visual field defects.

7.2 Methods

This study was undertaken with subjects recruited to undertake the following testing of binocular visual function as outlined in **Chapter 6**. Participants were recruited in response to outreach via stroke support groups, social media outreach, practice-based notices and communication with other local optometric practices, further information on participant recruitment in **Chapter 5**. Details of visual field findings were drawn upon from the results of **Chapter 5**. This study was undertaken in three parts;

With appropriate intermediate (1m) optical correction in place Log Contrast Sensitivity (LogCS) was measured monocularly. Following these subjects underwent testing at near using the Pattern Glare Test (Institute of Optometry, London, UK). Testing was undertaken at 40cm in accordance with the instrument's instructions (Wilkins and Evans 2001; Evans and Stevenson 2008). Scoring was recorded for the presence of visual effects when viewing the low spatial frequency grating (pattern 1), the medium spatial frequency grating (pattern 2) and the high spatial frequency grating (pattern 3), finally the difference between the medium and high spatial frequency gratings were calculated to derive the mid-high difference. While the examiner was masked from the results of the reference standard examination undertaken in **Chapter 5**, no masking was undertaken in this study.

Statistical analysis was undertaken using SPSS (IBM SPSS Statistics for Macintosh, Version 29.0.1.0 Armonk, NY: IBM Corp). To examine the effect of pattern glare on the different sized cohorts of subjects to assess the impact of the presence of field defects, a one way analysis of variance (Kruskal-Wallis H test) was used. A significance level of α=0.05 was used for all tests, Where post-hoc testing was undertaken a Bonferroni correction was undertaken to reduce the risk of a Type I error. Quantitative measures were assessed for normality using the Shapiro-Wilk test.

For the final part of this study participants then moved on to select the optimal spectral filter (Intuitive Overlays, Institute of Optometry, London, UK), before undertaking the Wilkins Rate of Reading Test (Institute of Optometry, London, UK). The test was completed in accordance with the instrument's instructions, with subject's rate of reading and error being measured twice with overlay in position and twice without (See **Chapter 4**), from which a rate of reading and error score were calculated.

A two way mixed design repeated level analysis of variance was employed incorporating one between subject factor (stroke subject / control subject) and one within subject factor (with filter / without filter). As previous studies, this study received ethical approval from the Health and Life Sciences Ethics Committee of Aston University (HLS21005) and was conducted in accordance with the requisites of the Declaration of Helsinki (2013).

7.3 Results

Due to the presence of ocular pathology reducing best corrected acuity two subjects were unable to complete this task, one from each cohort. In total 21 subjects with a history of stroke and 25 control subjects completed the study. With the removal of these subjects the stroke cohort consisted of 13 male and 8 female subjects, ranging in age from 49-89 years old (mean 72.0 years, SD+/-11.01years), with a mean time since stroke of 5.62 years (SD+/-3.55 years). Of these subjects 6 had visual field loss secondary to their stroke. Control subjects consisted of 9 male and 16 female subjects with a mean age of 69.68 years (SD+/-11.47), with 1 having coexisting field loss. No significant differences in gender (unpaired T-test: t=-1.774, df=44, p=.084) or age (unpaired T test: t=.710, df=44, p=.482) were present within these groups. Analysis found no significant difference in either distance (Kruskal-Wallis H test: χ^2=.858, df=2, p=.651) or near (Kruskal-Wallis H test: χ^2=.555, df=2, p=.758) acuity for between cohorts.

7.3.1 Contrast Sensitivity

Measures of contrast sensitivity (**Table 7-2**) found high degrees of correlation between eyes (ICC: .797 95%CI .637-.886, F[47,47]=4.915, p<.001) with no significant difference was observed between cohorts (Kruskal-Wallis H test: [right] χ^2=3.550, df=2, p=.170; [left] χ^2=1.614, df=2, p=.446), or between stroke and control subjects (Mann-Whitney U test: [right] p=.354, [left] p=.456).

	Stroke cohort			Control cohort		
	Median	Range	IQR	Median	Range	IQR
LogCS - right eye	1.35	0.90 - 1.55	0.50	1.50	1.05 - 1.65	0.15
LogCS - left eye	1.42	0.90 - 1.55	0.28	1.42	0.75 - 1.65	0.30

Table 7-2. Data of the median, range and interquartile range of findings of contrast sensitivity (LogCS) of right and left eyes between cohorts.

7.3.2 Pattern Glare Test Results

Analysis of pattern glare score found different scores between low, medium and high spatial frequency targets across cohorts (F[2, 88]=27.511, p<.001), with few symptoms of pattern glare exhibited when viewing a low spatial frequency target compared to a medium (paired T test: P<.001) or high spatial frequency target (Paired T test: p<.001), with greater symptoms of pattern glare exhibited viewing medium spatial frequency target compared to a high spatial frequency target (Paired T test: p=.043). When factoring for cohort, significant difference was observed (F[2, 88]=2.196, p=.047).

Spatial frequency	Stroke (mean ± SD)	Stroke$_{VF}$ (mean ±SD)	Control (mean ±SD)
Low	0.20 ± .56	0.40 ±0.50	0.40 ± 0.55
Med	1.73 ± 1.33	2.20 ±1.30	1.08 ± 0.91
High	1.20 ±1.56	0.80 ± 1.09	1.00 ± 1.04
Med-high difference	0.53 ± 1.72	1.40 ± 0.55	0.08 ± 0.75

Table 7-3. Summary of pattern glare scores for stroke subjects without visual field loss, Stroke subjects with visual field loss (Stroke$_{VF}$) and control subjects.

Between cohorts, while scores from low to high spatial frequency targets were consistent (F[1,44]=.025, p=.874), subjects within the stroke cohort exhibited significantly greater response to medium spatial frequency targets (F[1,44]=6.704, p=.013). A summary of pattern glare scores by cohort can be seen in **Table 7-3**.

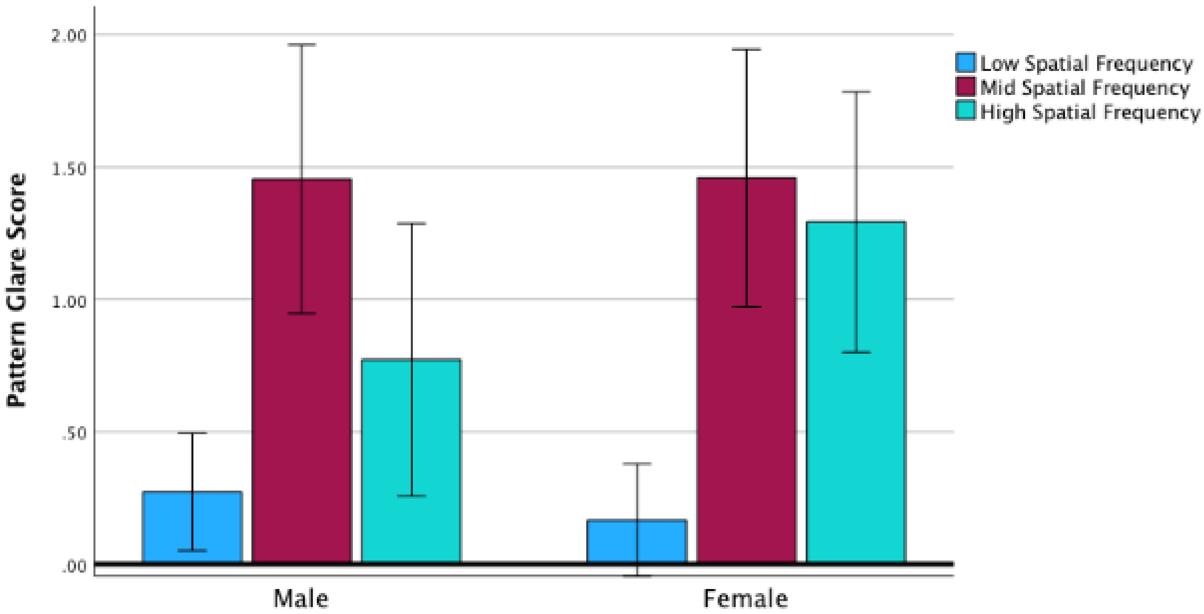


Figure 47. Mean pattern glare score for low, mid and high spatial frequency targets by gender. Error bars represent 95%CI.

When analysing for gender (**Figure 47**), similarly differences were observed between pattern glare symptoms at the different spatial frequency targets (F[2, 88]=25.401, p<.001), with lower scores for low spatial frequency targets compared to medium (Paired T test: p<.001) and high spatial frequency (Paired T Test: p<.001) targets, with lower response to higher spatial frequency targets compared to medium spatial frequency target (p=.065), no significant differences were observed in scores between genders (F[2,88]=1.790, p=.173).

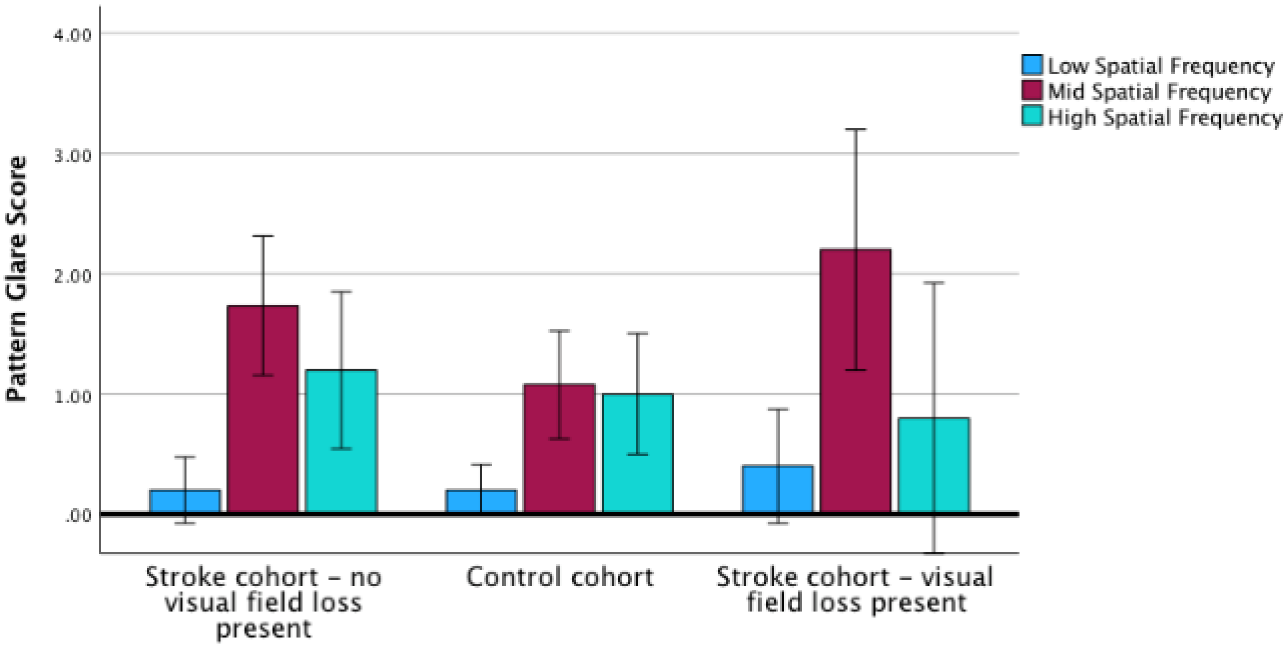


Figure 48. Mean pattern glare scores for low, mid and high spatial frequency pages by cohort. Error bars represent 95%CI.

Pattern glare score was found to be slightly higher in the stroke subjects with a visual field defect (**Figure 48**), with similar scores found in control subjects and stroke subjects without defect (Kruskal-Wallis H test: χ^2=1.450, df=2, p=.484). Significant difference in mid-spatial frequency pattern glare scores was found between cohorts (Kruskal-Wallis H test: χ^2=6.045, df=2, p=.049), with stroke subjects with field defects exhibiting greater scores than both stroke subjects without field defects (Mann-Whitney U test: p=.553), and control subjects (Mann-Whitney U test: p=.045). While stroke subjects without field defects exhibited greater pattern glare scores than controls, this was not found to be significant (Mann-Whitney U test: p=.078). Scoring for high spatial frequencies found greater degrees of pattern glare in the stroke subjects without field defect than other subjects, with stroke subjects with field loss exhibiting the lowest degrees of pattern glare on this test (Kruskal-Wallis H test: χ^2=.148, df=2, p.929).

Significant differences were observed in mid-high spatial frequency scores between cohorts (Kruskal-Wallis H test: χ^2=8.133, df=2, p=.017), with stroke subjects with field loss exhibiting greater mid-high difference scores than both stroke subjects without field loss (Mann-Whitney U test: p=.142) and control subjects (Mann-Whitney U test: p=.004). Stroke subjects without field loss were found to have slightly greater mid-high pattern glare scores than control subjects, though this was not significant (Mann-Whitney U test: p=.224).

When analysing more generally between subjects with a history of stroke and control subjects, Stroke subjects were more likely to exhibit significant pattern glare (Evans and Stevenson 2008) than control subjects (Pearson chi-squared: χ^2=6.878, df=1, p=.009), with 14 (67%) stroke survivors and 7 (28%) control subjects exhibiting either pattern glare scores >3 or a mid-high difference of 1 or greater.

The pattern glare test found significantly higher scores for stroke subjects when compared to control subjects when viewing the mid spatial frequency pattern (Mann-Whitney U test: p=.027), and the mid-high score difference (Mann-Whitney U test: p=.007). While scores were observed to be higher in the stroke cohort than the control cohort for the low (Mann-Whitney U test: p=.789) and high spatial frequency (Mann-Whitney U test: p=.815) pattern glare results this difference was not found to be significant.

While not significant, pattern glare score were found to be slightly higher in male subjects for low (Mann-Whitney U test: p=.386), and high spatial frequency (Mann-Whitney U test: p=.133) pattern glare scores as well as med-high difference score (Mann-Whitney U test: p=.093), no difference was noted between genders for medium spatial frequency pattern glare score (Mann-Whitney U test: p=.909).

7.3.3 Rate of Reading Test Results

A summary of the colour of intuitive overlay selected by cohort can be seen on **Figure 49**. Stroke subjects were found to be unable to read as quickly as control subjects (F[1,44]=10.752, p=.002), and were prone to making a greater number of errors when undertaking the rate of reading test (F[1,44]=4.891, p=.032). While the use of a overlay was found to have an impact on the reading speed (F[1,44]=7.151, p=.010), it was not found to make a difference the the number of errors recorded (F[1,44]=.010, p=.921). When considered together, interaction of factors identified that the use of filters was associated with an increase in the reading speed of stroke subjects (F[1,44]=5.285, p=.026), though no significant difference in error score was found (F[1,44]=1.517, p=.225).

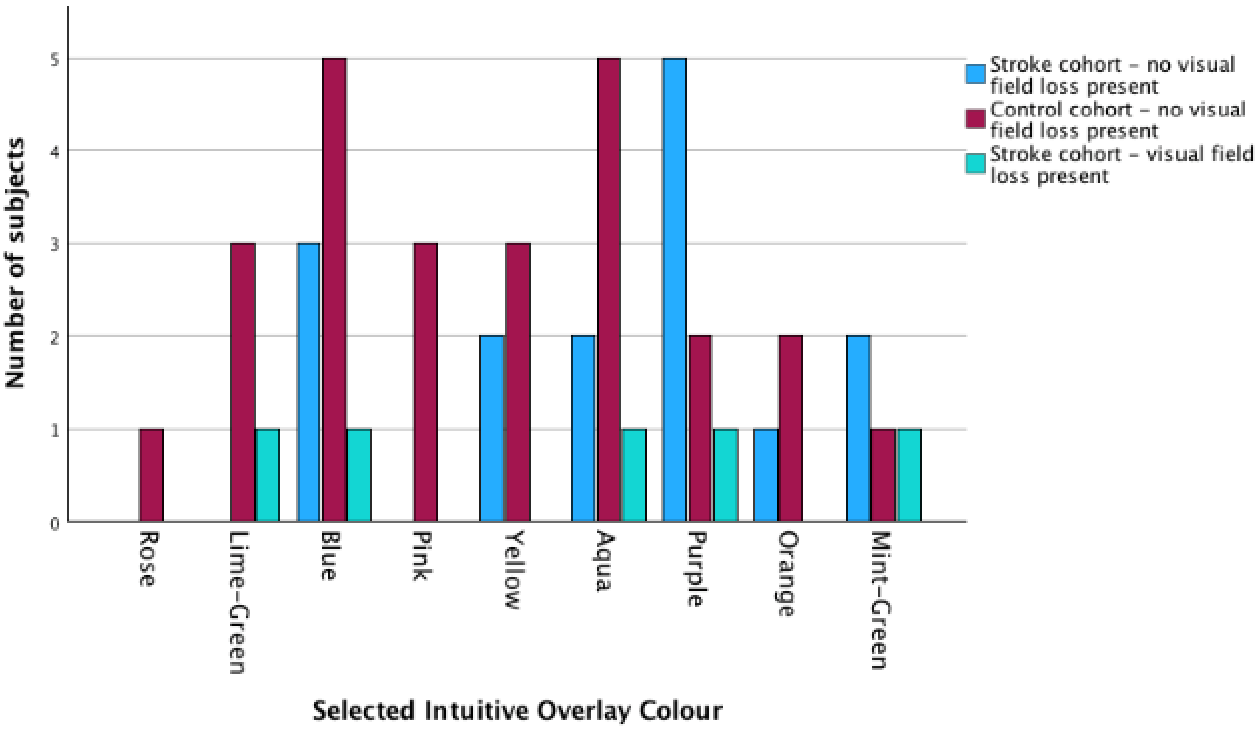


Figure 49. Intuitive Overlay colour selected by cohort.

With the use of an overlay a difference in reading speed (Kruskal-Wallis H test: χ^2=7.855, df=2, p=.020) was still observed between cohorts (**Figure 50**), with an improvement in reading speed observed within stroke subjects without field loss (Wilcoxon signed rank test: z=-2.646, p=.008), though little difference was observed in subjects with field loss (Wilcoxon signed rank test: z=-.944, p=.345). A summary of reading and error rates by cohort can be seen in **Table 7-4** and **Table 7-5** respectively.

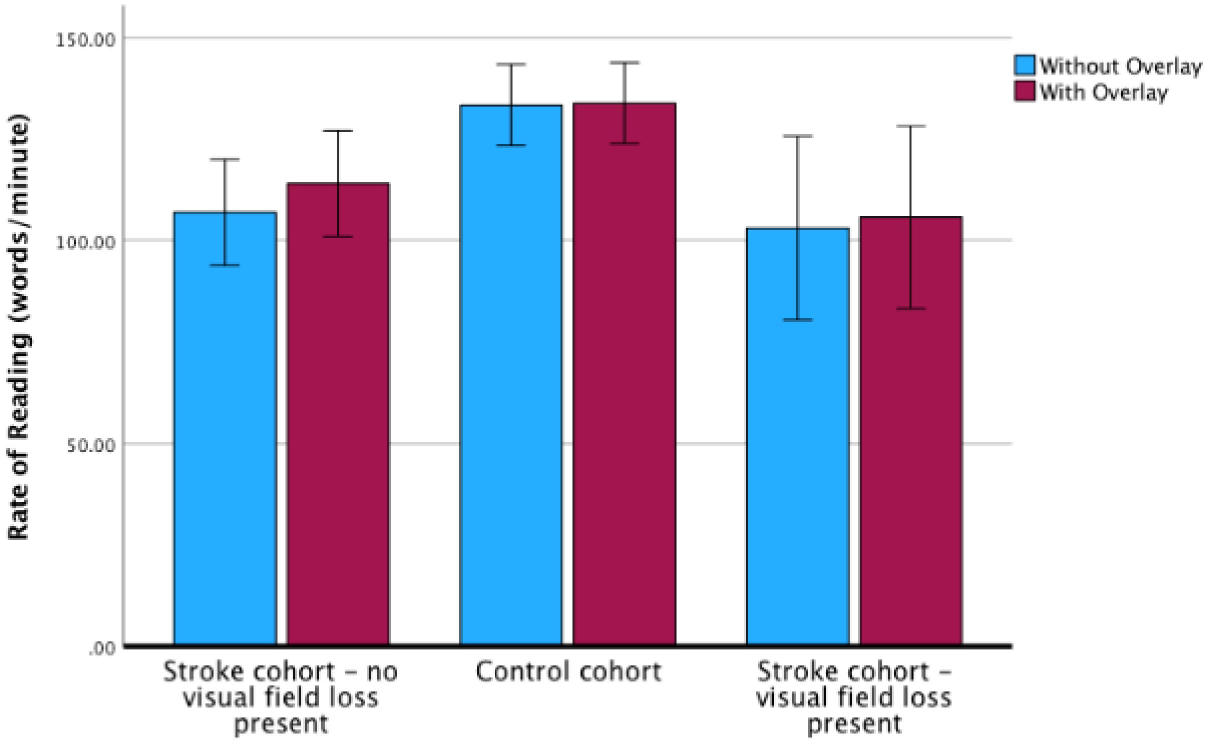


Figure 50. Results of rate of reading test with and without the use of intuitive overlays by cohort. While reading rate was lower across stroke cohorts, the use of an overlay was observed to improve this, though not significantly in those with co-existent field defects. Error bars represent 95%CI.

While the number of errors made remained lowest in control subjects and highest in stroke subjects with field loss (**Figure 51**), this difference was not found to be significant (Kruskal-Wallis H test: χ^2=5.715, df=2, p=.057). With the use of overlay control subjects continued to outperform stroke subjects both with (Mann-Whitney U test: p=.027) and without field defects (Mann-Whitney U test: p=.026), with stroke subjects without field defects outperforming those with defects (Mann-Whitney U test: p=.553).

Rate of Reading Test	Stroke (mean ± SD)	Stroke$_{VF}$ (mean ± SD)	Control (mean ± SD)
Without overlay	106.86 ± 26.13	103.00 ± 23.36	133.36 ± 24.62
With overlay	113.96 ± 25.29	105.70 ± 18.11	133.80 ± 25.65

Table 7-4. Summary of reading speeds measured using the Wilkins Rate of Reading Test (words/minute) for stroke subjects without visual field loss, Stroke subjects with visual field loss (Stroke$_{VF}$) and control subjects.

Female subjects were found to have slightly higher reading rate ($F[1,44]=.186$, $p=.669$) and error score ($F[1,44]=.059$, $p=809$) than male subjects, though this was not found to be significant (**Figure 52**). No significant difference in error scores was observed between genders (**Figure 53**) While the use of coloured overlays were found to increase the reading speed in both groups ($F[1,44]=5.413$, $p=.025$), it was found to make little difference in error score ($F[1,44]=.038$, $p=.846$). No significant interaction effect was observed between gender and overlay use ($F[1,44]=.746$, $p=.392$) or error score ($F[1,44]=.038$, $p=.846$).

Error Score	Stroke (mean ± SD)	$Stroke_{VF}$ (mean ± SD)	Control (mean ± SD)
Without overlay	2.13 ± 1.51	1.60 ± 2.04	1.10 ± .98
With overlay	2.03 ± 1.30	1.40 ± 1.19	1.24 ± 1.10

Table 7-5. Summary of error scores observed from the Wilkins Rate of Reading Test for stroke subjects without visual field loss, Stroke subjects with visual field loss ($Stroke_{VF}$) and control subjects.

The habitual rate of reading (Kruskal-Wallis H test: $\chi^2=11.619$, df=2, $p=.003$) and error score (Kruskal-Wallis H test: $\chi^2=6.215$, df=2, $p=.045$) was found to differ between cohorts. Control subjects were found to exhibit higher reading speeds than stroke subjects both with (Mann-Whitney U test: $p=.019$) and without field defects (Mann-Whitney U test: $p=.002$). Controls were also found to exhibit lower error scores when undertaking the rate of reading test than stroke subjects both with (Mann-Whitney U test: $p=.666$) and without defects (Mann-Whitney U test: $p=.026$). While a greater number of errors were made by stroke subjects with full visual fields than those with field loss (Mann-Whitney U test: $p=.119$), this group was found to exhibit a greater reading speed (Mann-Whitney U test: $p=.735$).

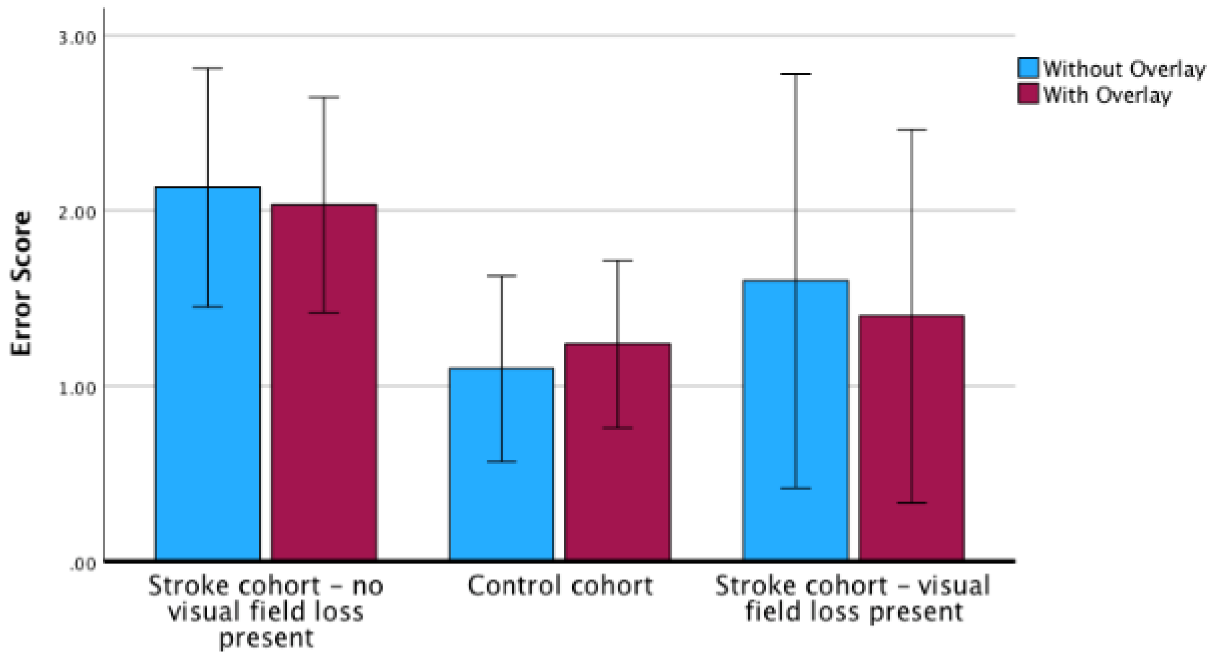


Figure 51. Results of error scores whilst undertaking the Wilkins Rate of Reading Test by cohort, comparing performance with and without the use of intuitive overlays. Whilst those with a history of stroke exhibited greater errors, this was more notable in those without field defects than those with them. No significant difference in performance was observed in any cohort when using overlays. Error bars represent 95%CI.

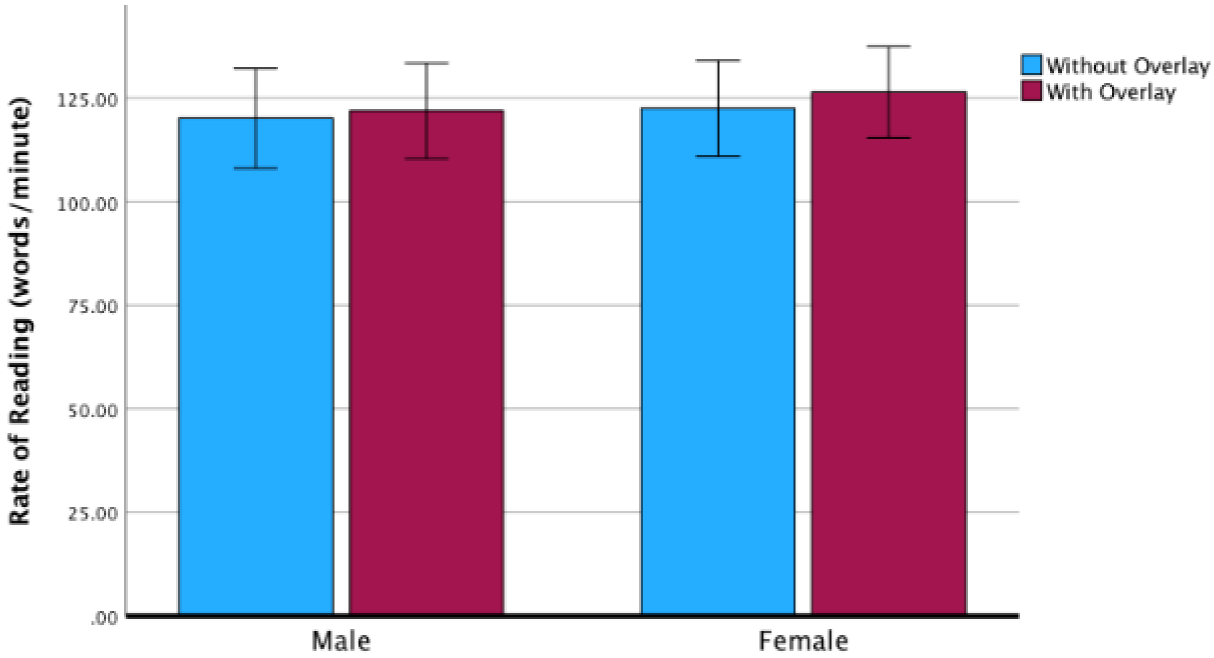


Figure 52. Results of reading speed with and without the use of overlays by gender. No significant difference was observed. Error bars represent 95%CI.

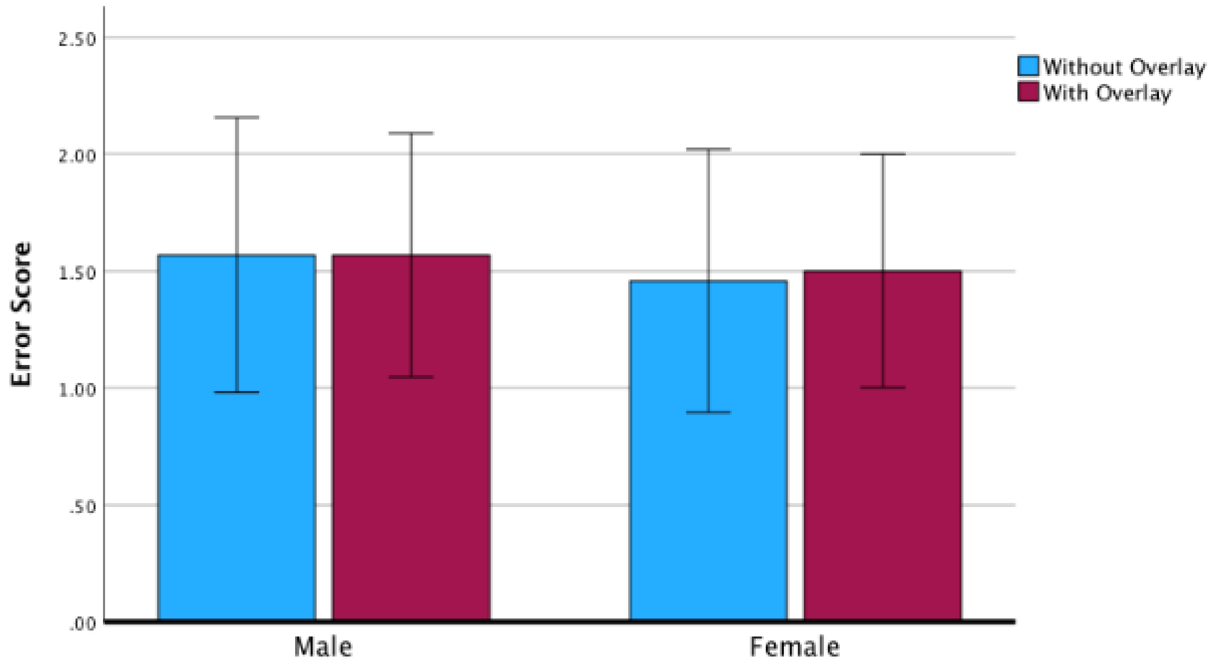


Figure 53. Error score observed while undertaking the Wilkins Rate of Reading Test with and without the use of intuitive overlays by gender. No significant differences in error rates were observed. Error bars represent 95%CI.

7.4 Discussion

This study has found greater degrees of pattern glare symptoms from stroke subjects compared to controls, with the greatest differences observed in those subjects with coexisting visual field defects. The disparity in pattern glare scores between stroke and control groups was especially prominent when subjects were exposed to medium spatial frequency targets. Clinically significant pattern glare is considered to be present when a medium-high difference score of over 1 or a medium spatial frequency score of 4 or greater are found (Evans and Stevenson 2008). These frequencies are known to be particularly discomfort-inducing for individuals with neurological sensitivities, as they closely align with the visual system's peak sensitivity to contrast (Wilkins et al. 1979; Fernandez and Wilkins 2008; Juricevic et al. 2010). The increased medium spatial frequency with consistent responses between cohorts to high spatial frequency target resulted in a higher mid-high difference score within the stroke cohorts.

Though the use of coloured overlays was associated with an overall improvement in reading rate in the stroke cohort, this benefit was primarily observed in participants without visual field defects. Stroke survivors demonstrated an average improvement of 5.4% in reading speed with the use of an overlay; however, those without field loss exhibited a greater average increase of 6.7%, consistent with the findings previously reported by Beasley and Davies(2013a). By contrast, participants with field defects derived minimal benefit, with only a 2.6% improvement observed. While modest, these improvements are similar to the improvements in reading rate observed in some previous studies into the impact of coloured overlays on reading rate (Bouldoukian et al. 2002; Evans and Joseph 2002; Kriss and Evans 2005; O'Leary and Evans 2006). Unlike previous work (Beasley and Davies 2013a) this study found no significant improvement in error score with the use of coloured overlay between cohorts.

Pattern glare has been postulated to result from cortical hyperexcitability, with strong neurological response in the visual cortex to mid-range spatial frequency stimuli. This response has been found to be more readily observed in low contrast than other spatial frequencies and may interfere with vision, through disruption of cortical inhibition (Chronicle and Wilkins 1996; Wilkins and Evans 2022), resulting in increased cortical activity, giving rise to perceptual distortions that may be uncomfortable to look at. While objective electrophysiological correlates of these symptoms have been observed (Arakawa et al. 2000; Huang et al. 2003), their cortical origin is not well understood. Investigations into other visual conditions have proposed that cortical excitability may increase following loss of vision (Coltheart 2018; Painter et al. 2018).

While previous research (Beasley and Davies 2012) has identified greater susceptibility to pattern glare in stroke survivors, the findings of this study would indicate that these may be further intensified in stroke survivors with visual field defects, where the compromised visual pathway may amplify the neural sensitivity mid spatial frequencies, resulting in increased symptoms of pattern glare.

Beasley and Davies (2012; 2013a) proposed that the increased prevalence of visual stress symptoms and improved reading rates using coloured overlays in stroke survivors as a phenomenon stemming from cortical hyperexcitability. Cortical hyperexcitability has been observed to occur following field loss in neurological disease (Carmichael 2012; Painter et al. 2018; O'Brien et al. 2020). Coloured overlays are thought to operate by reducing perceptual anomalies associated with visual stress, supporting the visual system to view triggering stimuli more comfortably (Wilkins and Evans 2022). While no definitive cause is known, it is postulated that the appropriate overlay when used rearrange cortical activity to reduce overaction of hyperexcitable regions of the cortex (Wilkins et al. 1994; Wilkins 2016; Wilkins et al. 2022; Wilkins and Evans 2022).

Like previous investigations, the use of coloured overlays improved the rate of reading within the stroke cohort, though this was more pronounced amongst those subjects without visual field defect. Subjects with field loss however exhibited more limited benefit despite the increased pattern glare score observed. Additionally, this study found no significant difference in the rate of reading errors with the use of coloured overlays, suggesting that the overlays' impact was primarily on reading speed rather than accuracy. While the use of coloured overlays did improve performance of the stroke cohort, the reading speed remained below that of the control group. This indicates that while overlays may offer some benefit, they do not fully compensate for the reading difficulties experienced by stroke survivors.

While the findings of this study are largely consistent with Beasley and Davies (Beasley and Davies 2012; Beasley and Davies 2013a), this study goes on to identify that stroke survivors with field loss experience greater symptoms of pattern glare and reading impairment than those without field loss, but despite this finding this group appear to be minimally responsive to the use of coloured overlays. This would suggest the loss of field to be a significant factor in both the presence of pattern glare and the reduced reading performance, but that the underlying mechanism may differ from those without field loss.

In the absence of screening/testing for neglect, it is unclear what influence this may have had on the rate of reading reported. While reduced reading performance has been observed to occur in the presence of visuospatial neglect, it is unclear whether the reading impairment is a direct result of the neglect (Moore et al. 2020), interference from flanking text (Rich and Palmer 2023; Gurd et al. 2024) or an indirect effect of inappropriate oculomotor behavior (Behrmann et al. 2002; Speedie et al. 2002). It is possible that these subjects' reading ability was impacted primarily by their diminished field of vision and the need for compensatory scanning or head movements, which would be expected to disrupt the smooth progression required for reading.

While some attention has been given to the fixational eye movements undertaken in loss of visual field (Schuett et al. 2008; Zihl 2010), as highlighted in **Chapter 6** eye movements within this cohort of stroke subjects were not found to be significantly worse than the control cohort. Indeed, stroke subjects without field loss were notable for the poorer eye movement they exhibited compared to both the control cohort and stroke survivors with field loss. It is possible then that while eye movements may be affected by cortical injury, the findings of this study combined with **Chapter 6** suggest these may not be the driver to the poorer reading performance observed. In addition to slower reading rates, stroke survivors also demonstrated a slightly higher frequency of reading errors during testing, though this was not found to be significant. While the use of coloured overlays may provide subtle support to stroke survivors with field loss, it is likely that a combination of factors are in operation with structural loss of field, subclinical anomalies of eye movements and other cortical factors rather than visual stress alone.

The magnocellular deficit theory of pattern glare postulates that visual stress and associated symptoms arise due to disruption to visual-temporal processing. Given the role of the magnocellular system in maintaining visual stability (Padula et al., 2017; Stein, 2001; 2014; 2019) the disruption of peripheral vision following stroke would be expected to impede this, providing a reason why those with visual field loss would be more susceptible to the symptoms associated with pattern glare. While this may provide some degree of explanation to the poorer reading performance with visual field defects, no other assessment of magnocellular function was undertaken. While this theory anticipates reduced contrast sensitivity in affected subjects especially across low spatial frequencies, the evidence for this is mixed (Skottun 2000). Similarly, the results of contrast sensitivity testing in this study were equivocal.

While the use of coloured overlays and lenses remain popular with eye care professionals and educators in ameliorating reading difficulties, the evidence supporting their efficacy in this task tends to be weak and inconsistent. One systematic review (Griffiths et al. 2016) found no strong evidence to the benefit of any of the systems of colour prescribing in the improvement of reading. They highlight that where studies are well controlled, differences in reading performances were less overt, attributing the results to placebo or Hawthorne effects rather than improvement due to the coloured lens / overlay, recommending against their use. Another systematic review (Evans and Allen, 2016) was more selective in their approach, analysing studies that actively selected for subjects with symptoms of visual stress. While acknowledging the limitations of the published evidence, they reported that coloured filters could be useful in the alleviation of symptoms and improve performance in individuals with visual stress.

Reading is a complex skill that relies on coordinated visual information processing, top-down attentional control, and higher-level linguistic processes involving multiple cortical centres and neural networks (Hwang et al. 2009; Ball 2012; Arrington et al. 2014; Amso and Scerif 2015; Staples and Graves 2020). It has been found that parafoveal vision, while not essential, plays a key role in word identification and guiding eye movements during reading (Gall et al. 2010). In hemianopia, parafoveal vision loss impairs processing of text while reading and alters eye movement patterns. While it may be anticipated that a right hemianopia would impair reading, it has been observed that left field loss frequently gives rise to greater difficulty (Behrmann et al. 2002; Rich and Palmer 2023; Gurd et al. 2024), while individuals who are well adapted to a right hemianopia may read at near normal levels (Zihl 2010). Within this study three subjects exhibited a left sided field loss (see **Table 5-9**).

While numerous studies have explored visual strategies to minimise the scotoma size (Pollock et al. 2019) and mitigate perceptual disruptions following stroke (Hazelton et al. 2022), there is currently no strong evidence supporting their effectiveness. Some studies have shown that saccadic visual search training can lead to both statistically and clinically significant improvements in reading performance among individuals who have developed reading impairments following stroke who have coexisting field loss (Schuett 2009; Kuester-Gruber et al. 2021; Kuester-Gruber et al. 2024). Although this involves practising non-typical eye movements that may pose cognitive challenges, it has demonstrated promising outcomes, with some studies reporting even greater improvement in older participants (Pambakian et al. 2004). This form of training can be particularly convenient for stroke survivors, as it can be completed at home, allowing for flexibility in the rehabilitation process. However, some oversight is essential; if not conducted correctly, the training may result in limited transfer of skills to real-world reading tasks (Hazelton et al. 2021).

This study has several limitations that potentially impact upon the utility of these findings. The study was conducted from a primary eye care practice, with a number of subjects recruited attending this branch for the provision of their eye care. As people actively attend routine eye care services, it is likely these would be more attentive to visual symptoms than the general population, reporting their symptoms more readily and skewing results. Despite information provided in the subject recruitment process on the nature of this study, the presence of this study occurring in a private setting may have raised concerns in potential subjects around possibility of costs, a concern frequently raised about eye care services at large (Hayden 2012; Association of Optometrists 2022; College of Optometrists 2023a). As a practice-based investigation, this study exhibited limitations in the severity and diversity of subjects investigated. Future investigation would benefit from being undertaken within a more neutral setting such as an academic or secondary care setting and aim to recruit a greater number of subjects across the spectrum of stroke severity to better understand the impact of this condition and the impact of coloured overlays as interventions in this group.

The participants in this study may not be representative of the broader population of stroke survivors. Post stroke sequelae vary widely and given this study was undertaken in a primary eye care setting it is likely that this cohort may reflect a less severely affected group seen in secondary care or larger population-based studies. While no assessment of visual neglect was undertaken, no participants exhibited overt symptoms of visuospatial neglect. It is however possible that a sizable minority of stroke subjects may have experienced this anomaly. Without testing it is not possible to appraise the impact of this anomaly on the procedures undertaken. As such this study likely does not capture cases where more severe neurological or functional deficits are present and would result in possible underreporting of the severity and giving limited guidance in terms of the interventions investigated in stroke survivors with more complex needs.

While no significant differences were observed in contrast between the groups under investigation, it should be noted that contrast testing did not strictly adhere to the instructions outlined for the Thomson XPert 3Di chart (Thomson Software Solutions, Hatfield, UK). While testing was undertaken on subjects typically around mid-day following several hours of use, no calibration was undertaken on the instrument prior to measurement. As a result, the absence of observed difference must be interpreted with caution. As such it is unclear whether this reflects a true absence of difference between groups, a potential limit of digital contrast sensitivity testing (Thayaparan et al. 2007), or by a potential floor effect arising from inadequate calibration. As such, future assessment should ensure strict adherence to instrument instructions to improve confidence in the reliability of measures observed.

While the Wilkins Rate of Reading Test has been popular in ophthalmic research assessing binocular vision anomalies (O'Leary and Evans 2006), ocular diseases (Eperjesi et al. 2004; Ridder et al. 2013) and the effects of coloured overlays on the reading rates (Wilkins et al. 1996a; Jeanes et al. 1997; Scott et al. 2002; Beasley and Davies 2013a), it is more limited in terms of its wider applicability. The test relies upon rapid automised naming of random words in meaningless sequence. As such it does not reflect real world reading, where emphasis is placed not only upon identification but also on linguistic comprehension. While the test has been found to be useful intra-individual changes (Wilkins et al. 1996b; Gilchrist et al. 2021), and as such useful for measuring changes based upon interventions, the results found cannot be considered to represent reading performance more generally.

As observed in **Chapter 6**, some caution is required in interpretation of these findings Post hoc power calculations of mean differences observed between stroke and control survivors for the subjects of this study exhibit a power of 0.49 for medium differences, and 0.83 for large differences, while the power associated with the analysis of variance measurements is found to be 0.48 for medium effects and 0.87 for large effects. This therefore must be borne in mind when reviewing these findings. There is some debate on the benefit of such post-hoc power calculations (see **Chapter 9** for further discussion), as the measurement with associated 95% confidence interval may be considered as the range of variances consistent with the observed data, where the true effect size may be found (Smith and Bates 1992; Levine and Ensom 2001). Reflecting upon the findings considering the variance observed, while differences between cohorts were observed for the measures conducted in this study, significant variance was observed. It would be reasonable to suspect that differences may be more subtle than observed within this study, and that further investigation is warranted with a larger cohort to reduce the risk of errors.

This study was undertaken after the studies outlined in **Chapter 5** and **Chapter 6**. Stroke survivors are particularly vulnerable to fatigue (Cumming et al. 2016), which can impact cognitive and visual processing abilities, with the effect that participating in these studies may have exacerbated this. The tasks undertaken in this study require sustained concentration, which can be challenging on stroke survivors and may have affected their performance on the tests conducted in this study. Having conducted this study after the other experiments, it may be that some of the differences may be attributable to a fatigue effect rather than reading impairment.

The significant relationship between visual field loss and both pattern glare and reduced reading speed highlights the need for investigation of the factors that influence reading speed post stroke. While a number of studies have identified aberrant eye movements or parafoveal loss as the source of these issues, neither of these explain the findings of this study. While a general improvement in reading performance was observed within the stroke cohort, the limited response of stroke survivors with field loss suggests that while coloured overlays may have a role to play in the mitigation of symptoms of pattern glare, eye care professionals should recognise that these interventions may serve as adjuncts and that these do not address the complex range of processing deficits associated with post stroke reading difficulties.

Chapter 8 An investigation into retinal structure in stroke survivors: An Optical Coherence Tomography (OCT) study.

8.1 Introduction

The neuroretina, having structural similarities to the brain, shares a common embryonic origin as well as similar vasculature and physiology (Girach et al. 2024). The retina exists as an extension of the diencephalon having a blood-retinal barrier that is structurally similar to the blood-brain barrier. Many of the changes that are observed in the retinal vessels are associated with changes in the cerebral vessels after cortical insult (Kwa et al. 2002; Ikram et al. 2006a; Ikram et al. 2006b; Moss 2015). Several retinal anomalies have been demonstrated to be associated with a greater risk of stroke such as narrowing of the retinal arterioles (De Silva et al. 2011; Vuong et al. 2015; Hughes et al. 2016), widening retinal vein calibre (Ikram et al. 2006a; McGeechan et al. 2009), the presence of cholesterol emboli within the retinal vasculature (Yin Wong and Klein 2002), diabetic retinopathy (Eriksson et al. 2024) and even macular degeneration (Wieberdink et al. 2011) though this latter point is contentious (Fernandez et al. 2015). This makes the retina a potentially useful surrogate for non-invasive investigation of potential changes that may occur following cerebrovascular accidents.

Multi-modal widefield retinal imaging is frequently encountered within primary eye care practice and is used to support the diagnosis, management and monitor changes to retinal structures where ophthalmic anomalies are identified. The Optos Monaco (Optos PLC, Dunfermline, UK) is a combination scanning laser ophthalmoscope (SLO) and optical coherence tomographer (OCT) capable of undertaking colour retinal imaging, fundus autofluorescence and scanning of the posterior pole of the eye (see **Chapter 4**).

Cerebrovascular accidents affecting the visual pathway are frequently followed by acute and delayed neuronal cell death. With the ischaemic core undergoing necrotic changes, while the penumbra undergoes apoptotic changes (Nitatori et al. 1995; Du et al. 1996; Gorman 2008). Following this insult, retrograde degeneration is frequently observed, occurring following stroke as well as other conditions (Gupta et al. 2009; Kanamori et al. 2012; Balk et al. 2014; Herro and Lam 2015; de Vries-Knoppert et al. 2019; You et al. 2021; Romaus-Sanjurjo et al. 2022). Retrograde degeneration is believed to occur following disruption of axonal transport (Jindahra et al. 2009; Jindahra et al. 2012), though this appears to be strongly linked to demyelination (Dyck et al. 1990; Raff et al. 2002).

Retrograde degeneration has been observed to occur in several studies (Jindahra et al. 2012; Keller et al. 2014; Herro and Lam 2015; Yamashita et al. 2016), with thinning of retinal ganglion cell and nerve fibre layer observed following stroke in a number of cases (Tatsumi et al. 2005; Park et al. 2013; Hokazono and Ribeiro Monteiro 2019; Newman-Wasser et al. 2019). Following cerebrovascular accident, those subjects with field loss have been found to exhibit thinner retinal nerve fibre layers and ganglion cell layers than control subjects (Bianchi Marzoli et al. 2023) and than those without field loss

(Rashid et al. 2021), highlighting two of their subjects exhibiting retinal thinning consistent with the pattern of their field defect one year following stroke. This does appear to be variable (Lee et al. 2020), with a significant number of stroke survivors initially experiencing field loss that resolve within the first year not affected by retinal thinning (Rashid et al. 2021). It is not uncommon that stroke survivors do not undergo visual assessment (Rowe et al. 2009; Sand et al. 2012; Stalin et al. 2024a), and given the lack of attention historically to OCT imaging following cerebrovascular accidents, it is likely that retrograde neuronal degeneration, like many ophthalmic sequelae, goes underdiagnosed (Lamirel et al. 2009; Nolan et al. 2015; Girach et al. 2024).

While OCT is a useful tool in imaging of the internal structures of the eye, these instruments are frequently limited by the restricted nature of their databases (Banc & Ungureanu, 2021b; N. Mehta & Waheed, 2020b; Nakayama et al., 2023b). While a comparison may be made against the database selected by the instrument manufacturer, this limits the use of analytic tools to measures of statistical variance from the database's normal. These instruments can be used to effectively determine change in image parameters over time, however in the absence of overt pathology, this frequently requires a series of seven or more scans to be consistent (Bradley et al. 2023b).

Visual field assessments are a useful tool to investigate the visual system following cerebrovascular insult. Due to their linear structure, an insult in the vicinity of the visual pathway can give rise to specific patterns of defects. This makes visual field assessment a useful surrogate tool in lieu of neuroimaging (Donaldson and Margolin 2021). As highlighted in **Chapter 2**, there is a paucity of data around optimal methods of field testing in stroke survivors, with kinetic perimetry giving rise to greater agreement with imaging of lesion location than automated approaches (Wong and Sharpe 2000). Within the eye care setting, this is frequently not achievable, with static automated perimetry being more widely employed (Tuck and Crick 1994; Artes et al. 2003).

Despite these insights, evidence on retinal thickness changes after stroke, both in the presence and absence of field loss remain inconsistent. As a commonly used instrument in primary eye care practice, changes in OCT parameters offer useful insights to clinicians in providing the optimal care to their patients. This study will investigate the impact of a history of stroke as well as the presence of visual field loss upon retinal thickness, ganglion cell complex, optic nerve head and neuroretinal rim parameters on a cohort of stroke and control subjects, to investigate how this may be best deployed to contribute to examination and ongoing care in stroke survivors.

8.2 Methods

This study is a cross-sectional study undertaken following completion of the study undertaken in **Chapter 7**. Subjects completed automated perimetry using the Henson 7000 instrument using the single stimulus approach of testing, wearing appropriate near point correction. Following this, subjects undertaking this study underwent pharmacological dilation using Tropicamide 1% w/v. Following a break of 30 minutes imaging was undertaken on the subjects using the Optos Monaco. Subjects underwent Optomap Ultra-Widefield (UWF) imaging, Optomap UWF autofluorescence (AF) imaging, Optos OCT line scan centred on the fovea, Optos OCT retina topography scan centred on the fovea and Optos OCT optic nerve head topography scan. Further details of techniques may be found in **Chapter 4**. Following completion of the examination, the examiner undertook slit lamp examination and intraocular pressure measurement to ensure no adverse effects following use of the pharmacological agent. The examiner was not masked from the subject's status for this study. Analysis was undertaken using SPSS software (IBM SPSS Statistics for Macintosh, Version 29.0.1.0 Armonk, NY: IBM Corp). All quantitative measures were assessed for normality using the Shapiro-Wilk test. Where normality was present parametric tests were applied, with non-parametric approaches used for non-normally distributed results. Analysis was undertaken to investigate retinal parameters between stroke and control cohorts as well as in the presence and absence of field defects. Due to uneven sample sizes a one way analysis of ranks (Kruskal-Wallis H test) was used to investigate between different cohorts. For testing a significance level of α=0.05 was applied, where post hoc analysis was undertaken a Bonferroni correction was applied. This study adhered to the requirements of the Declaration of Helsinki (2013) and received ethical approval from the Health and Life Sciences Ethics Committee of Aston University (#HLS21005). Written consent was received from participants in advance of participating in this study.

8.3 Results

8.3.1 Central Retinal Thickness

All stroke (22) and control (26) subjects from the diagnostic accuracy study reported in **Chapter 5** proceeded to participate within this study, a breakdown of participant information can be found in **Table 5-4** and **Table 5-5**.

A summary of the thickness parameters can be seen in **Table 8-1**. Retinal thickness was similar across cohorts except in the outer nasal (Kruskal-Wallis H test: χ^2=13.659, df=2, p=.001) and temporal (Kruskal-Wallis H test: χ^2=8.160, df=2, p=.017) retinas of the left eye. In these areas (**Figure 54** and **Figure 55**) stroke subjects without field loss were found to exhibit thinner retinas temporally (Mann-Whitney U test: p<.001), while stroke subjects with field loss were found to have slightly thinner retinas temporally (Mann-Whitney U test: p=.004) thought this was not significant. While the outer nasal retinal thickness in this eye was thinner in stroke subjects with field defects than control subjects without field loss, this was not found to be significant (Mann-Whitney U test: p=.049), and no other differences were observed between cohorts. Within the stroke cohort, when examining for gender, no significant difference in retinal thickness was observed across any central retinal thickness parameter.

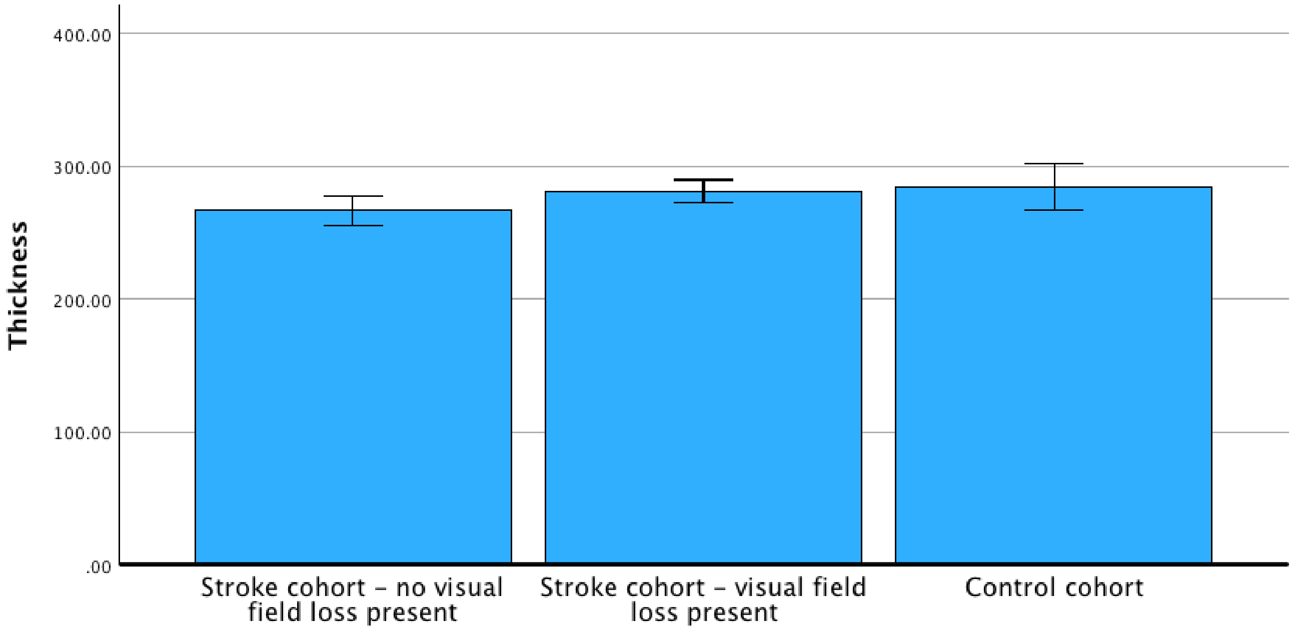


Figure 54. Left eye outer temporal retinal thickness by cohort (μm). Error bars represent 95% CI

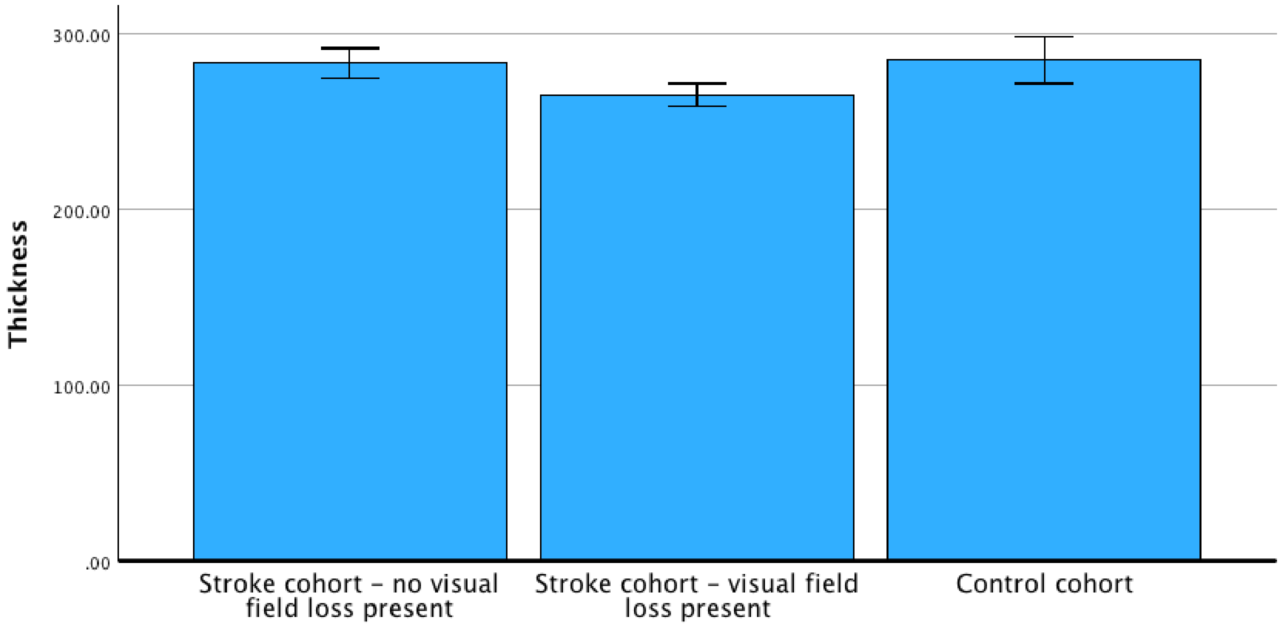


Figure 55. Left eye outer nasal retinal thickness by cohort (μm). Error bars represent 95% CI

8.3.2 Retinal Ganglion Cell Layer

Similarly to the central retina, examination of the thickness of the retinal ganglion cell complex was found to have no significant differences in the right eye (**Table 8-2**), though superior temporal (Kruskal-Wallis H test: χ^2=7.532, df=2 , p=.023), inferior temporal (Kruskal-Wallis H test: χ^2=13.131, df=2, p=.001), superior nasal (Kruskal-Wallis H test: χ^2=10.493, df=2, p=.005) and inferior nasal (Kruskal-Wallis H test: χ^2=8.540, df=2, p=.014) regions of the left eye were observed exhibit differences between cohorts.

Retinal location	Stroke (mean ± SD)	Control (mean ± SD)	p
Central retina - Right eye	270.50 ± 30.36	264.47 ± 29.78	.736
Inner superior retina - Right eye	318.41 ± 20.13	313.14 ± 13.26	.352
Inner temporal retina - Right eye	309.27 ± 18.89	303.04 ± 13.54	.568
Inner inferior retina - Right eye	310.41 ± 25.85	311.81 ± 15.15	.888
Inner nasal retina - Right eye	318.95 ± 17.29	320.29 ±16.92	.891
Outer superior retina - Right eye	271.77 ± 15.59	275.66 ± 17.38	.295
Outer temporal retina - Right eye	267.77 ± 27.74	259.61 ± 10.02	.407
Outer inferior retina - Right eye	266.40 ± 16.38	261.38 ±10.81	.212
Outer nasal Retina - Right eye	286.91 ± 16.91	282.19 ± 11.74	.307
Central retina - Left eye	270.09 ± 35.91	265.57 ± 26.04	.855
Inner superior retina - Left eye	316.86 ± 21.00	314.57 ± 14.22	.498
Inner temporal retina - Left eye	311.63 ± 20.44	314.71 ± 13.73	.151
Inner inferior retina - Left eye	314.04 ± 20.66	310.23 ± 12.47	.894
Inner nasal retina - Left eye	317.04 ± 18.50	306.19 ± 15.96	.168
Outer superior retina - Left eye	283.41 ±29.46	273.19 ± 10.37	.087
Outer temporal retina - Left eye	271.63 ± 25.98	278.95 ± 16.29	.017
Outer inferior retina - Left eye	265.81 ± 18.84	262.33 ± 11.77	.266
Outer nasal Retina - Left eye	264.57 ± 15.01	283.86 ± 17.85	.001

Table 8-1. Summary of central retinal thickness (μm) by ETDRS area for both eyes across stroke and control subjects. p value results represent one way analysis of rank difference between stroke and control subjects both with and without field loss.

Further investigation found that subjects from the stroke cohort with field loss exhibited thinner ganglion cell layer thicknesses than control subjects with no loss in the superior-nasal (Mann-Whitney U test: $p=.004$) and inferior nasal (Mann-Whitney U test: $p=.019$) ganglion cell layer, while stroke survivors without field loss were found to have thinner inferior temporal (Mann-Whitney U test: $p<.001$) and superior temporal (Mann-Whitney U test: $p=.006$). ganglion cell layers than those stroke survivors with field loss.Thickness profiles of the superior nasal, inferior nasal, inferior temporal and superior temporal ganglion cell layers between cohorts can be seen on **Figure 56** ,**Figure 57** , **Figure 58**, and **Figure 59**.

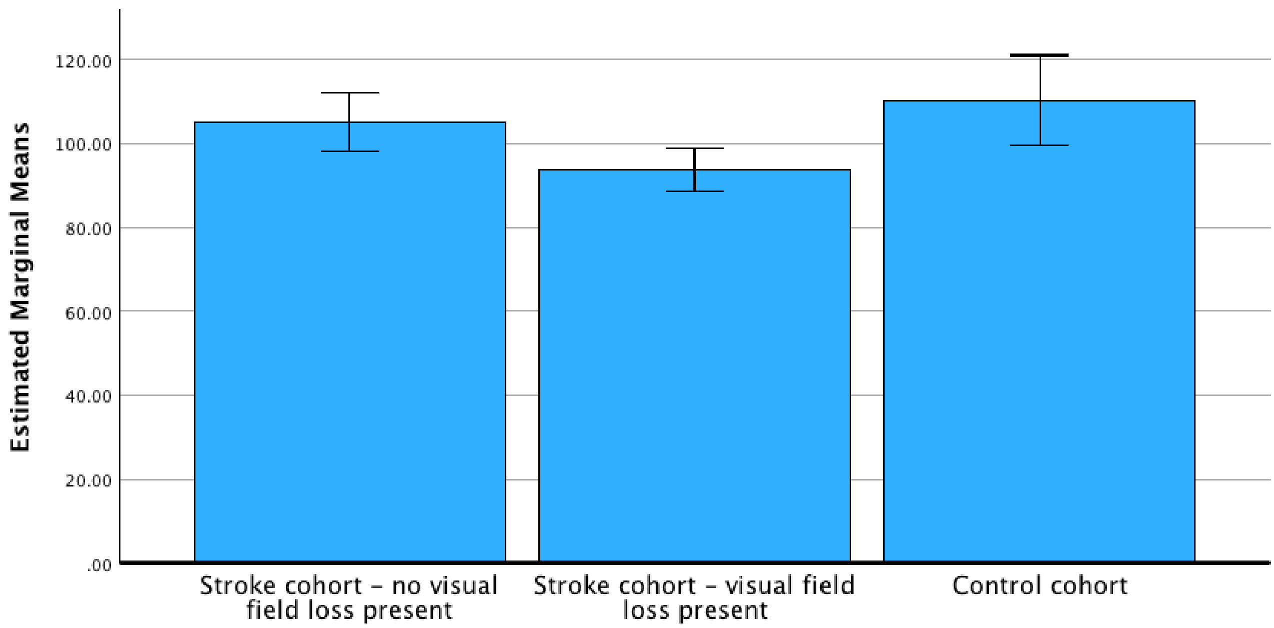


Figure 56: Left eye superior nasal ganglion cell thickness (μm). Error bars represent 95% CI

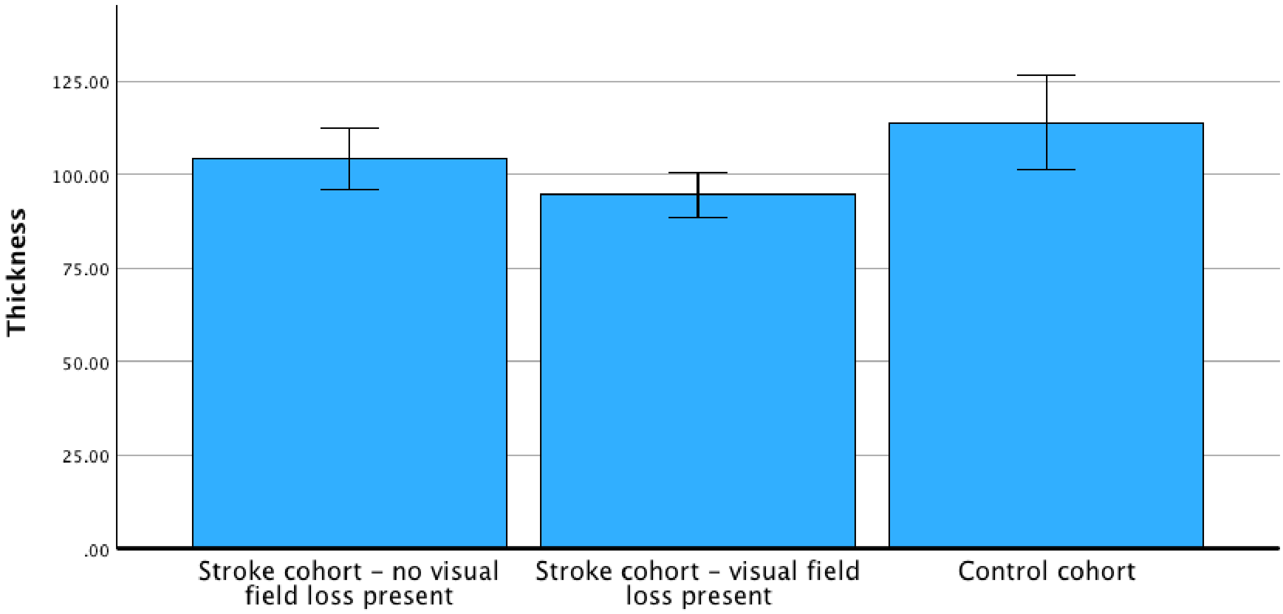


Figure 57: Left eye inferior nasal ganglion cell thickness (μm). Error bars represent 95% CI

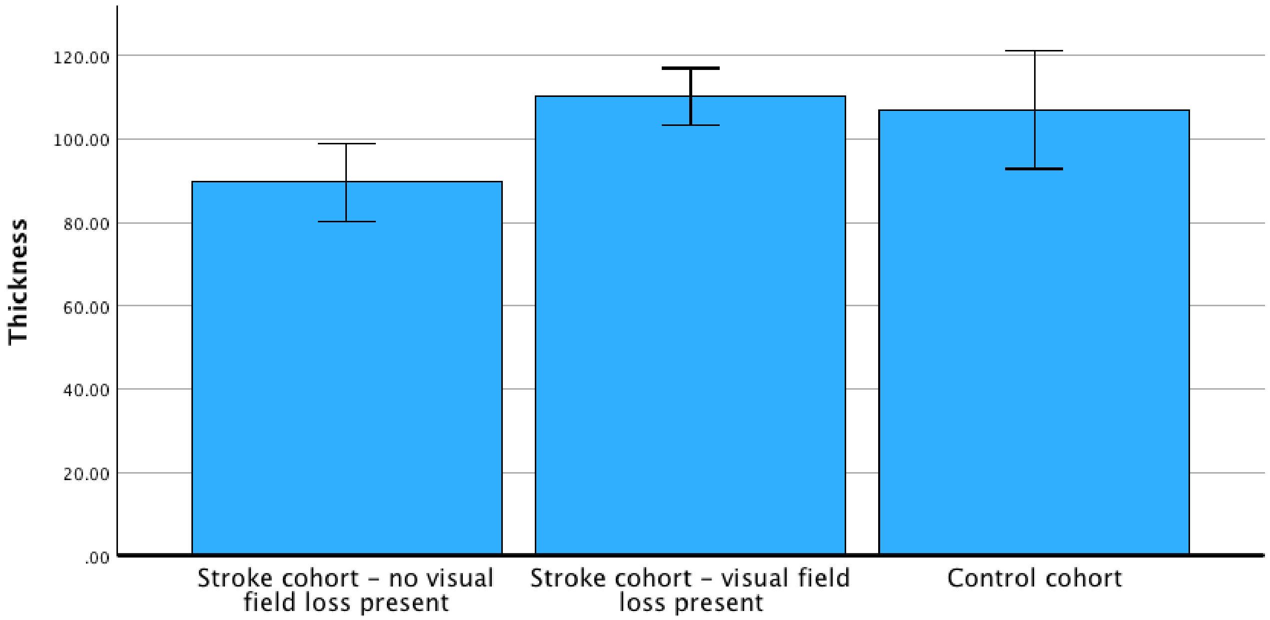


Figure 58: Left eye inferior temporal ganglion cell thickness (μm). Error bars represent 95% CI

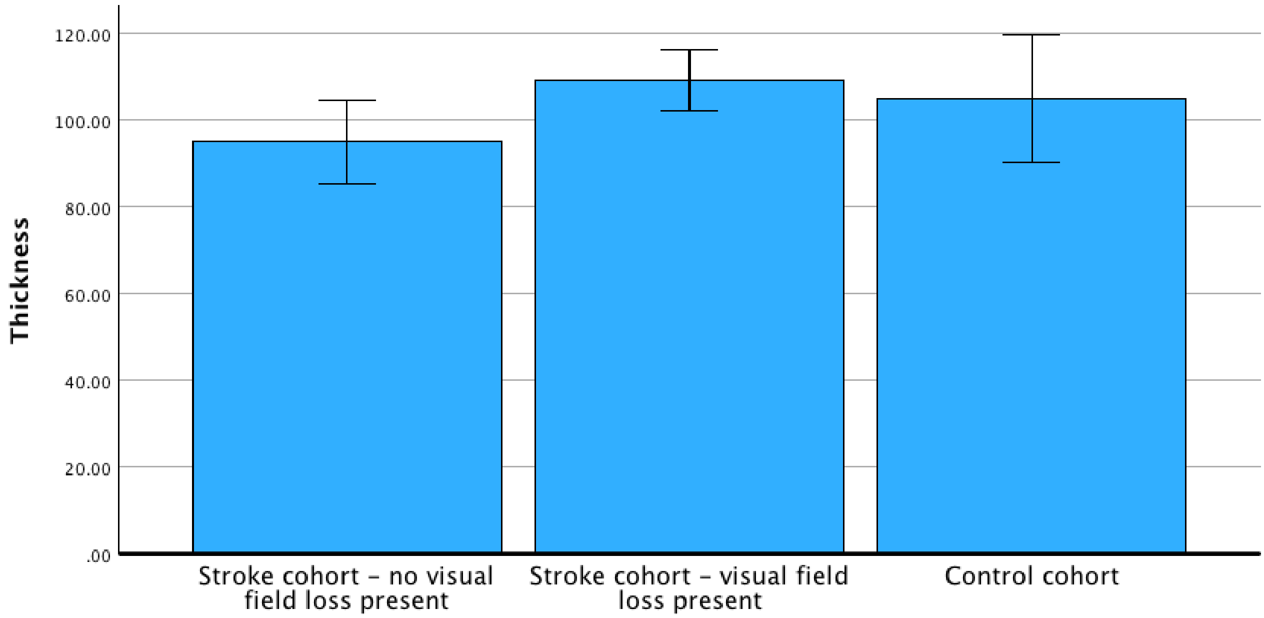


Figure 59: Left eye superior temporal ganglion cell thickness (μm). Error bars represent 95% CI.

No significant difference was observed between cohorts for either superior (Kruskal-Wallis H test: χ^2=2.302, df=2, p=.316) or inferior hemifield thickness (Kruskal-Wallis H test: χ^2=2.250, df=2, p=.325) in the right eye. While subjects with field loss exhibited thinner inferior hemifield thicknesses in the left eye, the difference was not significant between cohorts (Kruskal-Wallis H test: χ^2=5.794, df=2, p=.055). Within the stroke cohort, female subjects were found to have thinner superior-nasal (Unpaired t test: t(19)=-2.635, p=.016) and inferior nasal (Unpaired t test: t(19)=-2.150, p=.045) retinal thicknesses in the left eye than their male counterparts, no other significant differences were observed across genders in either eye.

Ganglion cell region	Stroke (mean ± SD)	Control (mean ± SD)	p
Superior - Right eye	99.10 ± 9.04	105.69 ± 20.44	.715
Superior-nasal - Right eye	108.35 ± 10.98	112.95 ± 7.68	.214
Inferior-nasal - Right eye	109.45 ± 11.32	112.95 ± 11.13	.427
Inferior - Right eye	95.75 ± 12.17	99.81 ± 8.24	.511
Inferior-temporal - Right eye	89.50 ± 9.98	97.13 ± 9.61	.440
Superior-temporal - Right eye	89.20 ± 6.72	89.86 ± 6.02	.924
Superior hemifield - Right eye	98.50 ± 8.40	102.73 ± 7.70	.316
Inferior hemifield - Right eye	98.15 ± 10.19	102.04 ± 8.45	.325
Superior - Left eye	101.85 ± 12.26	101.60 ± 11.86	.111
Superior-nasal - Left eye	93.82 ± 13.51	106.60 ± 12.48	.005
Inferior-nasal - Left eye	94.60 ± 16.92	107.10 ± 14.03	.014
Inferior - Left eye	97.55 ± 11.97	98.43 ± 17.22	.128
Inferior-temporal - Left eye	94.60 ± 16.29	109.34 ± 19.62	.001
Superior-temporal - Left eye	98.15 ± 21.07	108.17 ± 15.12	.023
Superior hemifield - Left eye	101.60 ± 11.80	101.43 ± 11.13	.210
Inferior hemifield - Left eye	99.90 ± 12.24	100.48 ± 16.25	.055

Table 8-2. Summary of thickness of ganglion cell regions (μm) for both eyes across stroke and control subjects. p value results represent one way analysis of rank difference between stroke and control subjects both with and without field loss.

8.3.3 Optic Nerve and Neuro Retinal Rim

Analysis of the optic nerve parameters found no significant differences between cohorts (**Table 8-3**) or genders. Similarly, analysis of the neuro-retinal rim thickness found no significant differences between cohorts (**Figure 60**). Further examination of the stroke cohort found female subjects tended to have thicker superior (Unpaired t test: t(18)=-2.256, p=.036) and temporal (Unpaired t test: t(18)=-2.742, p=.013) nerve fibres in their left eyes, no other differences were observed between cohorts.

Disc parameter	Stroke (mean ± SD)	Control (mean ± SD)	p
Disc area - Right eye	2.05μm^2 ± 0.2μm^2	2.10 ± 0.59	.073
Cup area - Right eye	0.41μm^2 ± 0.15μm^2	0.44μm^2 ± 0.23μm^2	.505
NRR area - Right eye	1.64μm^2 ± 0.19μm^2	1.66 μm^2 ± 0.42μm^2	.270
Horizontal C/D ratio - Right eye	0.39 ± 0.06	0.41 ± 0.09	.875
Vertical C/D ratio - Right eye	0.45 ± 0.07	0.46 ± 0.08	.925
Cup/disc area ratio - Right eye	0.19 ± 0.06	0.19 ± 0.07	.945
Mean cup depth - Right eye	0.20μm ± 0.12μm	0.21μm ± 0.12μm	.560
Max cup depth - Right eye	0.34μm ± 0.16μm	0.35μm ± 0.14μm	.710
Disc area - Left eye	2.05μm^2 ± 0.25μm^2	2.01μm^2 ± 0.49μm^2	.115
Cup area - Left eye	0.43μm^2 ±0.13μm^2	0.41μm^2 ± 0.19μm^2	.145
NRR area - Left eye	1.62μm^2 ± 0.22μm^2	1.65μm^2 ± 0.32μm^2	.171
Horizontal C/D ratio - Left eye	0.41 ± 0.06	0.49 ± 0.08	.176
Vertical C/D ratio - Left eye	0.49 ± 0.07	0.48 ± 0.08	.360
Cup/disc area ratio - Left eye	0.21 ± 0.06	0.19 ± 0.06	.263
Mean cup depth - Left eye	0.19μm ± 0.12μm	0.21μm ± 0.11μm	.737
Max cup depth - Left eye	0.35μm ± 0.16μm	0.37μm ± 0.13μm	.644

Table 8-3. Summary of optic nerve head characteristics across both eyes across stroke and control subjects. p value results represent one way analysis of rank difference between stroke and control subjects both with and without field loss.

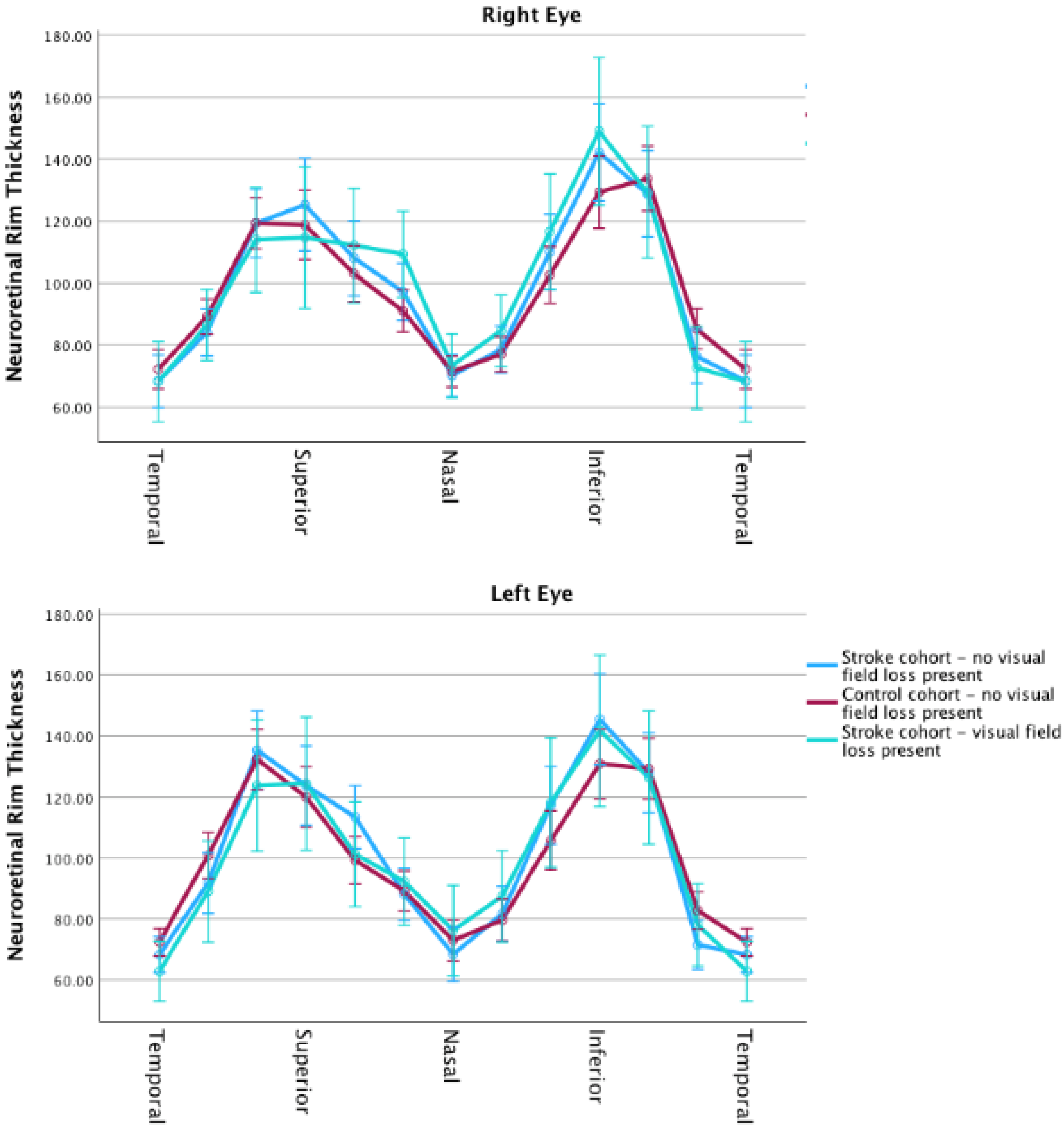


Figure 60. Neuroretinal rim thickness (µm) between cohorts. No significant difference was observed between cohorts for either eye.

8.5 Discussion

This study has identified the presence of subtle thinning in the outer retina of the left eye in subjects with a history of stroke, notably this thinning was not consistent between stroke survivors who did or did not exhibit concurrent visual field loss. Interestingly, no significant differences were observed between stroke and control cohorts in terms of optic nerve head or neuroretinal rim integrity. The findings of this study are however limited by the small sample size. While previous investigations have reported small (Hokazono and Ribeiro Monteiro 2019; Liang et al. 2022) and large (Tatsumi et al. 2005; Park et al. 2013; Newman-Wasser et al. 2019; Lee et al. 2020; Rashid et al. 2021) effects observed between cohorts, the findings of this study would suggest subtle thinning of the peripheral retina and ganglion cell layer may be observed in stroke survivors. Post hoc power analysis would suggest that for the detection of small effect size, the power of the one-way analysis of ranks would be 0.08. Even where direct comparison between stroke and control groups is considered to detect thinning within the stroke cohort (one tailed t-test) the power would be 0.17. This is further reflected by the significant variance on confidence intervals observed between the different cohorts. While sufficient power is present to confirm that large differences between stroke and control participants (power 0.86) is likely to not be present in this study, any statement on low or medium effects risks erroneous conclusions. As such should this approach be used again in future, it may serve to provide guidance on investigation of retinal thinning following stroke, the findings of this study should not be considered definitive.

Previous studies have documented thinning of the neuroretinal rim and ganglion cell layer in stroke patients, with changes found in both individuals with and without measurable visual field defects (Tatsumi et al. 2005; Park et al. 2013; Hokazono and Ribeiro Monteiro 2019; Newman-Wasser et al. 2019; Lee et al. 2020; Rashid et al. 2021). Many of these findings suggest a structural-functional relationship, where thinning observed in OCT testing corresponds to functional loss observed in perimetry. The consistency between structural OCT changes and field loss in some cases implies that retinal and optic nerve changes could serve as indicators of post-stroke damage, particularly in the interneuronal layers involved in primary visual processing. However, in this current study, while one case (**Figure 61**) did show this correspondence, this was not a trend observed consistently across all subjects with field loss, indicating that this relationship may not be universal. In particular, the potential for subclinical retinal changes following cerebrovascular accidents highlight the outer retina as a vulnerable region to degeneration following these episodes. This would suggest that while OCT-based structural changes might reflect visual field deficits in some cases, other variables may influence these structural changes, preventing a straightforward structural-functional association in every case.

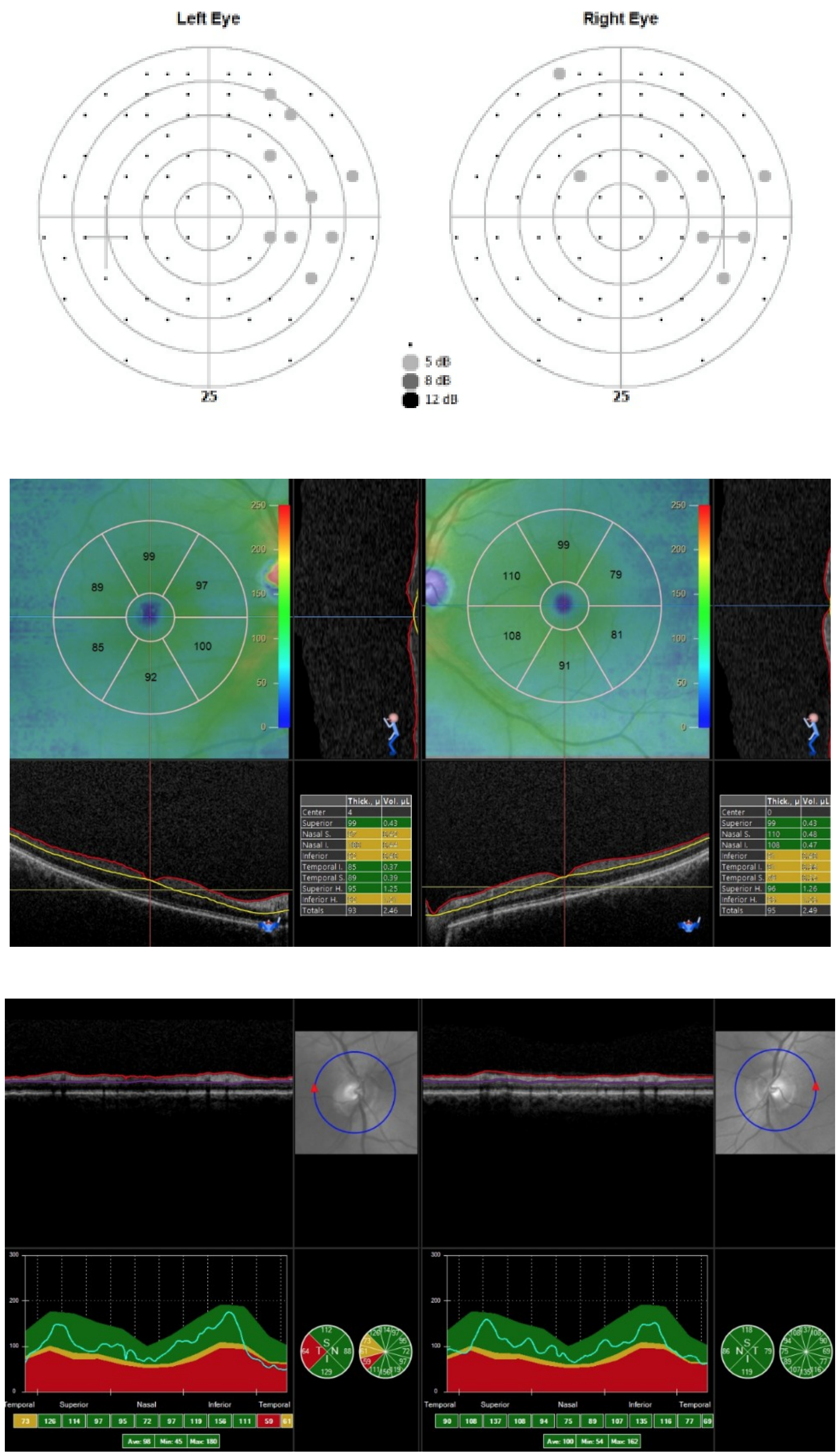


Figure 61. Field loss, RGC layer and NRR profile of subject 15 (stroke cohort, VF loss), exhibiting right sided relative homonymous scotomas with NRR and RGC layer thinning. While the retinal thinning correlates with the corresponding areas of loss of peripheral sensitivity, it is notable that only the right NRR exhibits corresponding thinning relative to the normative database.

Unusually, within this cohort no significant anomalies of the optic nerve head or neuroretinal rim were observed, even where field loss was present, contrasting with findings from some previous research. This difference might point to variability in how the neuroretinal rim responds to stroke-related damage across different patient populations, which may not always correlate with field loss detected on perimetric testing as would be anticipated. This has been observed in other conditions (Klistorner et al. 2009; Nilforushan et al. 2012; Alonso-Plasencia et al. 2019; Donaldson and Margolin 2021), and would suggest that the pattern of loss may be more complex. Differences in patient demographics, stroke location, stroke severity, time since stroke onset and instrumentation likely contribute to the lack of uniformity in findings across studies. For example, some research has suggested that neuroretinal rim thinning only becomes evident over a more extended period post-stroke, typically observable after a year (Rashid et al. 2021; Ye et al. 2022). In this study, only two subjects had experienced their stroke less than a year prior to participation, and with the exception of these cases, loss of retinal thickness would be expected to have been present were it going to occur. This would indicate that neuroretinal rim thinning is not an inevitable consequence of stroke, particularly in cases where visual field loss is absent.

As the only part of the central nervous system that is visible for direct examination, the neuroretina provides a unique, accessible window to assess the structural integrity of the brain and infer potential functional changes (Mutlu et al. 2017; Mutlu et al. 2018; Chua et al. 2021). Sparing of the axons making up the neuroretinal rim may suggest that retrograde degenerative changes are selective, potentially affecting those peripheral nerve fibres whilst having minimal impact on the overall thickness of the nerve fibre layer. While some studies investigating retrograde degenerative changes following neurological insult have reported degenerative changes to affect interneuronal thickness to the level of the inner nuclear layer (Green et al. 2010a; Abegg et al. 2012; Sriram et al. 2012; Kaushik et al. 2013; Ong et al. 2015; Mutlu et al. 2017; de Vries-Knoppert et al. 2019; Sotirchos et al. 2020), there is some disparity to the extent of these changes, with some studies finding no differences in retinal parameters following cortical insult (Heßler et al. 2015; Sayin et al. 2015). The literature suggests that the degree of retinal changes following cerebrovascular accident likely varies depending upon the location of insult, with damage to larger vessels giving rise to greater degeneration (Zhang et al. 2006; Tao et al. 2012) and insult on the visual pathway providing more explicit patterns of nerve fibre and ganglion cell layer degeneration than those adjacent or elsewhere in the brain (Bridge et al. 2011; Jindahra et al. 2012; Park et al. 2013; Millington et al. 2014; Mutlu et al. 2018; Ye et al. 2022). While thinning associated with functional loss has been reported (Rashid et al. 2021), others have found thinning of nerve fibre and ganglion cell layers in the eye ipsilateral to lesion location (Kwapong et al. 2022; Ye et al. 2022), suggesting instead impaired blood flow to the ipsilateral ophthalmic artery and choroid as the source of this degenerative thinning.

Measurements of parameters may be further confounded by the impact of other ocular anomalies that may coexist in the presence of cerebrovascular injury and may confound results. In addition to macular anomalies (Elsharkawy et al. 2021; Metrangolo et al. 2021; Wu et al. 2021; Heckenlaible et al. 2024; Hu et al. 2024), OCT parameters may appear or be altered in the presence of large optic nerves (El-Dairi et al. 2011; Chen and Kardon 2016), optic nerve anomalies (Bussel et al. 2014b; Hood and Raza 2014; Geevarghese et al. 2021), developmental anomalies (Oh et al. 2007; Maldonado and Toth 2013; Bassi and Mohana 2014; Jain et al. 2020; Sibony et al. 2021), ocular injury (Wylegala et al. 2009; Ryan et al. 2013; Oladiwura et al. 2014), and even in strabismus (Oka et al. 2013; Meng et al. 2023), though this latter point is contentious (Altintas et al. 2005; Ersan et al. 2013). Additionally databases may be limited in the scope and size of their datasets, highlighting the limits of their use as a tool for standalone investigation of retinal changes following brain injury (Nakayama et al. 2023).

Choroidal circulation is thought to contribute over 80% of vascular supply to the eye (Nickla and Wallman 2010) and it has been postulated that changes to the retinal vessels and ocular choroid may reflect similar changes in the cortical choroid (Erskine and Herreral 2015; Kajita et al. 2024). Investigation of choroidal blood flow is complex as significant variation may be observed between individuals due to the individual differences in distribution of end arteries within the choroid (Singh Hayreh 1990; Takahashi et al. 1996; Albrecht May and Rutkowski 2019). While investigations into vascular flow have identified choroidal thinning following stroke (Li et al. 2021; Gonzalez-Marrero et al. 2022; Kwapong et al. 2022; Wan et al. 2022), these have focussed on the central retina with little attention paid to peripheral vasculature.

The findings of this study support the view that retrograde degenerative changes frequently supposed as the cause of nerve fibre layer thinning may not account for the retinal changes observed post stroke. The selective vulnerability of the outer retina may indicate a distinct vascular origin at play impacted by other factors such as ischaemia, oxidative stress or possible inflammatory responses (He et al. 2023). Further investigation is warranted to assess retinal thickness changes following cerebrovascular accident, accounting for anatomic and morphological changes in retinal vasculature in the affected area of retina. Such work may provide insight into the drivers of retinal changes following neurological events, especially where the locus of the lesion does not fall on the visual pathway.

Investigations into the presence of field loss following stroke frequently present significant heterogeneity in methodology (Rowe et al. 2013a; Rowe et al. 2017), with field loss being quantified using a variety of methods such as static automated, kinetic and even confrontation fields. This study utilised suprathreshold automated perimetry, using a device that assesses the field following establishment of a central threshold (see **Chapter 4**). While popular in primary care, the device was initially designed for the identification of glaucomatous loss, with a sampling pattern set for sensitivity in this role. While the device serves to identify the presence of depressions in retinal sensitivity, it is not designed or optimised for detecting changes secondary to neurological origin. While overt field losses such as hemianopia may be readily observed, it is possible that subtle pattern loss may go unnoticed due to the instrument's sampling strategy.

This is the first study to employ the Optos Monaco device for retinal imaging and OCT measurements in post-stroke patients. While this instrument has been reported to provide reliable imaging that correlates well with other OCT devices, there are known discrepancies in retinal thickness measurements between this and other instruments (Enghelberg et al. 2022). Difference in image quality may also be observed between systems, with greater resolution being observed with other contemporary devices (Enghelberg et al. 2022). With deterioration in image quality, accuracy in retinal segmentation algorithms may be impaired, resulting in discrepancies in thickness measurements compared with other instruments. This may be exacerbated in the presence of lenticular opacities particularly in older subjects where the presence of media opacities may further impair imaging. Because of this, the Optos Monaco may yield slightly different values, making it near impossible to directly compare these results to those from studies employing other devices. Despite this, OCT instruments are based upon consistent imaging principles and remain highly effective in detecting retinal pathology. In the case of neurological insult where retinal changes may arise sometime after the episode and with sufficient testing (Bradley et al. 2023), this approach may offer a potentially sensitive method of monitoring for subtle changes over time, offering valuable insights even if inter-device variations exist.

While limited, these measurements add to the body of literature investigating the presence of retinal thinning following stroke. The absence of direct structural-functional mapping is a phenomenon that has been observed in other works and warrants investigation to further understand the mechanisms influencing post-stroke retinal thinning. Future longitudinal studies would be beneficial to determine if these retinal changes are progressive leading to degeneration over time. With better understanding, retinal imaging may serve as a useful surrogate of cortical integrity, with the potential of further integration of ocular health into the broader framework of stroke recovery.

These findings have previously been presented as a poster:

Maciver M. Wolffsohn J.S., & Logan N. (2024, Sept) *An investigation into retinal thickness in stroke survivors with and without visual field loss.* Poster presented at the 6th Interdisciplinary Postgraduate Research Conference, Aston University. Birmingham

Chapter 9 Conclusions

Clinicians in primary eye care frequently encounter patients with a history of stroke. While in many cases these patients may have been minimally impacted, some experience significant visual issues. While research and professional bodies have provided recommendations on the care of patients with other neurological and cognitive anomalies, similar recommendations have not been made for patient's visual issues following stroke.

While a range of ocular sequelae affecting the visual system have been reported following stroke - affecting visual, ocular health, oculomotor and binocular systems (Bodis-Wollner, 1972; Ciuffreda et al., 2007; Clatworthy et al., 2013; Darling et al., 2003; Dos Santos & Andrade, 2012; Munk et al., 2023; Padula & Argyris, 1996; Pitzalis et al., 2005; Rowe, 2009, 2010, 2011; Rowe et al., 2011, 2013b, 2013a, 2017, 2019; Rutner et al., 2006; Suchoff et al., 2008) - investigations into the best approaches to conduct ocular examinations for this group are limited. Research into the evidence base for ophthalmic diagnostic examinations is limited generally (American Optometric Association 2015; American Optometric Association 2023), but the stroke population is further underrepresented. This can result in a number of individuals who have experienced stroke struggling to access elements of primary eye care, frequently being recommended to inappropriately attend secondary care providers due to the presence of visual anomalies following stroke. It was this latter point that the author had observed to occur on several occasions in primary eye care practice that led to this work.

Examination of the published evidence base identified limited information on the appropriate diagnostic approaches to be used in this population. This initial review highlighted a limitation of the evidence base in other areas. During clinical practice much of the management approaches used by clinicians for anomalies of binocular vision are reliant upon information that is derived mainly from healthy subjects who frequently are younger than the typical stroke survivor. As such this may not accurately represent the typical post-stroke binocular visual system, or even that of those older subjects present as controls. While previous research reported upon the presence of pattern glare (Beasley and Davies 2012; Beasley and Davies 2013b) and the improvement in reading performance in stroke survivors with the use of chromatic overlays (Beasley and Davies 2013a), the impact of post stroke field loss was not investigated in detail, with only a single case study present in the literature (Beasley and Davies 2013b). While field loss is a long-recognised sequela of cerebrovascular accidents in many patients, evidence was mixed as to the retinal changes that may occur following this loss.

This thesis sought to develop and trial a test battery with the potential to be used in primary eye care practice to provide an appropriate baseline visual examination for patients with a history of stroke. Additionally, this work sought to investigate the binocular status of stroke survivors, comparing them to age matched controls, providing an overview of the normal binocular profile in this population. This study investigated the impact of field loss on the presence of pattern glare as well as the impact of this field loss on the response to the use of chromatic overlays. Finally, an investigation of retinal thickness was undertaken to assess changes in retinal thickness that may have arisen secondary to the cerebrovascular event, to provide additional guidance to the clinical professional in delivery of primary eye care to this demographic.

Appropriate visual care of stroke survivors exhibiting symptoms of possible visual deficits require examination using procedures that are clinically appropriate and efficient. Within this group there is greater risk of fatigue (Cumming et al. 2016), attention and communication difficulties (Wray et al. 2019) and where the clinician may attempt to separate elements of the assessment to multiple sessions to reduce the cognitive impact risk of non-attendance (Marzolini et al. 2016). The review of literature undertaken in **Chapter 2** on the diagnostic methods highlighted the limitations on the evidence base for the procedures used in ophthalmic examination on patients with a history of stroke. Those studies exhibited small sample sizes and design limitations, raising concerns over their generalizability to stroke survivors. In the absence of strong evidence to support diagnostic procedures or formal guidance to the appropriate approaches, the development of an instrument could serve as an interim solution to aid primary eye care professionals in the provision of care to this group.

While access to hospital-based eye care services for acute stroke patients has improved over the past decade (Hepworth and Rowe 2019), gaps remain, particularly in community-based services (Rowe 2010b; Rowe 2011b; Rowe 2017a; Stalin et al. 2024a; Stalin et al. 2024b). Many regions lack commissioned community eye care programs specifically tailored for stroke patients, and the accessibility of such services may be further hindered by perceptual and financial barriers (Hayden 2012; Association of Optometrists 2022; College of Optometrists 2023a). Many patients face challenges in accessing primary eye care due to limited knowledge of eye health issues or the perceived financial burden of examination and optical appliances. Even among practitioners, time and financial constraints may limit the extent of care provided. This inequity in service provision is compounded by variability in diagnostic approaches, with some practitioners modifying their testing based on time limitations or the likelihood of follow-up appointments. With a lack of sensitive visual screening tools and reliance on patient-reported symptoms it has been suggested that the prevalence of visual impairments post-stroke is likely underreported (Cockburn 1983; Rowe 2011b; Baxter et al. 2013; Rowe 2013). With an aging population and increasing stroke survival rates, it is likely that many of these patients will have their visual care provided in a primary eye care setting. **Chapter 3** reports on the development of a novel consensus-based minimum diagnostic test battery providing a standardized approach to the visual examination of stroke survivors. The test battery developed consisted of many test procedures that would be considered to constitute a comprehensive eye examination, sharing many features of the routine eye examination or sight test outlined within the College of Optometrists' Guidance for Professional Practice (**Table 2-1.**) While primarily designed for use within the primary care setting the test battery could potentially be used to detect, monitor, and manage visual anomalies post-stroke in a range of settings.

Evaluation of this test battery was undertaken and reported upon in **Chapter 5**, where the battery was assessed against the findings of a typical sight test provided in primary eye care practice. While significant agreement was observed within measures of refraction, refractive outcome, visual acuity, the presence of corneal anomalies, intraocular pressure and examination of the structures of the posterior pole, discrepancies were noted in the assessment of anterior segment, peripheral retinal anomalies and binocular vision testing where a greater prevalence of anomalies were observed by the test battery. However, the battery was insensitive to visual neglect and peripheral field loss—common post-stroke impairments—due to the absence of neglect screening items, automated or confrontation perimetry, and a reliance on the Amsler grid, which was inadequate for assessing peripheral vision. Frequently encountered following stroke, these deficits can have a significant impact upon mobility, reading ability, and can have implications on other tasks such as driving (Ruben et al. 2001; Azouvi et al. 2006; Bartolomeo 2021; Rowe et al. 2011; Stein 2022). As indicated above, the trial battery may be readily considered as a thorough eye examination, recognisable as the standard to which many optometrists are trained, and to the recommendations provided by guidance by professional bodies (Association of Optometrists 2015; College of Optometrists 2023b). While the battery identified a greater prevalence of anomalies compared to the reference standard assessment, this highlights the limitations of typical sight testing undertaken in primary eye care practice. It is unclear how these limitations, particularly the increased observation of ocular surface, binocular vision and peripheral retinal anomalies in the trial battery examination relates to clinical outcomes. Indeed, where visual anomalies such as peripheral vision loss go undetected, these have significant risks of further potential problems for the patient such as safe navigation. Should a patient with field loss (especially where sensory neglect is present) continue certain day-to-day tasks such as driving this has the potential to result in life-threatening consequences. Further investigation is necessary to determine whether the contemporary sight testing sufficiently addresses the needs of stroke survivors, and whether disparities between this and a comprehensive examination translates to improved clinical outcomes or patient care.

The presence of anomalies of eye movements, coordination and an increased presence of binocular vision anomalies have been reported within stroke survivors (Pedersen and Troost 1981; Leff et al. 2000; Ciuffreda et al. 2007; Suchoff et al. 2008; Rowe 2010a; Rowe 2011a; Rowe et al. 2013b; Stein 2022). While various interventions for eye movement, vergence, and binocular vision rehabilitation have been proposed, these remain largely unvalidated (Padula 1988; Pollock et al. 2011; Padula et al. 2012; Hill et al. 2015; Chang et al. 2016; Smaakjær et al. 2018; Axelsson et al. 2019). Closer evaluation however identifies that most existing studies rely upon case reports or small case series rather than robust randomized trials, and indeed much of the normative data typically reported in orthoptic training texts is the result of older studies in healthy pre-presbyopic, or early presbyopic populations (Ogle et al. 1967; Stidwill and Fletcher 2011; Scheiman and Wick 2013; Evans 2022). **Chapter 6** reported upon a cross-sectional evaluation of the binocular vision profile of stroke survivors and age matched control subjects. While poorer performance in eye movements was observed in stroke survivors than controls, surprisingly those subjects with field defects performed better than those without defects. Contrary to what might be expected, little difference was observed when assessing general orthoptic measures between cohorts, with similar levels of sensory fusion, heterophoria, fusional vergence ranges and stereopsis observed between cohorts. Despite this it is notable that the measures across both cohorts differed from published normals commonly referred to in authoritative texts. While this study provides limited insight into differences in binocular function between stroke survivors and controls, it provides new normative data for the typical binocular vision profile of patients in later presbyopia. While a limited number of subjects were able to complete measurement of fixation disparity curves at near, for those that were able to complete, the profile of control subjects was similar to those reported by Ogle (1967), while a greater incidence of base in acceptance (Type III) and binocular instability (Type IV) was observed within the stroke survivors. This final point suggests that alterations of binocular profile following stroke may be more complex, with post stroke symptoms resulting from subtle alterations of binocular control of retinal slip rather than significant loss of motor fusional ability.

Previous work by Beasley and Davies identified the increased presence of pattern glare in subjects with a history of stroke (Beasley and Davies 2012), an improvement in reading speed with the use of coloured overlays (Beasley and Davies 2013a) and reported upon the use of chromatic overlays to reduce symptoms of pattern glare in a patient with a history of stroke with visual field loss (Beasley and Davies 2013b). **Chapter 7** undertakes similar work, where like these previous studies that increased pattern glare scores and improved reading speeds using chromatic overlays within stroke survivors compared to controls. Notably elevation in pattern glare scores was observed to occur primarily for the mid-spatial frequency target, elevating the total score and, by extension the mid-high difference score. While the mid-spatial frequency target aligns with the visual system's peak sensitivity to contrast (Fernandez and Wilkins 2008), no difference in low contrast resolution was observed between cohorts. While stroke survivors with associated field loss were observed to exhibit greater pattern glare scores, marginal improvement was observed in reading speed when using overlays. Contrary to previous investigations no significant change in reading error scores were observed between cohorts when using coloured overlays. While the origin of the symptoms has been suggested to be the result of cortical hyperexcitability with the use of chromatic overlays reducing this response (Carmichael 2012; Bargary et al. 2015; O'Brien et al. 2020; Wilkins et al. 2022), these findings would suggest that a different mechanism may be present in stroke survivors who exhibit visual field loss.

Finally, **Chapter 8** undertook a cross-sectional investigation to investigate retinal thickness changes that occur following stroke both with and without coexistent field loss compared to a control cohort. While a single case of retinal thinning was observed that followed a retinotopic pattern of loss, the majority of OCT parameters exhibited no significant differences between cohorts. Sub-clinical thinning of the peripheral retina was measured to be present in stroke survivors without field loss, with no significant thinning observed in those with field loss. These findings highlight that field loss present may not correlate with structural findings at the retinal, neuroretinal rim or optic nerve head on OCT testing which may be influenced by factors other than retrograde degeneration in the presence of field loss. While no firm conclusion may be drawn from these findings, they contribute to the ongoing debate on the nature of post-stroke retinal changes. While the findings are more in line with the theory that many retinal changes observed post stroke are likely the result of vascular ischaemia, due to the low sample size, other theories cannot be excluded.

9.1 Practical implications of findings

Ophthalmic providers, especially those with limited experience may have difficulty in the selection and application of diagnostic procedures when managing patients with complex histories (Faucher et al. 2012). When addressing presentations outside their experience of routine care provision - due to lack of confidence or concern over examination time – may refer or direct patients to other sources of provision without examination (Parkins et al. 2018). This thesis sought to develop an instrument that could be employed by eye care professionals of all levels to aid in the provision of ophthalmic care to stroke survivors. The test battery developed is simple and may be undertaken using instrumentation readily available in primary care practice. Indeed, its contents may be considered as that of a good eye examination, sharing a number of features with the College of Optometrists' recommendations for the routine eye examination or sight test (**Table 2-1**). The outcomes of this test battery were observed to be consistent with many of the outcomes of conventional testing, while sensitive to the identification of ocular surface, peripheral retinal and anomalies of binocular vision. Given the limitation of the Amsler test within the instrument identification of field loss (or indeed the lack of sensitivity to macular pathology), the findings of **Chapter 5** would suggest that the substitution of this procedure with automated perimetry may be of greater benefit in the detection of peripheral anomalies that may be present following stroke (Zhang et al. 2006).

Similarly, while we may suspect that based on the absence of symptoms alongside documented of field loss in at least one participant (8) raises the question of unidentified visual neglect. This sole observation falls short of the expected prevalence reported in the literature (Esposito et al. 2021). Given the asymptomatic nature of the anomaly and the absence of testing procedures employed this is another area of weakness within the test battery. While a number of formal testing approaches may be employed to assess perception and spatial awareness in stroke survivors (Cermak and Hausser 1989; Ten Brink et al. 2018; Chiu et al. 2019; Friedman and Leong 1992), a range of simple chairside testing approaches can be used to examine for visual neglect, with simple paper-based tests such as the line bisection, star cancellation and clock drawing test being easily incorporated into an ophthalmic examination (Agrell et al. 1997; Plummer et al. 2003; Molenberghs and Sale 2011; Moore et al. 2022). Similarly, several simple tests may be employed to explore reading ability and visual stress (**Chapter 7**) screen for anomalies of spatial awareness and visual midline shift (Padula and Argyris 1996; Cohen et al. 2013; Padula et al. 2017) and screen visual perceptual skills such as laterality and visual memory (Scheiman 2011; Cohen et al. 2013). While this modified test battery may not be of routinely useful to the experienced clinician, its linear structure and ease of application would be expected to be easily applied within the clinical setting by less experienced clinicians (Faucher et al. 2012).

While inexperienced clinicians may be concerned about the complexity of managing patients with a history of stroke, this thesis has identified that stroke survivors require a thorough examination, assessing the visual, binocular, and refractive systems as well as ocular health. This examination may also benefit from perceptual screening for visual neglect in order best support patients in accessing rehabilitation. Where onward referral was indicated, or where an inexperienced clinician wishes to undertake referral the importance of comprehensive testing should not be understated, serving as a useful basis for secondary care clinicians in both the identification of the key visual differentials as well as providing an overview of the ocular status of affected patients. Reducing the risk of duplication and unnecessary testing following referral, improving the targeting of care in a timely manner without unduly burdening the patient with additional procedures.

Binocular vision in older people is poorly evidenced with a limited number of studies undertaken in presbyopic subjects (Freier and Pickwell 1983; Yekta et al. 1989; Pickwell et al. 1991; Palomo Álvarez et al. 2006). The findings of this work suggests that while heterophoria may be similar to published data, vergence ranges fall below those frequently reported in key training texts. This is important to clinicians providing care as it is necessary to recognise that ‘standard’ diagnostic criteria may not be appropriate for this demographic. Somewhat surprisingly the outcomes of this would suggest that clinicians need not be concerned over the history of stroke when evaluating the binocular vision of a patient and may consider their visual status similar to those without a history of brain injury. Given the limited knowledge of normative measures in older age groups, further investigation to identify these, stratifying for age would be useful to provide a better understanding the changes that occur, and set a suitable baseline to investigate interventions for binocular vision anomalies within this age group. Consideration should be given to the equipment employed in future investigation into binocular testing within these groups. While historically ophthalmology and orthoptic investigation has centred heavily on measurement of the motor system, optometry research has focussed more upon employing more naturalistic testing such as the Malett Unit (Karania and Evans 2006; Conway et al. 2012; Myklebust and Riddell 2016; Evans 2022), though the value of this measurement compared to other measures of fixation disparity has been debated (Sheedy and Saladin 1977; Sheedy 1980; London and Crelier 2006). While instrumentation for motor testing such as the Maddox rod and prism bars may be familiar to UK based clinicians, other methods of heterophoria testing may be more consistent and repeatable (Rainey et al. 1998a), and phoropter based procedures may be more applicable given their growing adoption within the UK and widespread use internationally. One of the challenges within this work due to the small and uneven sample sizes is that those subjects selected may not be representative of stroke survivors and indeed controls at large, and assessment with greater, more evenly distributed samples may provide more robust data.

While oculomotor control was observed to be poorer within the stroke cohort, unexpectedly this was worse in those stroke subjects without field loss. Previous studies have observed poorer eye movement control in the presence of field loss (Pambakian et al. 2004; Butler et al. 2009; Wiecek et al. 2012). This leads to the suspicion that subjects within this study were better adapted to the visual anomalies present than those stroke subjects without field defect, a feature previously observed by Zihl (2010). One challenge is the limited evidence base supporting the clinical evaluation of saccade and pursuit measures in practice. While a range of procedures are available to the clinician, the repeatability, inter and intra-clinician reliability and even validity of many of these procedures remains unknown. Without replication, caution should be exhibited when relying upon the results of these, and further investigation using either objective technology or validated clinical procedures should be employed.

As with previous work (Beasley and Davies 2012), this study found an increased presence of pattern glare was observed in the stroke cohort. Notably with significant increase in symptoms when viewing the mid spatial frequency target, especially where field defects were present. When encountering patients with a history of stroke, clinicians should be sensitive to the presence of symptoms of pattern glare and ready to investigate whether the use of overlays would benefit these patients, being cautious in cases of field loss. While both the mid spatial frequency and mid-high difference score have been identified as significant measures of pattern glare, this study's findings suggest that within this cohort the mid spatial frequency score alone may be the most useful indicator for symptoms of pattern glare. While it may be tempting to consider the other target pages redundant, it should be noted that the first and third page of this test serve the supplementary purpose of instructing and control for suggestibility or potential malingering (Evans and Stevenson 2008).

While a variety of possible origins have been suggested for these symptoms no definitive cause has been identified. Electrodiagnostic studies within susceptible individuals may be of use in identifying the origin of these symptoms, which with better understanding may provide insight into possible avenues of management. Likewise, this approach may be beneficial in attempting to identify why stroke survivors with field defects have limited improvement in their reading performance when using chromatic filters, as this approach has been useful in both observing physiological changes (Yadav and Ciuffreda 2015), responses to treatment (Yadav et al. 2014) and response to coloured ovelays (Yadav and Quan 2022) in other neurological conditions. Indeed these symptoms may be of multifactorial origin and that other theories with further investigation may better explain this lack of improvement in this group. A useful avenue to explore would be the presence of other perceptual deficits and the impact on their presence on the alteration of reading speed and accuracy with chromatic filters.

While the findings of this study contradict previous work with no significant differences in low contrast sensitivity observed between stroke and control subjects (Bodis-Wollner 1972; dos Santos and Andrade

2012; Clatworthy et al. 2013), the use of a conventional contrast sensitivity test rather than an electronic platform (Thayaparan et al. 2007) and other measures of perceptual function may provide insight to developing a new paradigm of understanding of these phenomena. Another angle that may be investigated would be to assess the impact of selected intuitive overlays compared to the use of a simple a blue or yellow overlay (Stein 2014) with possible follow-up investigating of whether those subjects that do respond to overlays would benefit from precision tinting with colorimetry, comparing the outcome of this with a cosmetically similar coloured appliance.

When providing advanced imaging in primary care to patients, this study suggests that retinotopic thinning may be less frequently encountered in the presence of field defects than expected. While an important finding where present, clinicians should be aware of possible subtle retinal thinning, and where present, should consider the use of tracking software to monitor. While the implications of this thinning are unclear these changes should raise awareness in the clinician and make them sensitive to pathologic changes that may be observed. One weakness in this study was the absence of data collection in respect to the laterality of stroke affecting this cohort. While previous work has reported ipsilateral retinal thinning following stroke (Kwapong et al. 2022; Ye et al. 2022), and left hemisphere strokes dominate, the data of laterality would have been useful in supporting the proposition that thinning of the retina is the result of poor vascular flow, which the data in this study is insufficient to report. Studies in OCT changes following stroke tend to give rise to disparate findings and given the complex patterns of retinal changes following stroke, may benefit from large scale studies factoring the area of brain damage to better understand the patterns of change in the neuroretina following cerebrovascular insult.

This study presents several key findings. Although its primary aim was to develop a diagnostic test battery suitable for use in community optometry settings, the resulting instrument described in **Chapter 3** shares many elements of the routine eye examination outlined in the College of Optometrists' guidance for professional practice for the routine eye examination or sight test (**Table 2-1**). The College of Optometrists provides guidance for clinicians over several areas of clinical practice. This guidance is provided for practitioners as a benchmark to base their typical examination against, though it should be noted that (subject to meeting the minimum regulatory requirements of the Opticians Act 1989) it is not mandatory to complete all elements listed. The Opticians Act (1989) requires an optometrist to undertake an examination of the internal and external surface of the eye and associated structures in its immediate vicinity for the purpose of detecting signs of injury, disease or abnormality in the eye or elsewhere. As such there is the potential for variability to be observed between clinicians in terms of testing procedures and protocol. Substantial variation has been reported in the processes followed when patients present with a range of visual symptoms (Shah et al. 2008; Shah et al. 2009d; Shah et al. 2009a; Shah et al. 2009b), raising the question whether a ‘standard sight test’ exists.

Although the test battery was developed through a structured Delphi process (**Chapter 3**) with the aim of establishing a specialised protocol for examining stroke survivors, many clinicians may recognise its components as resembling those of a thorough eye examination. However, the findings presented in **Chapter 5** indicate a concerning disparity: that standard sight tests typically conducted within community optometric practice often lack the depth of assessment required to adequately address both the visual needs of stroke survivors. Even though all optometrists are trained to perform detailed ocular assessments, the reality observed in clinical practice suggests that time and commercial constraints, as well as clinician assumptions may result in examinations that do not fully address the patient's needs (Shickle et al 2015; Swystun and Davey 2021). This highlights a critical gap between training, clinical guidelines, and real-world practice, underscoring the need for stroke survivors to receive patient centred care addressing their specific visual needs even when not under the care of experienced, specialist clinicians. This work has also emphasised the increased presence of symptoms of visual stress, encouraging clinicians to consider investigating these symptoms as well as exploring these options with patients to identify supplementary appliances that may improve their visual comfort and quality of life. The findings of this study provide a better understanding of the eye movements and coordination following brain injury, setting a baseline of expectations to provide more appropriate orthoptic care to those with symptomatic anomalies. And finally, this work adds to the body of literature of the changes that may be observed in the retina following stroke.

9.2 Limitations

In the absence of sufficient evidence on diagnostic techniques for this study's target demographic the iterative Delphi process was used. While this has been used in other studies within optometry (Myint et al. 2010; Goodrich et al. 2013; Davey et al. 2017; Evans et al. 2017; Holmes and Myint 2018), it relies upon convergence of agreement within an expert panel. While diversity of perspective and extensive subject specific knowledge has been observed to improved rigour in responses the impact may be more limited within a more homogenous group (Linstone and Turoff 1975; Powell 2003; Ibiyemi et al. 2016). While invitations were sent to prominent specialists and circulated with professional bodies, health centres, stroke support and research organisations, this study's respondents were largely homogenous with responses from experienced clinical optometrists and experienced optometrists with an interest in behavioral optometry. As such the instrument design is heavily focused on core tenets of optometric practice. While the battery was useful in detecting typical ophthalmic manifestations of stroke and other ocular anomalies, the perspectives of other experienced stroke specialists such as neurologists, neuro-ophthalmologists, occupational therapists or specialist orthoptists may have provided insight that could enhance the generalizability of the findings in this work. This issue is not unique to this study, shortly following completion of the work incorporated within **Chapter 3**, another research group (Rowe et al. 2019b) undertook a similar piece of work using the Delphi approach to develop outcome measures for visual screening and assessment. While a larger sample size was initially recruited (123), and significant attrition observed (51/123 completed 3 rounds), it is notable that their study was comprised primarily of occupational therapists and orthoptists including only a single ophthalmologist and no optometrists.

The Delphi process suffers from problems of consistency of approach. While the general principles of expert opinion, anonymity of response, iterative responses with feedback and statistical consensus are required there is often little in the way of further structure in the process, with issues of definition of expertise (Hasson and Keeney 2011; Keeney et al. 2011), what constitutes adequate consensus (Keeney et al. 2011; Barrett and Heale 2020), with criticisms that the technique rather than promoting consensus encourages conformity, suppressing divergent opinions (Keeney et al. 2011). While some have suggested that the weaknesses of the Delphi arise due to weakness in the process of applying the method (Hohmann et al. 2018), at the philosophical level the Delphi approach is a method of assessing expert agreement to derive truth, considering truth to be derived inductively from:

An empirical generalisation (or communication) is judged "objective," "true," or "factual" if there is sufficient widespread agreement on it by a group of experts. (Linstone and Turoff 1975)

However, highlighting,

The same dataset can be used to support either theoretical model. The point is that data is not information; information is that which results from the interpretation of the data (Linstone and Turoff 1975).

Ultimately, questioning whether the focus on the expert's knowledge is the pertinent issue, or whether the outcome of the Delphi process should be balanced with perspective arising from other political, sociological and psychological and ethical considerations (Linstone and Turoff 1975). This outlook explains variability of outcomes, though raises questions to whether this approach may be suitable in the provision of healthcare, where potential interventions would be expected to greater support than that of the opinion of (sometimes self) selected experts. To the greatest extent possible it would be expected that, medical decisions, guidelines, and other types of policies are based on and consistent with good evidence of effectiveness and benefit (Skelly and Chapman 2011), rather than relying only upon expert opinion. Structurally, the reliance on expert agreement to infer truth within the Delphi process reflects a form of inductive reasoning that may be based upon indemonstrable premises, an approach that if considered scientific may be readily criticised:

A subjective experience, or a feeling of conviction, can never justify a scientific statement, and that within science it can play no part except that of an object of an empirical inquiry. No matter how intense a feeling of conviction it may be, it can never justify a statement. (Popper 2002)

This is very different from the Delphi approach where the outcome arises as a synthesis of (potentially) conflicting ideas.

Whenever we propose a solution to a problem, we ought to try as hard as we can to overthrow our solution, rather than defend it. (Popper 2002)

While several alternative epistemological approaches may be applied, many frameworks employed within health (and scientific investigation more broadly) may be built upon assumptions that there exists limited evidence *for*, and which many other viable models may be equally explained *by*. Popper's emphasis on falsifiability emphasises that - in his opinion - consensus alone does not constitute evidence, reinforcing the need for consensus-derived models to undergo empirical testing.

While Popper's outlook on theories involves significant scepticism, viewing science as a:

system of hypotheses which in principle cannot be justified, but with which we work as long as the stand up to tests, and of which we are never justified in saying that we know they are 'true' or 'more or less certain' or even 'probable'. (Popper 2002)

This perspective raises a tension in practice, where clinical decision making is often grounded in a combination of observed signs, reported symptoms and the clinician's scientific understanding of physiology and pathology. The choice of treatment will be based on what the clinician's hypothesis of the cause, not in the absence of evidence of testing disproving the presence of the origin.

Within a healthcare context Popper's *positivist* outlook results in an inherent uncertainty in decision-making in the face of uncertainty.

Evidence-Based Practice offers a more pragmatic epistemological approach (Sackett et al. 1996; Satterfield et al. 2009). In this paradigm, empirical evidence is appraised in relation to its relevance, feasibility, and applicability to individual patients (Evans 2007). Integrating the best available evidence from research with clinical expertise and patient values, and provides a more nuanced foundation for care. Since the mid-1990s, this model has gained increasing prominence in both healthcare and optometric research (Rowe and Evans 2017), offering a valuable supplement to clinical judgment rather than a replacement for it. In the absence of strong evidence to support specific aspects of practice these consensus-based models provide a structured, provisional starting point for innovation. Models derived from these expert led consensus based activities should not be considered as static, but evolving frameworks subject to ongoing empirical scrutiny and refinement. Anomalies or failures a model, revealed through quantitative evaluation, could then prompt the development of superior models, advancing the field.

The developmental process… a process of evolution from primitive beginnings - a process whose successive stages are characterised by an increasingly detailed and refined understanding of nature. But nothing that has been or will be said makes it a process of evolution toward anything (Kuhn 2012)

While this work may serve to initiate a standardised approach to the development of the ophthalmic examination of stroke survivors, which eye care professionals may use to inform their clinical judgement (Atkins et al. 2004; Skelly and Chapman 2011). Future development should seek to test quantitatively where practice fails to achieve its aim - as was observed in this study – and look to mechanisms to enhance practice to improve the level of care provided or identify superior clinical approaches.

The instrument developed was tested against the results of a typical sight test undertaken in primary eye care practice. As such this testing does not adhere to the recommendations of the STARD guidelines for reporting diagnostic accuracy studies (Cohen et al. 2016). These guidelines recommend the use of a new test against a recognised *gold standard* assessment. While for some elements this was able to be undertaken (e.g. IOP), due to instrumentation this was not possible for all elements of the procedure. One of the challenges within ophthalmic testing is that several procedures have notable test-retest differences, with variation occurring on different times of day. As such the measurements taken represent a snapshot of the visual system, and the setting of testing should be arranged to minimise potential variation due to other factors such as fatigue. Undertaking examination assessing the newly developed instrument against those gold standard procedures rather than a conventional eye examination would provide a more robust assessment of diagnostic accuracy, with the gold standard assessments setting a true benchmark of presence.

As a trial based in clinical practice the techniques and procedures employed represent those undertaken in primary eye care practice daily. While effort was made to ensure standardisation, undertaking examination in a well-lit, quiet, calm environment using standard procedures, these measures cannot be expected to match those measures obtained within the standardised lab setting. While the author did provide some of the instrumentation for the course of the study, larger instruments used were those available in the research location. While many instruments were able to give objective measures, some instruments (such as retinoscopy or the use of the NSUCO test) relied upon the subjective interpretation of the examiner. While this instrumentation was able to provide measures useful in constructing this work, improvements upon this work could be made through the use of equipment more regularly employed within research settings, able to provide repeatable objective results.

A key limitation of this study was the poor uptake and incomplete responses to the health questionnaire, which was designed to collect information on participants' ocular and general health history, as well as self-reported symptoms. While a limited case history was obtained during the reference standard examination, the combined information from both sources offered a brief and superficial understanding of participants' visual experiences. This shortfall restricts the ability to explore potential associations between reported symptoms and measures taken of the binocular visual system, perceptual anomalies or functional measures such as reading rates. Consequently, the relationship between the elevated pattern glare scores and real-world visual discomfort, including symptoms experienced during tasks such as reading, could not be further investigated in this work. This limitation reduces the interpretability of the findings and limits the applicability of the results in clinical practice. Future studies should incorporate validated symptom questionnaires to support a more consistent, structured assessment of the functional impact of visual anomalies.

While the number of participants in this work was similar to that of Beasley and Davies (2012, 2013a), which was also undertaken in a private primary eye care setting, the subject numbers remain modest. Undertaking research in primary care has the potential to have challenges in recruitment. While most primary eye care providers provide eligible patients with care financed by the NHS, many potential subjects may have concern over undertaking research in such settings due to concern around possible pressure to purchase appliances following consultation. While outreach during recruitment was explicit on the nature of work being undertaken and how this was separate to the commercial operations of the business location. The hosting of this study within a primary private setting rather than a hospital or university clinic setting may have caused some potential subjects to decide against participation. Participant recruitment began as concerns over the COVID 19 pandemic began to subside. While public health and vaccination policies had achieved a level of control over severe illnesses in early 2022, the author experienced resistance among many older and frail individuals to attend routine eye care services, a feeling likely shared by vulnerable subjects such as being investigated in this study. Furthermore, stroke survivors with more complex needs are more likely to receive domiciliary care, and as such are less likely to present to primary eye care settings. As a result, the sample recruited for this study likely underrepresents more severe stroke related impairment, limiting the findings to the broader stroke population.

The delay between initial examination and follow-up examination led to a fair number of subjects choosing to withdraw from the study without completing it. A large minority of these subjects chose to withdraw between sessions, for a variety of reasons. Even where recruitment is successful, given the complexities of issues affecting potential subjects with a history of cerebrovascular disease, other factors may impact participation, and the quality of data collected. As Howard et al (2022) found in their study on automated tracking of saccades in subjects with homonymous field defects. Despite successful recruitment of 144 subjects, they were able to only gain meaningful data from 14 of those.

Given these limitations, a modest number of subjects were anticipated and thus there was a potential to limit the impact of findings. Given the nature of testing undertaken, the target demographic and number of participants recruited in a similar practice-based setting, it was anticipated that around 20-25 stroke survivors and a similar number of controls would be recruited for participation in this study. As such calculations of observed power were conducted following completion of the study. Somewhat unsurprisingly, where significance was observed within trials power tended to be high, while low significance tended to have an associated low power (Althouse 2021; Nuzzo 2021). While an important feature in planning studies, the limits of post-hoc power testing are well reported (Levine and Ensom 2001; Moher et al. 2010; Althouse 2021; Nuzzo 2021; Heckman et al. 2022), with post-trial interpretation of confidence intervals preferred to give insight to potential differences or effects (Smith and Bates 1992). Following completion of the study the 95% confidence interval enables observation of the spread of data, enabling visualisation of the potential effect of interventions, or differences between cohorts. This latter approach enables us to observe that across the results of **Chapters 5**, **6**, **7** and **8** that where present, differences between stroke and control subjects were modest. This does give insight to sampling for future work as to provide strong data across any of these areas larger sample sizes are warranted. Where future work was to be conducted, assessing the simple accuracy of the novel battery comparing the results of refractive, visual, binocular and ocular health findings a power analysis for a χ^2 indicates that the minimum sample necessary to provide a power of 0.8, an α=0.05 and moderate difference (w = 0.3, df=9) would be 174. Similarly, the minimum number of participants necessary to detect a moderate difference between groups of stroke subjects with field defects, without defects and controls statistical analysis would require a one way analysis of variance with power of at least 0.8 and α=0.05 for a medium difference (f=2.5) would require 159 subjects, while to detect a low effect (f=0.1) would require 969 subjects. To conduct a repeated measures analysis of variance (as done in **Chapter 7**) 98 subjects would be required - notably this figure is higher than the combined subject numbers of this work and Beasley & Davies (2013a). Where these areas, or similar work was to be undertaken, a much greater number of subjects would be necessary to reduce the risk of Type II errors, though as highlighted by Howard et al (2022) this level of recruitment may not guarantee adequate quality of data and greater numbers may need to be considered to enable some degree of redundancy. If undertaken again recruitment could be improved through collaboration with NHS and academic providers to identify and aid in recruitment of subjects as well as provide a neutral, non-threatening environment to facilitate investigations.

Over the course of this work the use of correction factors in post hoc testing was not consistent. Some debate exists around whether the use of correction factors should be used as a matter of course in post-hoc testing (Rothman 1990; Bland and Altman 1995; Savitz and Olshan 1995). The concern is that with multiple testing the risk of a type I error increases. When considering a true null hypothesis, with the criterion of α=0.05, where a trial is run there is a 0.95 probability of correctly identifying the null hypothesis to be true in each trial. However, if this is run on 20 occasions, the probability of achieving a correct result across all trials becomes $(0.95)^{20} = 0.36$. This results in the probability of achieving one significant result in error of 1-0.36 = 0.64, greater than the 0.05 expected. This may be avoided by use of correction factors such as the Bonferroni correction, a modification developed to offset this risk by reducing the α for repeated tests. Where a test is run on n occasions where the null hypothesis is true, the probability that no significant difference will be found will be $(1 - \alpha)^n$. If α is made suitably small, then the probability that none of the tests will find significance may be modified to 0.95. If any of the n tests has a p value lower than α then significance will hold at the 0.05 level. From this, it can be derived that $(1 - \alpha)^n \approx 1 - n\alpha$, setting $n\alpha = 0.05$, allows us to identify a suitable post hoc $\alpha = 0.05 / n$.

Several criticisms have been raised around the use of this approach, most notably articulated by Perneger (1998). This approach was originally devised as a correction method to aid decisions in repetitive measurements, not to assess evidence. This results in an approach suited to correction for errors of multiple sampling for discrete groups within tests rather than multiple testing within the same group. As such the correction may in fact be an inappropriate test for assessing a universal null hypothesis, where no association between any variables under observation is present and all observations occur by chance. One of the corollaries of the Bonferroni method is that the interpretation of significance for a test becomes dependent upon the number of other tests undertaken, while this may be relevant for repeated subgroup sampling, altering the interpretation of data based on the number of statistical tests performed would be inappropriate, especially where multiple tests may be undertaken but not reported upon. The Bonferroni correction by reducing the p value through multiple tests ultimately lowers the power of the test and potentially increases the risk of a type II error occurring. Despite this limitation the correction is useful where a large number of tests may be undertaken in order to reduce the risk of a type I error. To this end the correction was not applied in **Chapter 5** where post-hoc testing was undertaken in a largely exploratory manner, while the greater risk of multiple testing employed in **Chapter 6**, **7** and **8** necessitated its use (Armstrong 2014).

While masking other optometrists in assessing diagnostic utility of the instrument was achieved with support of branch colleagues, this was not the case with the studies reported upon in **Chapter 6**, **Chapter 7** and **Chapter 8** where the author undertook testing without masking of the subject's status. While procedures were undertaken in accordance with either manufacturer's instructions or guidance in training documentation, the absence of masking represents a source of bias affecting the results. While this could be improved by having these procedures such as retinal imaging undertaken by an examiner not involved in the recruitment process, in the case of the binocular vision, pattern glare and overlay assessments this may prove difficult to mask in a primary eye care setting, as these auxiliary procedures are rarely undertaken. In such a case this may benefit from greater support with the examiner undertaking dedicated assessments for the course of the study, masked to the status of the subject.

9.3 Conclusion and Suggestions for Further Work

This work has highlighted a number of areas where further investigation would be useful to support the care not only of patients with a history of stroke presenting in primary eye care practice but older patients more generally.

This study has highlighted that many older patients, but particularly stroke survivors attending community optometric practice frequently do not receive an adequate level of clinical care corresponding to their often-complex visual needs. The findings of **Chapter 5** highlight the shortcomings of many sight tests performed in community practice, with disparities in ocular surface and measures of binocular visual function. Within community optometric practice, stroke survivors require a thorough patient-centred examination. While this thesis sought to develop a (modified) test battery for use within this demographic (**Table 9-1**), the battery originally developed may be thought to consist of the key elements of a good eye examination, and recognisable as such as conducted by many optometrists around the world. What this work has identified is that the sight test provided in some community optometry practices falls short of the level of care necessary or that would be expected in this group. While not universal, further investigation would be useful to better understand the scale of the limitation of eye care services, as well as their impact upon patients (Rowe et al. 2009; Rowe 2010b; Hanna et al. 2024). Future work could also examine the component tests of a thorough sight test against a *gold standard* of testing of the parameters identified. From this a good indication of the diagnostic accuracy of each component procedure could be derived and where appropriate recommendations made to the optimal procedures to be employed to improve the clinical care to this group.

Much of the research undertaken into visual issues following stroke has either occurred retrospectively in primary care (Rutner et al. 2006; Ciuffreda et al. 2007; Suchoff et al. 2008; Smaakjær et al. 2018; Axelsson et al. 2019) or where prospectively undertaken, has occurred following referral for orthoptic investigations, frequently where concern has been raised over visual sequalae (Rowe 2010a; Rowe 2010b; Rowe 2011b; Baxter et al. 2013; Hepwort and Rowe 2019). While it has been recognised that in a minority of patient's visual loss immediately following stroke may resolve over the first few months (Gray et al. 1989; Çelebisoy et al. 2011; Rashid et al. 2021). This results in a potential skew of data, with primary care based studies potentially reporting more mild impairments, whilst hospital based studies may report more severe cases. Given the results found in this thesis, it is possible that some areas of understanding of the post-stroke visual system are the result of survivor bias (Rutner et al. 2006; Ciuffreda et al. 2007; Suchoff et al. 2008; Axelsson et al. 2019). While the Vision in Stroke group (Rowe et al. 2020; Rowe et al. 2022b; Rowe et al. 2022a) has begun more general prospective investigations into the visual effects experienced by stroke survivors similar work is warranted to investigate the profile of visual anomalies observed in a post-stroke cohort, both with and without visual symptoms. This work as well as previous investigations (Rowe 2010b; Stalin et al. 2024b; Stalin et al. 2024a) have identified potential gaps in the visual care received by stroke survivors, highlighting the inconsistency of approach provided as well as the perceived difficulties of access to services. The original purpose of the instrument developed in this thesis was to be usable in primary eye care locations, in order to improve access to eye care services for stroke survivors. However, in trialling this test battery it became apparent that the greater issue is the level of care provided during regular sight tests in contemporary practice in this demographic. An appraisal the scale of these issues would be useful in providing insight to the challenges faced by this patient group, and awareness to clinicians of the visual issues experienced and challenges faced by these patients, as was the case following the PrOVIDe study (Bowen et al. 2016) for individuals with dementia.

Like Rutner et al. (2006) this study has found an increased incidence of ocular surface anomalies present in survivors of stroke. Further investigation would be useful to assess the nature of ocular surface anomalies present – considering the diagnostic criteria outlined in DEWS II (Wolffsohn et al. 2017) – to appraise whether this group is in greater need of management of ocular surface anomalies. Were this to be found to be the case, as a cohort not typically represented within studies on ocular surface treatments, further work would be beneficial to identify the relative efficacy of the established treatment options for dry eye (Jones et al. 2017) within this cohort.

Given the potential for an increased risk of falls following field loss, investigation would be useful to appraise the post stroke patient experience of different approaches of refractive correction. Several different optical approaches have been developed to aid stroke survivors with field loss, notably the use of peripheral prisms to induce peripheral exotropia, increasing awareness within the blind field (Peli 2000; Bowers et al. 2012; Bowers et al. 2014; Houston et al. 2018b; Houston et al. 2018a). These devices however risk binocular confusion and suppression. The multiplexing prism, a newly developed device incorporating Fresnel and flat elements reduces some elements of the distortion, creating monocular confusion with associated lower contrast (Peli and Jung 2017). This design offers the potential for increased awareness within the blind field with reduced risk of diplopia, though investigation is warranted to assess how it compares to the use of peripheral prisms and sham treatments.

	Original Trial Battery	**Modified Examination**

Post-Stroke Diagnostic Battery	● Case History
	● Habitual distance acuity
	● Habitual near acuity
	● Measurement of pupil diameter
	● Pupil reflex testing
	    ○ Marcus-Gunn testing
	● Ocular motility (physiological H/X)
	● Retinoscopy
	● Subjective refraction
	    ○ JCC
	    ○ Corrected distance acuity
	        ■ Pinhole
	    ○ Binocular Balance
	● Distance cover test
	● Determination of near addition
	    ○ Corrected near acuity
	● Near cover test
	● Determination of intermediate addition
	● Near point of convergence
	● Amsler chart
	● Slit lamp examination
	    ○ Van Herick's test
	    ○ NaFl staining
	● Posterior Segment Exam
	    ○ Indirect ophthalmoscopy
		● Case History
		● Habitual distance acuity
		● Habitual near acuity
		● Measurement of pupil diameter
		● Pupil reflex testing
		    ○ Marcus-Gunn testing
		● Ocular motility (physiological H/X)
		● Retinoscopy
		● Subjective refraction & visual acuity
		● Distance cover test
		● Determination of near addition
		    ○ Corrected near acuity
		● Near cover test
		    ○ Determination of intermediate addition
		● Near point of convergence
		● Automated perimetry
		● Slit lamp examination
		    ○ Van Herick's test
		    ○ Sodium fluorescein staining
		● Posterior Segment Exam
		    ○ Indirect ophthalmoscopy

Follow-up procedures that should be considered.	● Habitual Distance Acuity
	● Pattern glare test
	● Wilkins rate of reading test
	● Pupil reflex test
	● Marcus Gunn swinging flashlight test
		● Perceptual testing
		    ○ Neglect (clock drawing / line cancellation)
		    ○ Visual perceptual skills (laterality, spatial deficiency, visual memory)
		    ○ Visual midline testing
		● Pattern glare test
		● Wilkins rate of reading test & coloured overlay testing

Table 9-1. Recommendations for key visual tests to be undertaken with stroke survivors. The original trial battery was derived from the Delphi study undertaken in **Chapter 3**. This trial battery broadly reflects the components of a thorough eye examination, and while it covers a range of conventional vision tests, it neglects several important areas such as perimetry and perceptual screening. Though as **Chapter 5** highlighted, despite its limitations this battery detected a greater number of binocular vision and ocular surface anomalies as well as peripheral retinal anomalies. A modified examination is proposed to address the shortcomings of the original replacing Amsler grid testing with automated perimetry and adding a range of visual perceptual screening tests that may support the identification of anomalies of visual processing.

While often recommended, there is little evidence to support the optimal approach for selecting optical appliances for stroke survivors, with investigations into risk of falls between multifocal and single vision lens use being equivocal (Verheyden et al. 2013). Prospective investigations are warranted to investigate the subjective preference, ease of use, and associated fall risk with different correction modalities. This should also assess whether appliances such as contact lenses may be of benfit, as these may reduce peripheral aberrations experienced when using spectacle corrections. Further investigation on this front could assess whether the use of multifocal or EDOF contact lenses could aid stroke survivors to continue with activities of daily living, whilst reducing the risk of falls from the distortion and defocus found in bifocal or multifocal spectacle corrections.

While several clinical procedures are widely used in practice, a number of these remain unvalidated, or of limited sensitivity. Appraisal of eye movement tests such as the NSUCO oculomotor test are required to confirm their normal ranges, appraise their validity and reliability in a general population and an appraisal of their accuracy compared to objective methods should be undertaken to provide clinicians with evidence of its usefulness. Similarly, the use of pupil testing, while widely used has been reported to have limited sensitivity (Olson et al. 2016), in the clinical setting. Similar appraisal against objective methods is warranted to identify whether this testing approach is useful in this cohort or whether potentially more sensitive objective examination is required.

The absence of published data on the normal functioning of the binocular vision system in older patients undermines the provision of care to this group. Studies should be undertaken to strengthen the understanding of normal orthoptic measures in the older population, stratifying by age to enable the identification of patterns of changes to be readily identified. Following this further investigation into the binocular vision profile in a larger sample of stroke survivors to enable identification of subtle differences that may be present within stroke survivors. This study should seek to stratify for not only those without visual field loss but also different patterns of loss to identify those most at risk of development of symptomatic binocular vision anomalies. Given the differing profile of forced duction curves observed within the stroke cohort, further work would be beneficial to understand the binocular visual response in this group. The increased presence of type III and IV curves within this cohort would suggest that anomalies are present in vergence adaptation (Schor 1979), with subjects poorly able to adapt to convergence demand, or indeed any vergence changes (London and Crelier 2006), serving as a potential origin to the symptoms reported within the literature. As highlighted earlier in this work, the management of a number of binocular vision anomalies is poorly evidenced generally, with recommendations for procedures in brain injury survivors based upon activities trialled in younger cohorts, unmasked studies or practitioner experience (Padula 1988; Padula et al. 2012; Scheiman and Wick 2013; Chang et al. 2016; Smaakjær et al. 2018; Axelsson et al. 2019). Prospective investigations are required to investigate the effect of orthoptic therapy upon both objective measures and subjective symptoms of binocular vision anomalies in stroke survivors to develop an evidence base for practice.

The presence of poorer eye movements in stroke survivors without field defects was a surprising finding, as previous studies had found poorer eye movements in the presence of field loss, with speculation that the inhibition of magnocellular processing was in part responsible for reading deficits observed (Zihl 2010). The results found in **Chapter 7** would suggest at least two potential causative pathways for visual stress following stroke, with those without visual field defects experiencing symptoms of pattern glare and improved reading with the use of coloured overlays, consistent with the results of Beasley and Davies (2012, 2013a), and another that experiences greater symptoms of pattern glare, with lesser relief using overlays. Future work could look to investigate eye movements associated with reading in this cohort using objective eye tracking instruments, a number of which are available as webcam based or spectacle-based instruments that may be employed in the clinical setting.

Given the associated, and frequently non-specific light sensitivity described by stroke survivors, baseline psychophysical assessment of visual function would be useful to aid in the identification of potential origins of some of these symptoms. The visual system's light adaption and dark adaption should be appraised to assess whether these are similar to matched controls. Contrast sensitivity, while within normal range within this study, was conducted sampling across the peak of the contrast sensitivity curve, sampling at lower spatial frequencies may enable detection of deficiencies if present. Similarly, the magnocellular system is sensitive to temporal change, so an appraisal of temporal frequency would be useful to assess changes that may be present. This approach would enable sampling from the parvo and magnocellular systems giving some indication of whether the symptoms experienced had originated from these pathways.

Cortical electrodiagnostic evaluation of those subjects both with and without field defects to assess whether these subjects experience cortical hyperexcitablility as postulated by previous authors. Where present this may enable identification of the cortical areas involved in order to develop a paradigm from which to investigate further. Electrodiagnositc assessment of the visual pathway would also be useful. While Padula and colleagues (Padula et al. 1994; Padula and Argyris 1996) investigated VEP responses following TBI, a similar investigation sampling across spatial frequencies would be useful to investigate possible objective correlates of pattern glare, and sampling at low contrast, lower spatial frequency and higher temporal frequencies may give some insight to the relative function of the visual pathways. As reported earlier, the use of coloured overlays has been observed in other neurological conditions to alter the evoked potentials of subjects in objective testing(Willeford et al. 2016; Yadav and Quan 2022), this would appear a natural next step in the investigation of the origin of the symptoms of pattern glare and light sensitivity reported in this cohort.

A number of large studies have been undertaken to investigate the patterns of retinal changes following stroke. The results of these studies have largely been heterogeneous with no consistent pattern to explain changes observed. This could be improved by a larger study investigating OCT parameters while factoring the location, type and severity of brain injury factoring the presence of field loss, with longitudinal appraisal to asses for change. Such a study may begin to enable stratification of retinal changes by location and density of neurological defects and may give some insight to the reason why some injuries that give rise to field loss do not result in axonal degeneration while others do.

Several alternative therapies may be investigated to whether they provide benefit to stroke survivors. While the neuroprotective effects of minocycline antibiotics are recognised in a stroke cohort (Bodis-Wollner, 1972; Malhotra et al., 2018), a single case study has reported upon possible restoration of visual field loss following the use of these agents (Skulskie and Tomsik 2011). These agents have demonstrated neuroprotective qualities (Malhotra et al. 2018), and are generally well tolerated in ischaemic stroke, though no strong evidence has been published for haemorrhagic stroke. Where field loss has occurred following ischaemic stroke prospective investigation of the effect of Minocycline on the prevalence of occurrence of chronic field loss could be investigated as a potential early stage treatment option for field loss.

This thesis aimed to developed and trial a new ophthalmic test battery for the diagnostic examination of patients with a history of stroke. Although the resulting protocol closely resembled a comprehensive eye examination, testing revealed gaps in the routine sight testing typically offered in community practice. Stroke survivors often present with complex and subtle visual impairments, necessitating comprehensive evaluation. The findings highlight the importance of delivering thorough and patient-centred eye care, with clinicians employing clinical judgement, attention to individual patient symptoms, and comprehensive assessment to ensure improved access to, and high-quality outcomes for, those with complex visual needs.

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Appendices

Appendix 1: Delphi Study - Ethical Approval

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21 November 2017 2017

FAVOURABLE ETHICAL OPINION – WITH CONDITIONS

Study Title: Fractured Vision: Optometric examination of patients following stroke

Reference Number: SFEC 2017-113

Date Submitted: 06 November 2017

Thank you for submitting your application to the Science Faculty Ethics Committee (SFEC) for ethical review in accordance with current procedures.

I am pleased to inform you that SFEC was content to grant a favourable ethical opinion of the above research on the basis described in the submitted documents listed at Annex A, and subject to standard general conditions (*See Annex B)*, and the following specific minor conditions:

Conditions[1]

A. The participant information sheet (PIS) gives conflicting expected times for completing the questionnaires. It states initially (in 'study summary') that each will take 30-40 minutes, then (in 'what will happen to me') that the first will take 30-40 but the second and third may take up to an hour, and

[1] The favourable opinion given is dependent upon the study adhering to the conditions stated, which are based on the application document(s) submitted. It is appreciated that Principal Investigators may wish to challenge conditions or propose amendments to these. In that case, please consider the favourable opinion *suspended*, and simply make your case for amending or discarding conditions in writing as you would an application resubmission following ethical review.

finally (in 'what are the possible disadvantages') that all three will take up to an hour and a half. Please clarify and make this consistent.

B. The participant information sheet discusses consent and states that this in implied by completing the questionnaire, please ensure this is made explicit at the start of the questionnaire itself.

C. In the Introduction email: please avoid university terms that will not have meaning to the participants (e.g. ‘the university N drive’). ‘Stored on a password protected drive within the University’s secure system’ would be more appropriate.

Advisory Notes[2]

i. Please ensure all embedded links work.

ii. The justification for the study could be more explicit about the rationale for why a standardised approach to testing in this patient group would be beneficial.

iii. The investigator states that the study will consist of three rounds of questionnaire in order to reach consensus, and has a reference supporting that this is 'frequently' achieved. There does not, however, seem to be consideration of what will happen if this is not achieved. This might be worth further thought.

Please resubmit an updated application form incorporating the changes as per the above conditions for the final SFEC records on this application.

If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact ethicssci@port.ac.uk who will circulate your queries to SFEC

Please note that the favourable opinion of SFEC does not grant permission or approval to undertake the research. Management permission or approval must be obtained from any host organisation, including the University of Portsmouth or supervisor, prior to the start of the study.

Wishing you every success in your research

Dr John Crossland
Vice Chair Science Faculty Ethics Committee

Annexes

A - Documents reviewed
B - After ethical review - Guidance for researchers

[2] The comments are given in good faith and it is hoped they are accepted as such. The PI does not need to adhere to these, or respond to them, unless they wish to.

Information:

Dr Chris Markham - PhD Supervisor
Dr Rebecca Stores - PhD Supervisor
Holly Shawyer - Faculty Administrator

Statement of compliance

SFEC is constituted in accordance with the Governance Arrangements set out by the University of Portsmouth

After Ethical Review

If unfamiliar, please consult the advice After Ethical Review (Annex B), which gives detailed guidance on reporting requirements for studies with a favourable opinion, including, notifying substantial amendments, notification of serious breaches of the protocol, progress reports and notifying SFEC of the end of the study.

Feedback

You are invited to give your view of the service that you have received from the Science Faculty Ethics Committee. If you wish to make your views known please contact the administrator at ethics-sci@port.ac.uk

ANNEX A Documents reviewed

The documents ethically reviewed for this application

Document	*Version*	*Date*
A-2017-113 MACIVER PI submission email		06 Nov 2017
B-2017-113 MACIVER Ethics Application V1	V1	06 Nov 2017

A - 1 ANNEX B - After ethical review - Guidance for researchers

1. This Annex sets out important guidance for researchers with a favourable opinion from a University of Portsmouth Ethics Committee. Please read the guidance carefully. A failure to follow the guidance could lead to the committee reviewing and possibly revoking its opinion on the research.

2. It is assumed that the research will commence within 1 year of the date of the favourable ethical opinion or the start date stated in the application, whichever is the latest.

3. The research must not commence until the researcher has obtained any necessary management permissions or approvals – this is particularly pertinent in cases of research hosted by external organisations. The appropriate head of department should be aware of a member of staff's research plans.

4. If it is proposed to extend the duration of the study beyond that stated in the application, the Ethics Committee must be informed.

5. Any proposed substantial amendments must be submitted to the Ethics Committee for review. A substantial amendment is any amendment to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the Committee that is likely to affect to a significant degree:
   (a) the safety or physical or mental integrity of participants
   (b) the scientific value of the study
   (c) the conduct or management of the study.

5.1 A substantial amendment should not be implemented until a favourable ethical opinion has been given by the Committee.

6. Researchers are reminded of the University's commitments as stated in the Concordat to Support Research Integrity viz:

- maintaining the highest standards of rigour and integrity in all aspects of research
- ensuring that research is conducted according to appropriate ethical, legal and professional frameworks, obligations and standards
- supporting a research environment that is underpinned by a culture of integrity and based on good governance, best practice and support for the development of researchers
- using transparent, robust and fair processes to deal with allegations of research misconduct should they arise
- working together to strengthen the integrity of research and to reviewing progress regularly and openly

7. In ensuring that it meets these commitments the University has adopted the UKRIO Code of Practice for Research. Any breach of this code may be considered as misconduct and may be investigated following the University Procedure for the Investigation of Allegations of Misconduct in Research. Researchers are advised to use the UKRIO checklist as a simple guide to integrity.

Appendix 2: Delphi Study – Participant Information Sheet

Dr Chris Markham PhD FHEA MHCPC
Head of School

UNIVERSITY OF PORTSMOUTH

School of Health Sciences and Social Work

University of Portsmouth
James Watson West 2 King Richard 1st Road
Portsmouth PO1 2FR
T: +44 (0)23 9284 4440
E: shssw@port.ac.uk

PARTICIPANT INFORMATION SHEET

Title of Project: Fractured vision: Optometric examination of patients following stroke

Name and Contact Details of Researcher(s): Mr Malcolm Maciver, School of Health Sciences and Social Work, University of Portsmouth, James Watson West, PO1 2DT. malcolm.maciver@port.ac.uk

Name and Contact Details of Supervisor (if relevant): Dr C Markham, Head of School, School of Health Sciences and Social Work, University of Portsmouth, James Watson West, PO1 2DT. chris.markham@port.ac.uk

Ethics Committee Reference Number: SFEC 2017-113

Invitation

We would like to invite you to take part in our research study. Joining the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you. The following notes outline what is involved in the study, and how much time this should take. Should you have any questions or wish clarification on part of the study please don't hesitate to contact the principal investigator, Malcolm Maciver, on malcolm.maciver@port.ac.uk.

The principal investigator is a qualified optometrist and PhD researcher at the University of Portsmouth, he is also involved with the delivery of the Masters in Optometry programme at the University of Portsmouth, leading two units on the MOptom course programme.

Study Summary

This study is designed to create a standardised eye examination battery for patients that present with a history of stroke. In many cases these patients have complex visual needs and some practitioners are hesitant to conduct examinations and provide vision care. This results in many patients having difficulty accessing primary eye care services within the community.

You have been contacted as we are looking for eye care or healthcare professionals with experience in the provision of visual care to brain injured patients. This study will consist of a series of 3 questionnaires which aims to develop a standard visual test battery for use on patients who have suffered a stroke. Each questionnaire should take around 30-40 minutes to complete and will be completed online.

What is the purpose of the study?

With an ageing population, stroke is becoming increasingly prevalent within western society. Many individuals who have suffered a stroke develop complex visual problems subsequent to their injury. In many cases primary care optometrists are the first eye care professionals to encounter these patients. Current guidance for the provision of care to patients following stroke is limited,

This study is a *Delphi Study* to develop a standard vision test battery that could be used by the primary care optometrist in clinical practice. The *Delphi Study* is a method used to find a group consensus using tiered questionnaires with feedback to participants at each step. This study consists of a series of questionnaires issued to multiple experts within the field. After each questionnaire is answered, the grouped (anonymous) results of the previous questionnaire are returned to participants with the next questionnaire. This multi-step method with grouped results is used to develop a consensus.

Why have I been invited?

You have been invited to this study as you are a vision or healthcare professional with a specialist interest in the provision of visual care to patients with acquired brain injury.

This study will consist of a small group of around 18-20 vision and healthcare professionals with a specialist interest in acquired brain injury. You have been approached to participate as you have been identified as an expert within this area, either through your publication(s), professional reputation or by recommendation by professional and non-governmental bodies.

Do I have to take part?

No, taking part in this research is entirely voluntary. It is up to you to decide if you want to volunteer for the study. We will describe the study in this information sheet. Completion of the questionnaire will be considered as consent at each stage of the study.

What will happen to me if I take part?

If you decide to take part you will be sent a questionnaire at three different points in time. These questionnaires will ask you about your thoughts on the visual examination of patients who have had a stroke. The first questionnaire should take around 30-40 minutes to complete. Subsequent questionnaires will be based on the (group) responses to the previous iteration, these will be issued with the anonymous group results of the previous questionnaire. The second and third questionnaire will take a similar period of time to complete.

Expenses and payments

This study is not funded, there are no expenses or payments for participation in this study.

Anything else I will have to do?

It is requested that participants do not discuss the contents or nature of this study with other eye care providers until after the submission of the final questionnaire.

What data will be collected and / or measurements taken?

The primary data from this study will be that collected from the questionnaires. Participant's contact data will be held by the principal investigator (see later). Data from questionnaires will be anonymised at collection by the online survey platform. Data will be collected using the online survey platform BOS.

What are the possible disadvantages, burdens and risks of taking part?

The major burden of taking part is time. This study will consist of three questionnaires at different time points which may take upto two hours of your time to complete.

What are the possible advantages or benefits of taking part?

Participation in this study will give you the opportunity to consider the views of other experienced eye care providers views on the visual assessment of patients following stroke. This will give the opportunity to reflect on your provision of eye care to patients following stroke in your practice.

Will my taking part in the study be kept confidential?

All participant personal data will remain confidential.

Anonymisation of participants from one another is a key feature of the method used within this study. All contact details that could be used to identify you as a participant within this study will be kept securely on an encrypted password protected file on the University of Portsmouth's N drive. Passwords / encryption access will be held by the principal investigator only.

The data, when made anonymous, may be presented to others at academic conferences, or published as a project report, academic dissertation or in academic journals or book. Anonymous data, which does not identify you, may be used in future research studies approved by an appropriate research ethics committee.

The raw data, which would identify you, will not be passed to anyone outside the study team without your express written permission. The exception to this will be any regulatory authority which may have the legal right to access the data for the purposes of conducting an audit or enquiry, in exceptional cases. These agencies treat your personal data in confidence.

The raw data will be retained for up to 10 years. When it is no longer required, the data will be disposed of securely or destroyed.in line with the University of Portsmouth's records management policy:
http://www.port.ac.uk/departments/services/corporategovernance/recordsmanagement/uop_retention/

http://www.port.ac.uk/accesstoinformation/policies/researchandknowledgetransferservices/filetodownlo ad,189755,en.pdf

What will happen if I don't want to carry on with the study?

As a volunteer you can stop any participation in the study at any time, or withdraw from the study at any time before, without giving a reason if you do not wish to. As all data collected within this study is anonymised at collection, should you withdraw from the study all data collected up until the point of withdrawal will be retained and included in the study. Once the research has been completed, and the data analysed, it will not be possible for you to withdraw your data from the study.

What if there is a problem?

If you have a query, concern or complaint about any aspect of this study, in the first instance you should contact the principal investigator Mr Malcolm Maciver (malcolm.maciver@port.ac.uk). If there is a complaint please contact the supervising academic Dr Chris Markham (chris.markham@port.ac.uk) with details of the complaint. The contact details for both the principal investigator and supervisor are detailed on page 1.

If your concern or complaint is not resolved by the researcher or their supervisor, you should contact the following member of Staff:

Dean of Science	Prof Sherria Hoskins
Faculty of Science	023 9284 3007
University of Portsmouth	sherria.hoskins@port.ac.uk
St Michael's Building	
White Swan Road	
Portsmouth	
PO1 2DT	

If the complaint remains unresolved, please contact:

The University Complaints Officer

023 9284 3642 complaintsadvice@port.ac.uk

Who is funding the research?

This research is unfunded. This study is supported by the University of Portsmouth. None of the researchers or study staff will receive any financial reward by conducting this study, other than their normal salary / bursary as an employee / student of the University.

Who has reviewed the study?

Research involving human participants is reviewed by an ethics committee to ensure that the dignity and well-being of participants is respected. This study has been reviewed by the Science Faculty Ethics Committee and been given favourable ethical opinion.

Thank you

Thank you for taking time to read this information sheet and for considering volunteering for this research.

Appendix 3: Delphi Study - Substantial Amendment (Round 2)

Malcolm Maciver
School of Health Sciences and Social Work
University of Portsmouth
Malcolm.Maciver@port.ac.uk

UNIVERSITY OF PORTSMOUTH

Science Faculty Ethics Committee
Science Faculty Office
University of Portsmouth
St Michael's Building
White Swan Road
PORTSMOUTH
PO1 2DT

023 9284 3379 ethics-sci@port.ac.uk

23 May 2018

FAVOURABLE ETHICAL OPINION – NOTIFICATION OF SUBSTANTIAL AMENDMENT

Study Title: Fractured Vision: Optometric examination of patients following stroke

Reference Number: SFEC 2017-113A Date Submitted: 17 May 2018

Thank you for submitting your proposal amendment to the Science Faculty Ethics Committee (SFEC) for ethical review in accordance with current procedures.

I am pleased to inform you that SFEC was content to grant a favourable ethical opinion of this proposal amendment on the basis described in the submitted documents listed at Annex A, and subject to standard general conditions (*See Annex B)*.

Please note that the favourable opinion of SFEC does not grant permission or approval to undertake the research. Management permission or approval must be obtained from any host organisation, including the University of Portsmouth or supervisor, prior to the start of the study.

Wishing you every success in your research

John C

Dr John Crossland
Vice Chair, Science Faculty Ethics Committee

Annexes

A - Documents reviewed
B - After ethical review - Guidance for researchers

Information:

Dr Chris Markham - PhD Supervisor
Dr Rebecca Stores - PhD Supervisor

Rose Barrand - Faculty Administrator

Statement of compliance

SFEC is constituted in accordance with the Governance Arrangements set out by the University of Portsmouth

After Ethical Review

If unfamiliar, please consult the advice After Ethical Review (Annex B), which gives detailed guidance on reporting requirements for studies with a favourable opinion, including, notifying substantial amendments, notification of serious breaches of the protocol, progress reports and notifying SFEC of the end of the study.

Feedback

You are invited to give your view of the service that you have received from the Faculty Ethics Committee. If you wish to make your views known please contact the administrator at ethics-sci@port.ac.uk

ANNEX A **Documents reviewed**

The documents ethically reviewed for this application

Document	*Version*	*Date*
A-2017-113 A Substantial Amendment PI submission email		17 May 2018
B-2017-113 A Updated Ethics Application - M Maciver (1)	V2	17 May 2018
C-2017-113 A .SubstantialAmendment.UP841674		17 May 2018

A - 1 ANNEX B - After ethical review - Guidance for researchers

1. This Annex sets out important guidance for researchers with a favourable opinion from a University of Portsmouth Ethics Committee. Please read the guidance carefully. A failure to follow the guidance could lead to the committee reviewing and possibly revoking its opinion on the research.

2. It is assumed that the research will commence within 1 year of the date of the favourable ethical opinion or the start date stated in the application, whichever is the latest.

3. The research must not commence until the researcher has obtained any necessary management permissions or approvals – this is particularly pertinent in cases of research hosted by external organisations. The appropriate head of department should be aware of a member of staff's research plans.

4. If it is proposed to extend the duration of the study beyond that stated in the application, the Ethics Committee must be informed.

5. Any proposed substantial amendments must be submitted to the Ethics Committee for review. A substantial amendment is any amendment to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the Committee that is likely to affect to a significant degree:
   (a) the safety or physical or mental integrity of participants
   (b) the scientific value of the study
   (c) the conduct or management of the study.

5.1 A substantial amendment should not be implemented until a favourable ethical opinion has been given by the Committee.

6. Researchers are reminded of the University's commitments as stated in the Concordat to Support Research Integrity viz:

- maintaining the highest standards of rigour and integrity in all aspects of research
- ensuring that research is conducted according to appropriate ethical, legal and professional frameworks, obligations and standards
- supporting a research environment that is underpinned by a culture of integrity and based on good governance, best practice and support for the development of researchers
- using transparent, robust and fair processes to deal with allegations of research misconduct should they arise
- working together to strengthen the integrity of research and to reviewing progress regularly and openly

7. In ensuring that it meets these commitments the University has adopted the UKRIO Code of Practice for Research. Any breach of this code may be considered as misconduct and may be investigated following the University Procedure for the Investigation of Allegations of Misconduct in Research. Researchers are advised to use the UKRIO checklist as a simple guide to integrity.

Appendix 4: Delphi Study - Substantial Amendment (Round 3)

Malcolm Maciver
School of Health Sciences and Social Work
University of Portsmouth
Malcolm.Maciver@port.ac.uk

Science Faculty Ethics Committee
Science Faculty Office
University of Portsmouth
St Michael's Building
White Swan Road
PORTSMOUTH
PO1 2DT

023 9284 3379 ethics-sci@port.ac.uk

27 June 2018
FAVOURABLE ETHICAL OPINION – NOTIFICATION OF SUBSTANTIAL AMENDMENT

Study Title: Fractured Vision: Optometric examination of patients following stroke

Reference Number: SFEC 2017-113A **Date Submitted:** 27 June 2018

Thank you for submitting your proposal amendment to the Science Faculty Ethics Committee (SFEC) for ethical review in accordance with current procedures.

I am pleased to inform you that SFEC was content to grant a favourable ethical opinion of this proposal amendment on the basis described in the submitted documents listed at Annex A, and subject to standard general conditions (*See Annex B)*.

Please note that the favourable opinion of SFEC does not grant permission or approval to undertake the research. Management permission or approval must be obtained from any host organisation, including the University of Portsmouth or supervisor, prior to the start of the study.

Wishing you every success in your research

Dr John Crossland
Vice Chair, Science Faculty Ethics Committee

Annexes

A - Documents reviewed
B - After ethical review - Guidance for researchers

Information:

Dr Chris Markham - PhD Supervisor

Dr Rebecca Stores - PhD Supervisor
Rose Barrand - Faculty Administrator

Statement of compliance

SFEC is constituted in accordance with the Governance Arrangements set out by the University of Portsmouth

After Ethical Review

If unfamiliar, please consult the advice After Ethical Review (Annex B), which gives detailed guidance on reporting requirements for studies with a favourable opinion, including, notifying substantial amendments, notification of serious breaches of the protocol, progress reports and notifying SFEC of the end of the study.

Feedback

You are invited to give your view of the service that you have received from the Faculty Ethics Committee. If you wish to make your views known please contact the administrator at ethics-sci@port.ac.uk

ANNEX A **Documents reviewed**

The documents ethically reviewed for this application

Document	*Version*	*Date*
A-2017-113B MACIVER PI submission email		27 Jun 2018
B-2017-113B MACIVER .up841674.MMaciver.Ethics	V3	27 Jun 2018

A - 1 ANNEX B - After ethical review - Guidance for researchers

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Dr Chris Markham PhD FHEA MHCPC
Head of School

School of Health Sciences and Social Work
University of Portsmouth
James Watson West
2 King Richard 1st Road
Portsmouth PO1 2FR
United Kingdom

T: +44 (0)23 9284 4440
E: shssw@port.ac.uk

PARTICIPANT INFORMATION SHEET

Title of Project: Fractured vision: Optometric examination of patients following stroke

Name and Contact Details of Researcher(s): Mr Malcolm Maciver, School of Health Sciences and Social Work, University of Portsmouth, James Watson West, PO1 2DT. malcolm.maciver@port.ac.uk

Name and Contact Details of Supervisor (if relevant): Dr C Markham, Head of School, School of Health Sciences and Social Work, University of Portsmouth, James Watson West, PO1 2DT. chris.markham@port.ac.uk

Ethics Committee Reference Number: SFEC 2017-113

Invitation

We would like to invite you to take part in our research study. Joining the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you. The following notes outline what is involved in the study, and how much time this should take. Should you have any questions or wish clarification on part of the study please don't hesitate to contact the principal investigator, Malcolm Maciver, on malcolm.maciver@port.ac.uk.

The principal investigator is a qualified optometrist and PhD researcher at the University of Portsmouth, he is also involved with the delivery of the Masters in Optometry programme at the University of Portsmouth, leading two units on the MOptom course programme.

Study Summary

This study is designed to create a standardised eye examination battery for patients that present with a history of stroke. In many cases these patients have complex visual needs and some practitioners are hesitant to conduct examinations and provide vision care. This results in many patients having difficulty accessing primary eye care services within the community.

You have been contacted as we are looking for eye care or healthcare professionals with experience in the provision of visual care to brain injured patients. This study will consist of a series of 3 questionnaires which aims to develop a standard visual test battery for use on patients who have suffered a stroke. Each questionnaire should take around 30-40 minutes to complete and will be completed online.

What is the purpose of the study?

With an ageing population, stroke is becoming increasingly prevalent within western society. Many individuals who have suffered a stroke develop complex visual problems subsequent to their injury. In many cases primary care optometrists are the first eye care professionals to encounter these patients. Current guidance for the provision of care to patients following stroke is limited, This study is a *Delphi Study* to develop a standard vision test battery that could be used by the primary care optometrist in clinical practice. The *Delphi Study* is a method used to find a group consensus using tiered questionnaires with feedback to participants at each step. This study consists of a series of questionnaires issued to multiple experts within the field. After each questionnaire is answered, the grouped (anonymous) results of the previous questionnaire are returned to participants with the next questionnaire. This multi-step method with grouped results is used to develop a consensus.

Why have I been invited?
You have been invited to this study as you are a vision or healthcare professional with a specialist interest in the provision of visual care to patients with acquired brain injury.
This study will consist of a small group of around 18-20 vision and healthcare professionals with a specialist interest in acquired brain injury. You have been approached to participate as you have been identified as an expert within this area, either through your publication(s), professional reputation or by recommendation by professional and non-governmental bodies.

Do I have to take part?
No, taking part in this research is entirely voluntary. It is up to you to decide if you want to volunteer for the study. We will describe the study in this information sheet. Completion of the questionnaire will be considered as consent at each stage of the study.

What will happen to me if I take part?
If you decide to take part you will be sent a questionnaire at three different points in time. These questionnaires will ask you about your thoughts on the visual examination of patients who have had a stroke. The first questionnaire should take around 30-40 minutes to complete. Subsequent questionnaires will be based on the (group) responses to the previous iteration, these will be issued with the anonymous group results of the previous questionnaire. The second and third questionnaire will take a similar period of time to complete.

Expenses and payments
This study is not funded, there are no expenses or payments for participation in this study.

Anything else I will have to do?
It is requested that participants do not discuss the contents or nature of this study with other eye care providers until after the submission of the final questionnaire.

What data will be collected and / or measurements taken?
The primary data from this study will be that collected from the questionnaires. Participant's contact data will be held by the principal investigator (see later). Data from questionnaires will be anonymised at collection by the online survey platform. Data will be collected using the online survey platform BOS.

What are the possible disadvantages, burdens and risks of taking part?
The major burden of taking part is time. This study will consist of three questionnaires at different time points which may take upto two hours of your time to complete.

What are the possible advantages or benefits of taking part?
Participation in this study will give you the opportunity to consider the views of other experienced eye care providers views on the visual assessment of patients following stroke. This will give the opportunity to reflect on your provision of eye care to patients following stroke in your practice.

Will my taking part in the study be kept confidential?
All participant personal data will remain confidential.
Anonymisation of participants from one another is a key feature of the method used within this study. All contact details that could be used to identify you as a participant within this study will be kept securely on an encrypted password protected file on the University of Portsmouth's N drive. Passwords / encryption access will be held by the principal investigator only.

The data, when made anonymous, may be presented to others at academic conferences, or published as a project report, academic dissertation or in academic journals or book. Anonymous data, which does not identify you, may be used in future research studies approved by an appropriate research ethics committee.

The raw data, which would identify you, will not be passed to anyone outside the study team without your express written permission. The exception to this will be any regulatory authority which may have the legal right to access the data for the purposes of conducting an audit or enquiry, in exceptional cases. These agencies treat your personal data in confidence.

The raw data will be retained for up to 10 years. When it is no longer required, the data will be disposed of securely or destroyed.in line with the University of Portsmouth's records management policy: http://www.port.ac.uk/departments/services/corporategovernance/recordsmanagement/uop_retention/ http://www.port.ac.uk/accesstoinformation/policies/researchandknowledgetransferservices/filetodownload,189755,en.pdf

What will happen if I don't want to carry on with the study?

As a volunteer you can stop any participation in the study at any time, or withdraw from the study at any time before, without giving a reason if you do not wish to. As all data collected within this study is anonymised at collection, should you withdraw from the study all data collected up until the point of withdrawal will be retained and included in the study. Once the research has been completed, and the data analysed, it will not be possible for you to withdraw your data from the study.

What if there is a problem?

If you have a query, concern or complaint about any aspect of this study, in the first instance you should contact the principal investigator Mr Malcolm Maciver (malcolm.maciver@port.ac.uk). If there is a complaint please contact the supervising academic Dr Chris Markham (chris.markham@port.ac.uk) with details of the complaint. The contact details for both the principal investigator and supervisor are detailed on page 1.

If your concern or complaint is not resolved by the researcher or their supervisor, you should contact the following member of Staff:

Dean of Science
Faculty of Science
University of Portsmouth
St Michael's Building
White Swan Road
Portsmouth
PO1 2DT

Prof Sherria Hoskins
023 9284 3007
sherria.hoskins@port.ac.uk

If the complaint remains unresolved, please contact:

The University Complaints Officer
023 9284 3642 complaintsadvice@port.ac.uk

Who is funding the research?

This research is unfunded. This study is supported by the University of Portsmouth. None of the researchers or study staff will receive any financial reward by conducting this study, other than their normal salary / bursary as an employee / student of the University.

Who has reviewed the study?

Research involving human participants is reviewed by an ethics committee to ensure that the dignity and well-being of participants is respected. This study has been reviewed by the Science Faculty Ethics Committee and been given favourable ethical opinion.

Thank you

Thank you for taking time to read this information sheet and for considering volunteering for this research.

Appendix 5: Feedback to Participants – Delphi Round 1

Fractured Vision: Optometric examination of patients following stroke
Feedback from Round 1

Recent investigation (Maciver *et al*, 2018) has found that there exists a limited evidence base for many optometric diagnostic investigative techniques in patients with a history of stroke. The initial round of the study sought to establish current practice among clinicians with experience in examining and providing ophthalmic care to patients who have suffered a stroke. Please find below a summary of the responses received from the first round of this study:

Question 1: What length of time do you think would be appropriate for conducting an eye examination on a patient who had previously suffered a stroke?

There were a range of answers provided with times ranging from 30 minutes to 3 hours, with most responses indicating an examination time under an hour.

Question 2: What tests or measurements (if any) would you request to be undertaken by auxillary staff prior to examination?

While some responses indicated a preference for clinicians to conduct all diagnostic testing, non-contact tonometry, visual field testing, fundus imaging and OCT were frequently delegated to auxillary staff to undertake prior to examination with the optometrist.

Question 3: What questions related to visual symptoms would you ask as part of your case history or patient interview?

Several key areas were common to respondents of this question these were:
- Distance and near vision
- Central vs peripheral vision
- Sensory/neurological disturbance (balance/spatial awareness)
- Diplopia
- Light/pattern sensitivity

Other key features were details of previous attendance and diagnosis made by specialist medical services.

Question 4: What questions would you ask about medical history during the case history or patient interview?

Respondents were keen to receive comprehensive details of patient's medical history, highlighted features included:
- Previous medical history
- Presence of hypertension
- Presence of hypercholesteroemia
- Presence of diabetes
- Current medications

Particularly regarding the stroke:
- Date of stroke
- Location of brain injury
- Current stroke specific treatments

Question 5: What lifestyle related questions would you ask during the case history or patient interview?

Responses centred around the patient's occupational status, their ability to continue habitual tasks comfortably and areas where patients experienced difficulty in day to day tasks such as reading, VDU use and hobbies.

Question 6: Describe (in detail) how you would assess the external eye and associated structures.

There was some degree of variation in preferred technique for anterior eye examination between respondents. Most respondents preferred a slit lamp examination, with ocular surface assessment using stains and lid eversion if symptoms were reported. While some respondents preferred to use direct ophthalmoscope with the option to use a supplementary lens to assess the anterior segment.

Question 7: Describe (in detail) how you would examine the internal structures of the eye.

Indirect slit lamp biomicroscopy using a wide field (90D) lens was the preferred option of respondents with many opting for supplementary ophthalmic imaging to support record keeping. Of note many respondents did not indicate a whether they would dilate the patient or not as part of their internal eye examination.

Question 8: Describe (in detail) any other tests that you would undertake to examine the health of the eye or visual system

There were several tests common to most responses:

- Pupil reflex testing
- Marcus-Gunn testing
- Perimetry
- Tonometry

In addition several respondents suggested more functional (real world) approaches to perimetry, and Amsler testing centrally.

Question 9: Outline the tests and/or measurements you would perform to assess the performance of the visual system

Respondents were uniform in their suggestion of distance acuity (aided and unaided). No preference was observed between Snellen and LogMAR scoring. Other tests suggested included colour vision testing by Ishihara and red desaturation, and contrast sensitivity testing.

Question 10: Outline the tests and/or measurements you would conduct during the refractive examination

Attempts to separate refraction from binocular vision can be artificial due to the significant link between the accommodative and vergence systems. For this feedback accommodation will be included under refractive tests while vergence related tests will be included under binocular testing.

Retinoscopic objective refraction was the preference for most practitioners, followed by Jackson Crossed Cylinder refraction with binocular balancing. Many practitioners also sought to undertake testing of the accommodative system (especially in pre-presbyopic subjects), testing near point of accommodation.

Other tests suggested for these patients included:

- Dynamic retinoscopy (MEM)
- Accommodative facility (+/-2.00)
- Fused crossed cylinder
- Positive & negative relative accommodation
- Determination of the AC/A ratio

Question 11: Describe the tests and/or measurements that you would conduct during the binocular examination

Attempts to separate refraction from binocular vision can be artificial due to the significant link between the accommodative and vergence systems. For this feedback accommodation will be included under refractive tests while vergence related tests will be included under binocular testing.

To assess heterophoria, respondents were evenly split between the use of the objective cover test and the use of a Maddox rod. Most respondents were also indicated a preference for fixation disparity findings to support their prescribing as well as near point convergence testing. Tests of fusion were rare and less than half of respondents chose to measure stereopsis. Physiological X/H testing of ocular motility was near universal with many practitioners also testing patient’s saccadic accuracy through observation and tests of inferred saccadic accuracy (DEM/KD test).

Question 12: How would your examination differ if the patient was pre-presbyopic?

Most respondents indicated the measurement of amplitude of accommodation.

Question 13: What other tests would you consider (not previously mentioned) to examine the eyes or visual system?

Other tests suggested by respondents:

- Wilkins Rate of Reading test
- IOO Pattern Glare test
- Alpha-Omega Pupil testing
- Optokinetic nystagmus testing
- Jump vergence
- Effect of typoscope on reading
- Dilation
- Red spot test
- Contact lens assessment

Question 14: How would your assessment vary if the patient was being seen under the General Ophthalmic Services (GOS) contract?

Responses to this question were mixed. Many respondents indicated that their assessment would altered in response to patients attending for assessment under the GOS contract. With many altering their response to provide a standard sight test.

Question 15: Any further comments?

Each patient encounter is unique and those patients who have presented with a history of stroke can have variable sequaele to the episode and may have a range of ocular complications. Such a questionnaire is challenging as it suggests commonality of ophthalmic difficulties between patients with a history of stroke. During the questionnaire respondents identified and outlined the importance of listening to the patient. Indicating that the content of their exam would often be fluid, tailored by the patient’s history and stated visual requirements.

Question 16: What is your professional background?

All participants within this study are GOC registered optometrists. Participants who have agreed to participate within this study come from a range of backgrounds in community, specialist, behavioral and hospital eye service practice.

The first questionnaire in this study sought to establish the procedures and routines used by experienced clinicians providing ocular and visual care to patients with a history of stroke. The second round of this study will move away from personal practice. The next questionnaire will instead consider the **recommendations you would make** to a *less experienced* and/or *less confident* clinician who has been informed that a patient with a history of stroke has made a tentative appointment with them. The questions within the second questionnaire will be based on the results summarised above.

Malcolm C Maciver BSc MOptom MCOptom
Principal Investigator

Maciver M., Markham C., & Stores R. (2018, March) *Methods of visual examination following stroke: A systematic review*. Poster presented at Optometry Tomorrow, the annual conference of the College of Optometrists. Birmingham.

Appendix 6: Feedback to Participants – Delphi Round 2

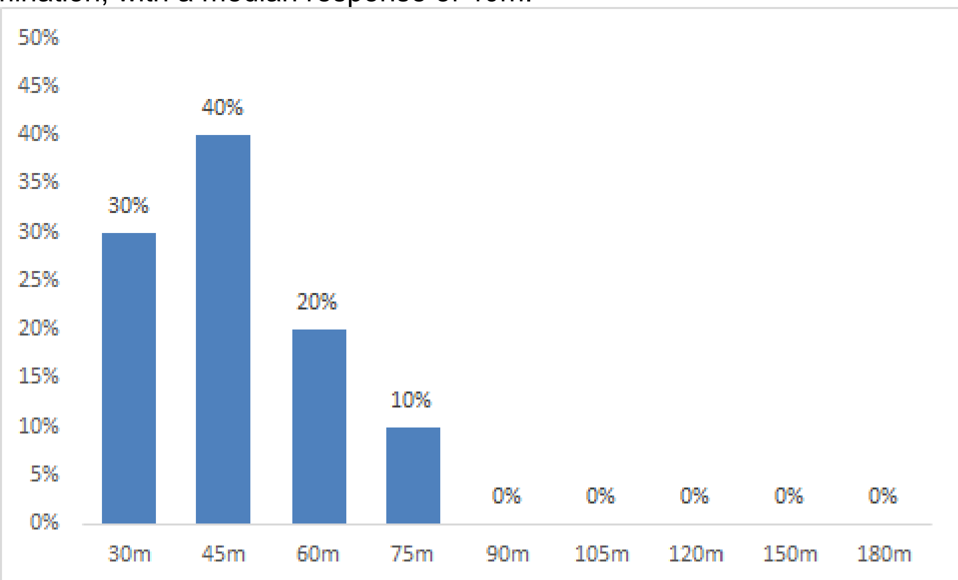
Fractured Vision: Optometric examination of patients following stroke
Feedback from Round 2

Following a review of the literature, it has been found that there is a paucity of evidence in the appropriate ophthalmic diagnostic procedures that should be used by clinicians providing vision care to patients with a history of stroke. The first round of this study sought to establish current clinical practice amongst clinicians with experience of examining and providing ophthalmic health and vision care to patients with a history of stroke. This second round took this information, and used it as a reference base for recommendations that experienced clinicians would make to a less experienced and/or confident clinician who was expecting to examine a patient with a history of stroke.

The results of this round identify the key diagnostic tests that would be recommended for use by an inexperienced clinician in ideal circumstances when examining patients with a history of stroke.

Question 1: How much time should be set aside in order to conduct a full eye examination?

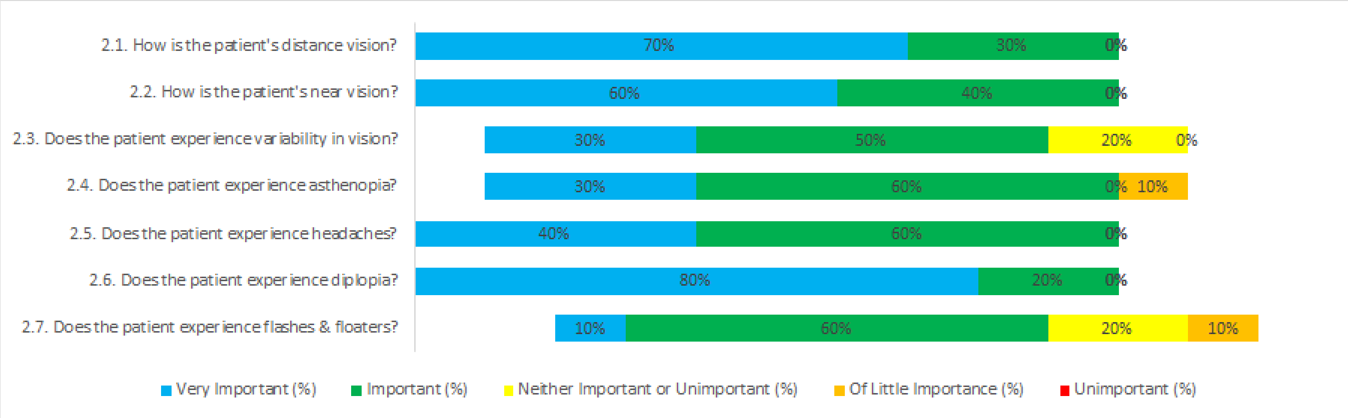
Respondents provided a range of responses indicating an extended period when compared to a standard examination, with a median response of 40m.



Recommended time to be set aside to examine a patient with a history of stroke

Question 2: Which of the following should be asked about as part of a case history?

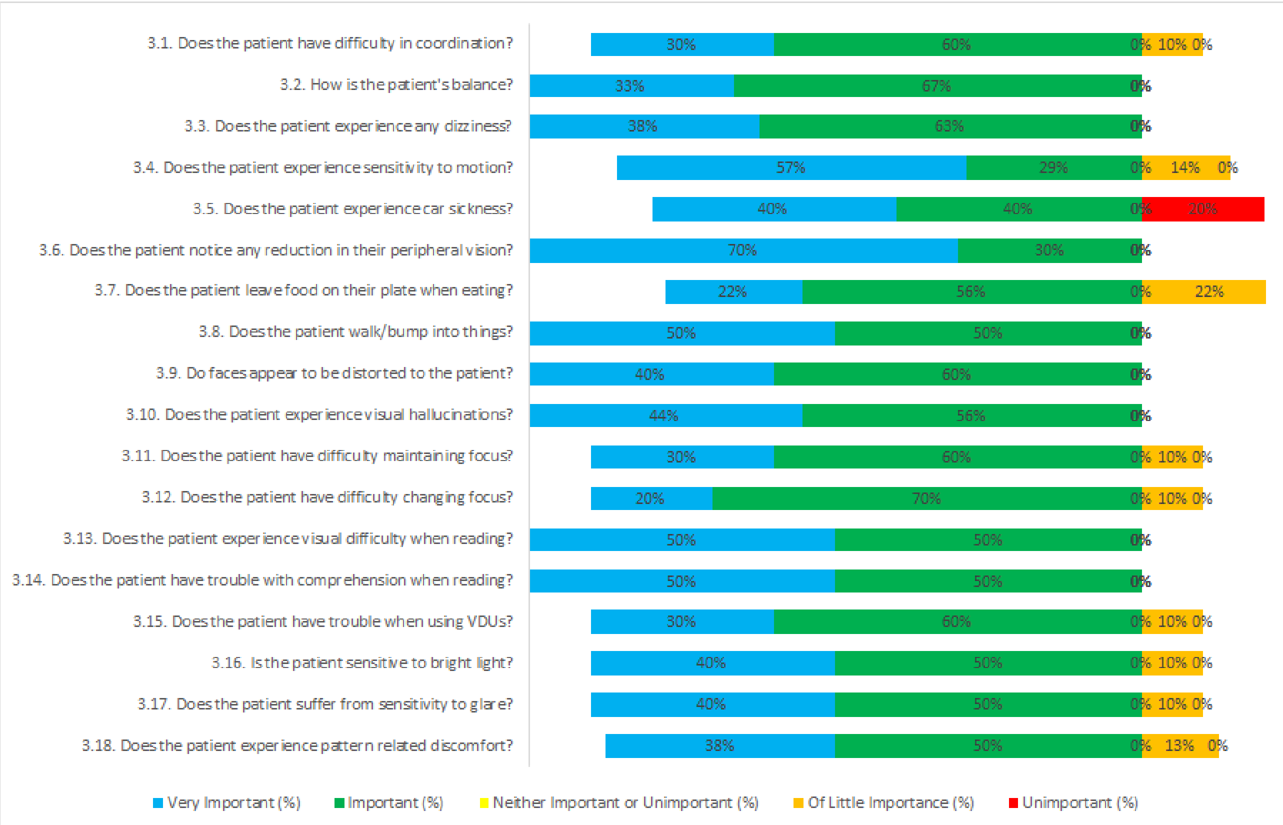
As indicated in the previous round of the study, case history featured as key to the identification of visual issues during examination. Most questions pertaining to general visual symptoms were considered to be an important part of the case history my most respondents.



Importance of visual symptoms when conducting a case history

Question 3: Which of the following questions should be asked regarding specific symptoms?

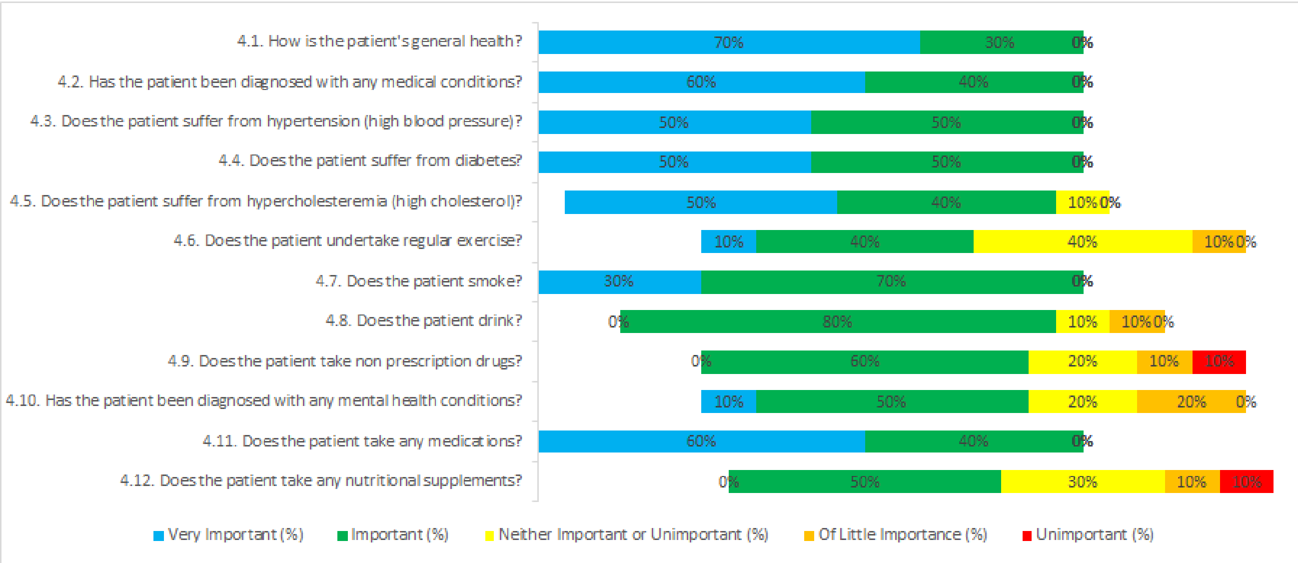
As indicated in the previous round of the study, case history featured as key to the identification of visual issues during examination. Unsurprisingly the questions pertaining to neurologically associated visual symptoms were considered to be an important part of the case history my most respondents.



Importance of neurological symptoms when conducting a case history

Question 4: Which of the following questions should be asked regarding the patient's medical history?

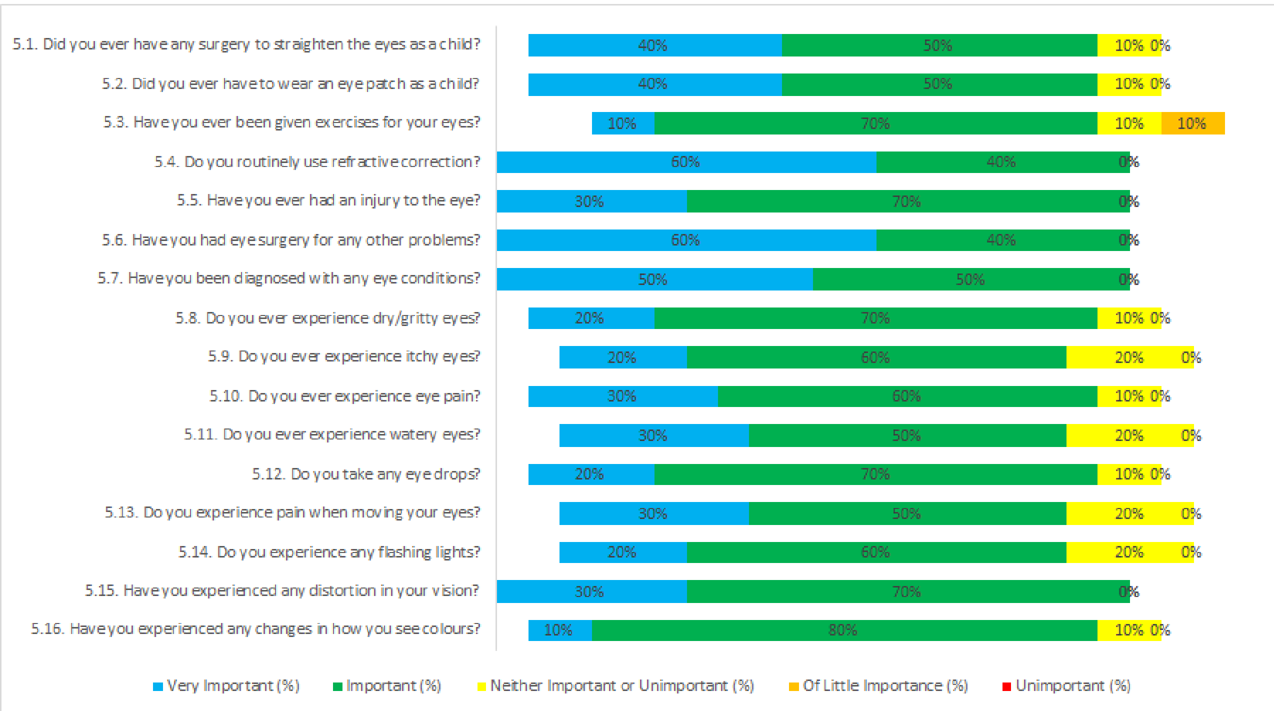
Like the questions pertaining to general visual symptoms, questions around patient's medical and medicinal history were considered to be significant by most clinicians.



Importance of medical and medicinal history when conducting a case history

Question 5: Which of the following questions should be asked regarding the patient's ocular history?

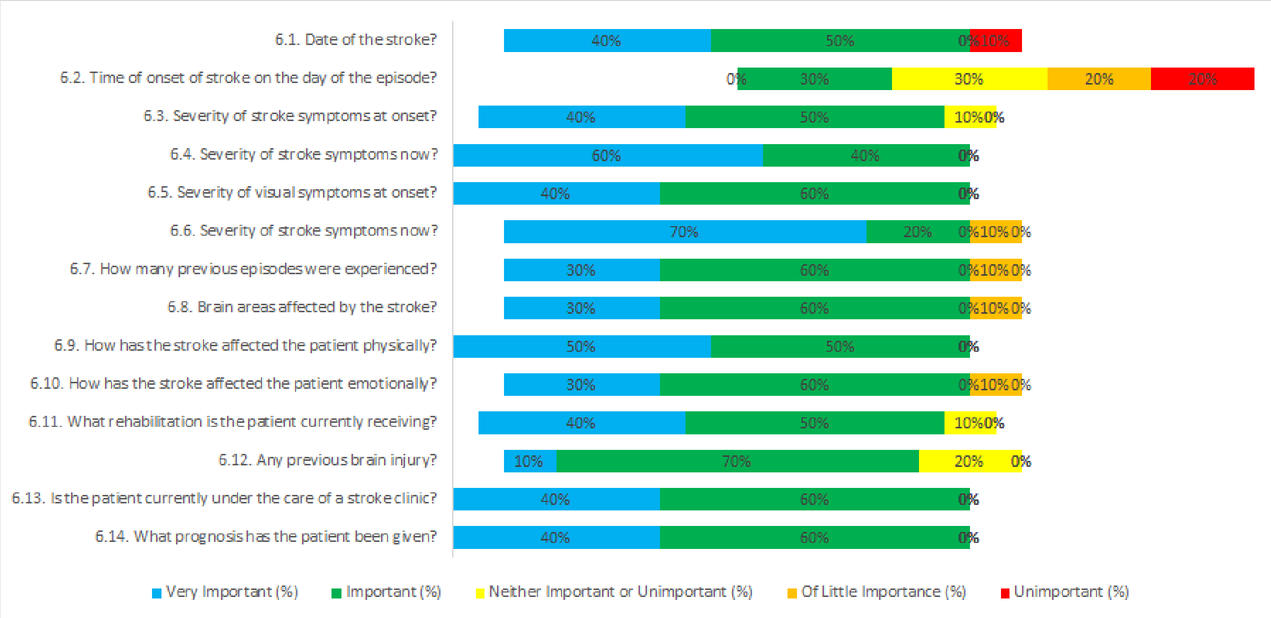
Features of personal ocular history where considered to be important to most practitioners when conducting ocular examination.



Importance of ocular symptoms when conducting a case history

Question 6: Which of the following questions should be asked regarding the stroke?

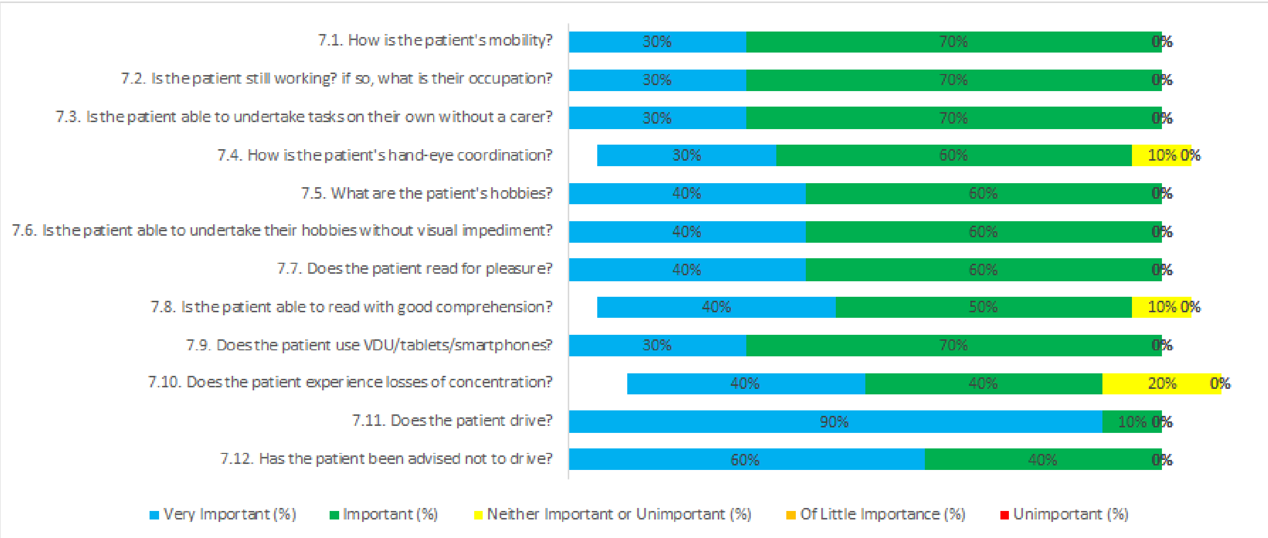
Most questions identified were considered to be of importance when considering the details of the stroke. While the timing of the episode during the day of the initial event was not considered of significance by many, details such as severity and visual symptoms at the time of the episode were considered important by most respondents.



Importance of stroke related information when conducting a case history

Question 7: Which of the following questions should be asked regarding the patient's lifestyle?

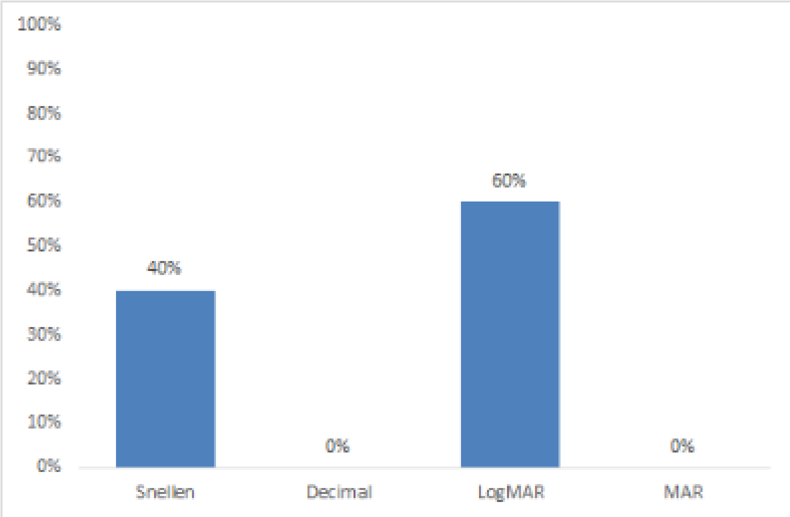
Similar to general history, visual symptoms and personal ocular history, the impact of the stroke on the patient's lifestyle options was considered to be of significance to most respondents. In particular the patient's driving status was considered to be highly significant to most respondents.



Importance of lifestyle information when conducting a case history

Question 8: What notation should be used to record distance acuity?

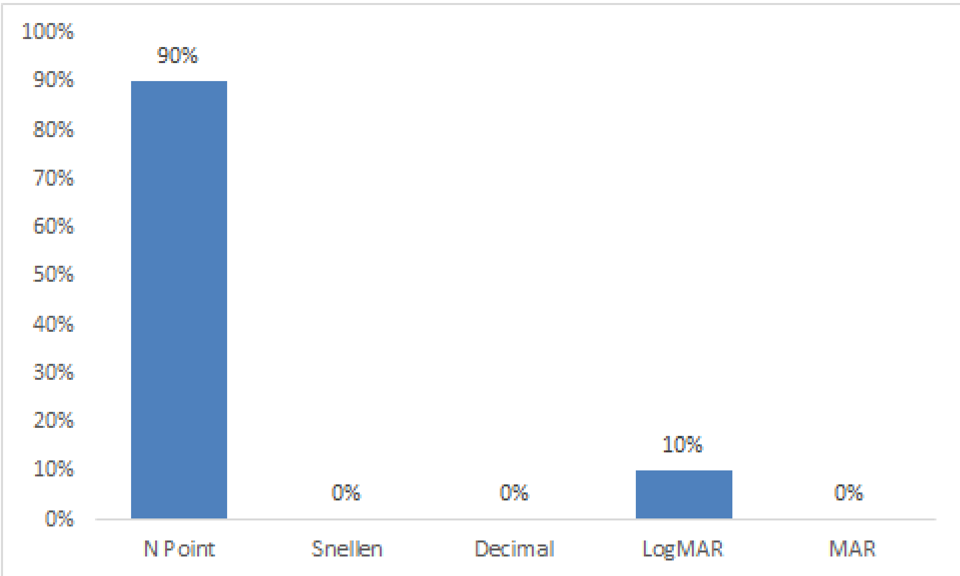
While many clinicians still opt for the traditional Snellen chart for assessing acuity, most respondents favoured the more repeatable LogMAR chart for the assessment of acuity.



Respondent's recommended method for assessment of distance acuity

Question 9: What notation should be used to record near acuity?

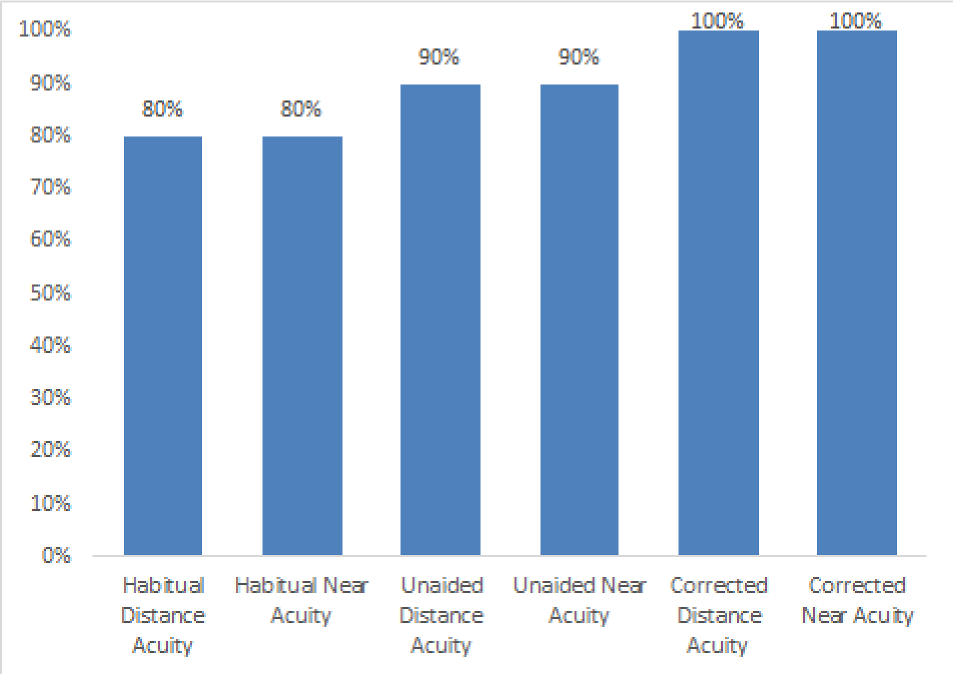
While many respondents favoured the LogMAR methodology for the assessment of distance acuity it is interesting to note that many prefer the more conventional Royal College of Ophthalmologists' N point series of test charts for the assessment of near vision.



Respondent's recommended method for assessment of distance acuity

Question 10: Which measures of acuity should be undertaken?

When considering patient's acuity, most respondents considered habitual and unaided acuity to be important measures of vision. All respondents considered best corrected acuity to be an essential measure.

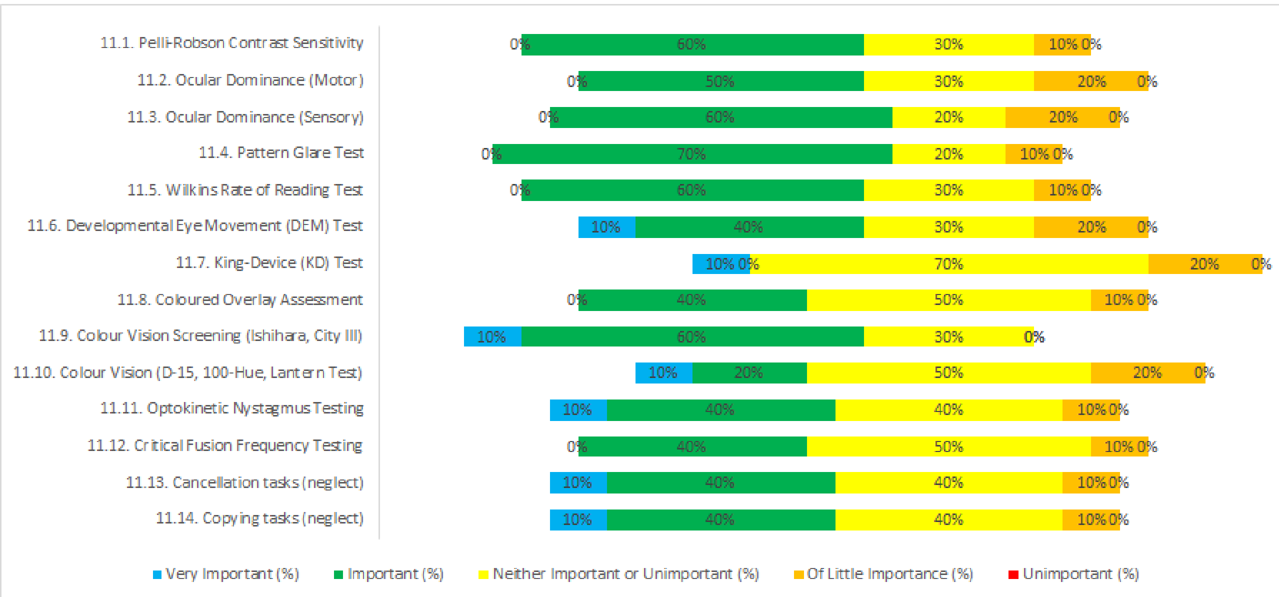


Respondent's recommended measures of acuity in a patient presenting with a history of stroke

Question 11: Which of the following tests of the visual system should be undertaken?

Generally a mixed response was gained from many respondents regarding the use of clinical tests. Key tests identified when examining the visual system (in addition to acuity) were:

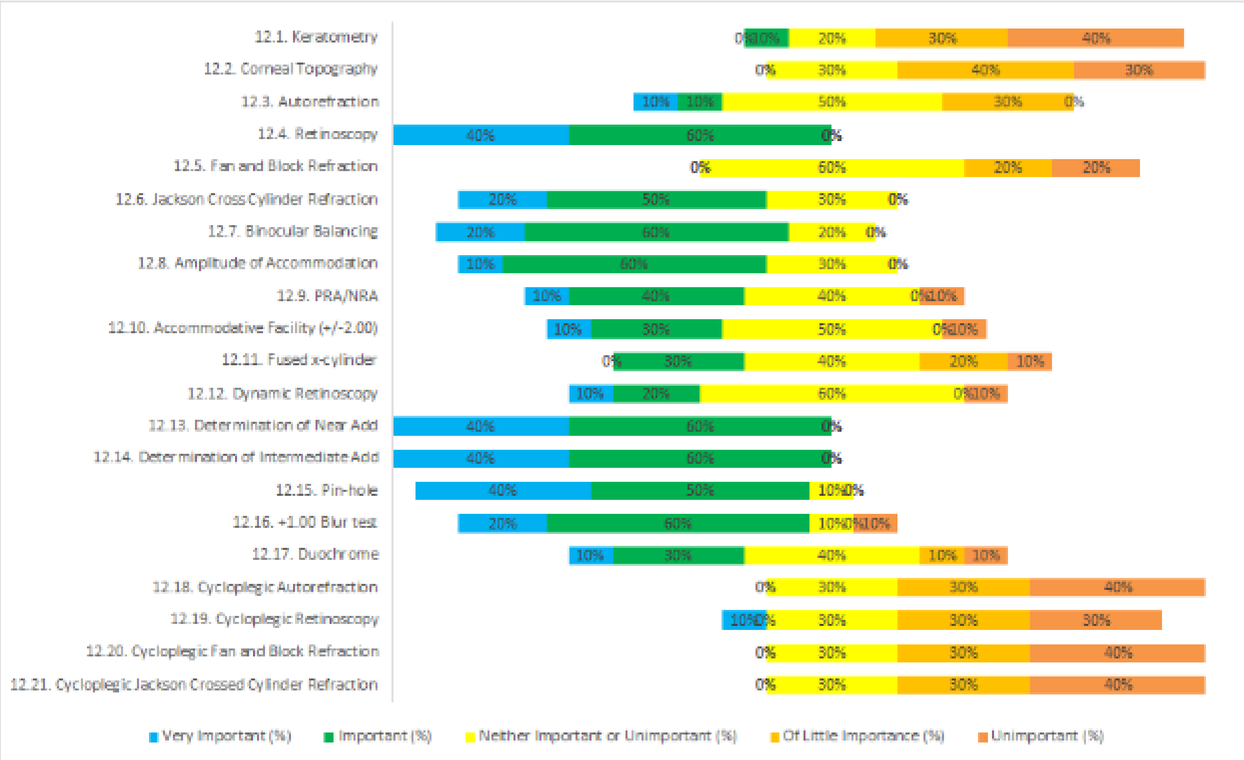
- Contrast sensitivity
- Sensory dominance
- Pattern glare test
- Wilkins rate of reading test
- Colour vision screening



Respondent's recommended assessments of the visual system in a patient presenting with a history of stroke

Question 12: Which of the following tests of the refractive system should be undertaken?

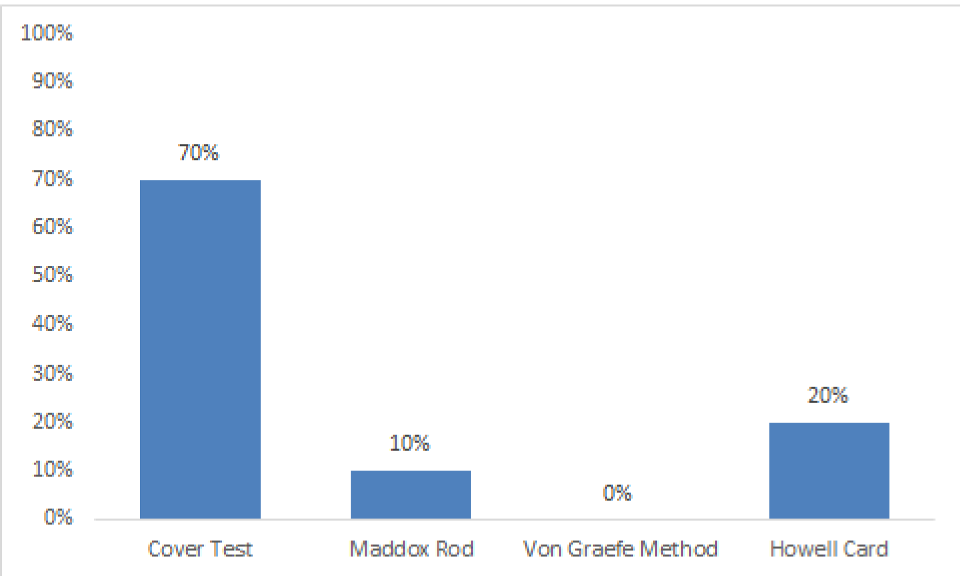
Respondents were clear that measures of corneal contour were largely not relevant when examining patients with a history of stroke. In addition, while refractive procedures were considered key, cycloplegic results were considered to be of limited use. It is of interest that many respondents gave a clear preference in objective refraction methodology, outlining a preference for the use of retinoscopic refraction in lieu of automated refractive methods.



Respondent's recommended methods of the refractive system in a patient presenting with a history of stroke

Question 13: Which of the following tests should be undertaken to assess the patient's distance oculomotor status?

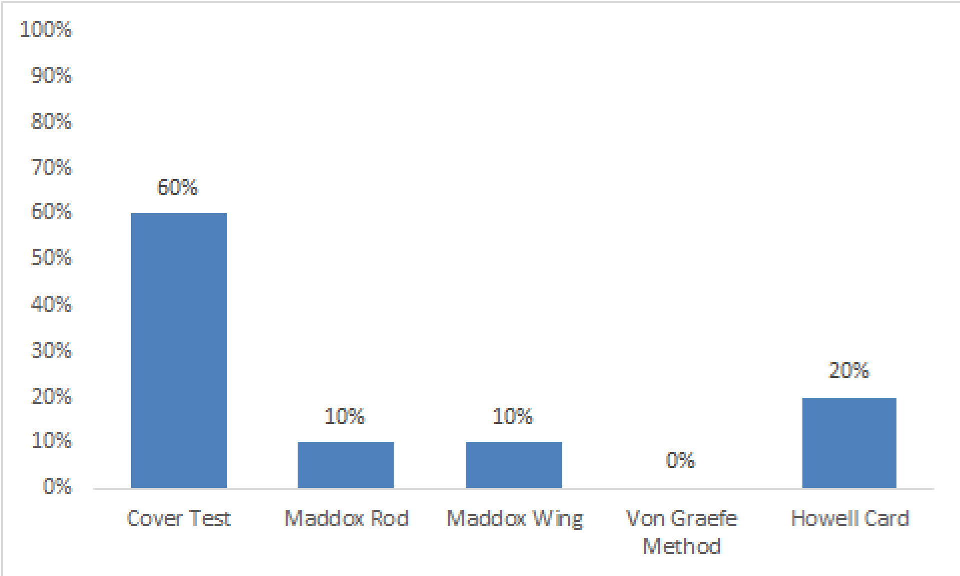
In many areas of optometry it is difficult for the clinician to limit their choice of assessment method as required by this question, as one respondent outlined (in comments section) many cases may require more than one method. This was considered and implemented to instead outline preferred method. Largely clinicians preferred the objective cover test to subjective methods when examining patients with a history of stroke.



Respondent's recommended method of measuring distance oculomotor status in a patient presenting with a history of stroke

Question 14: Which of the following tests should be undertaken to assess the patient's near oculomotor status?

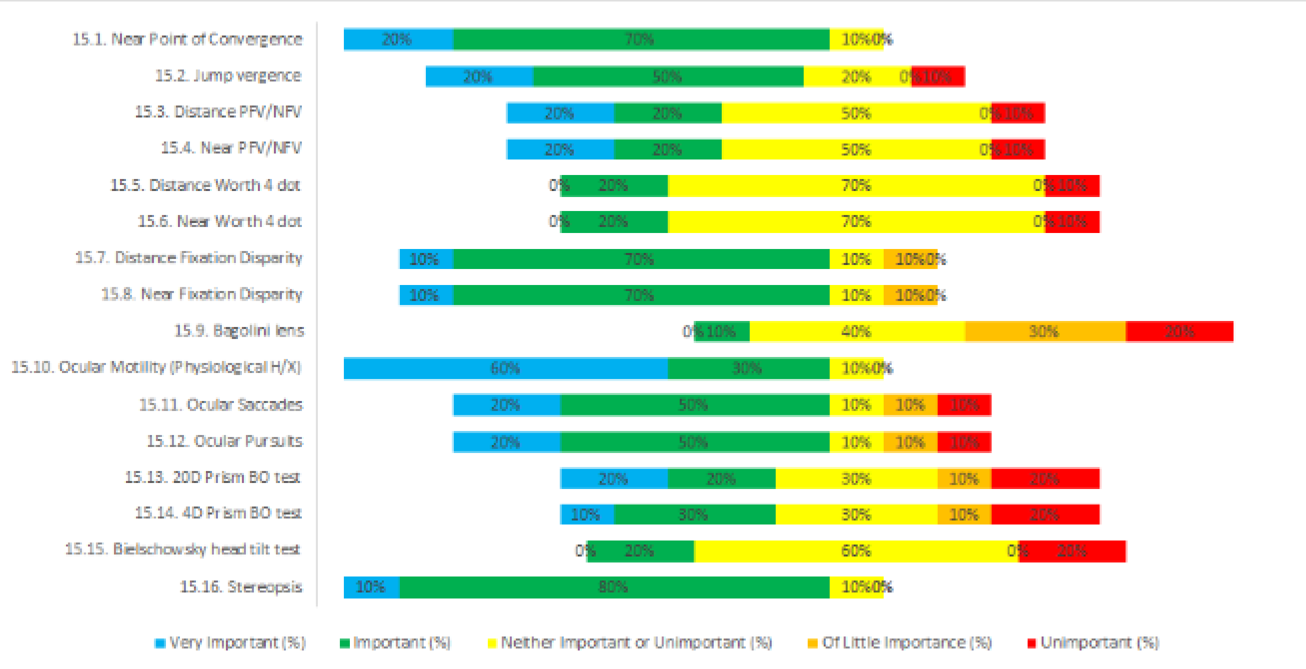
As with the assessment of distance oculomotor balance, many clinicians preferred the use of the cover test when considering near oculomotor balance. It is of note that for assessment of near OMB, more clinicians opted for other subjective dissociated methods of assessment.



Respondent's recommended method of measuring near oculomotor status in a patient presenting with a history of stroke

Question 15: Which of the following tests of binocular function should be undertaken?
Assessment of several key features of binocular vision were considered of great importance to respondents. In particular several tests were considered by most respondents to be useful to the exam of this patient demographic:

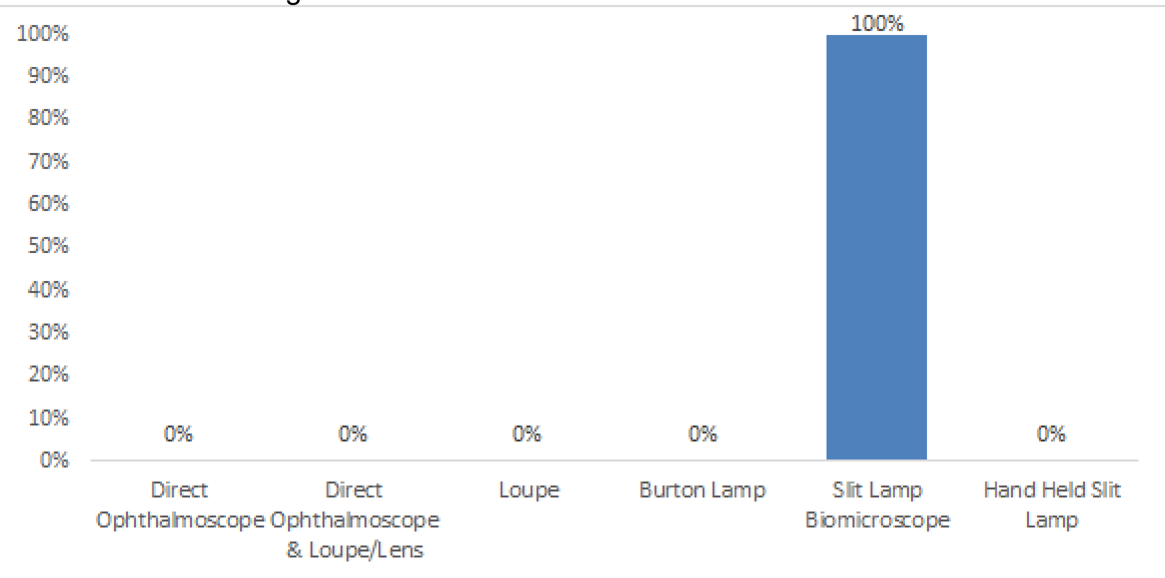
- Near point of convergence
- Jump vergence
- Distance fixation disparity
- Near fixation disparity
- Ocular motility (physiological H/X)
- Ocular saccades
- Ocular pursuits
- Stereopsis



Respondent's recommended of binocular function in a patient presenting with a history of stroke

Question 16: Which of the following instruments should be used to assess the anterior & external eye?

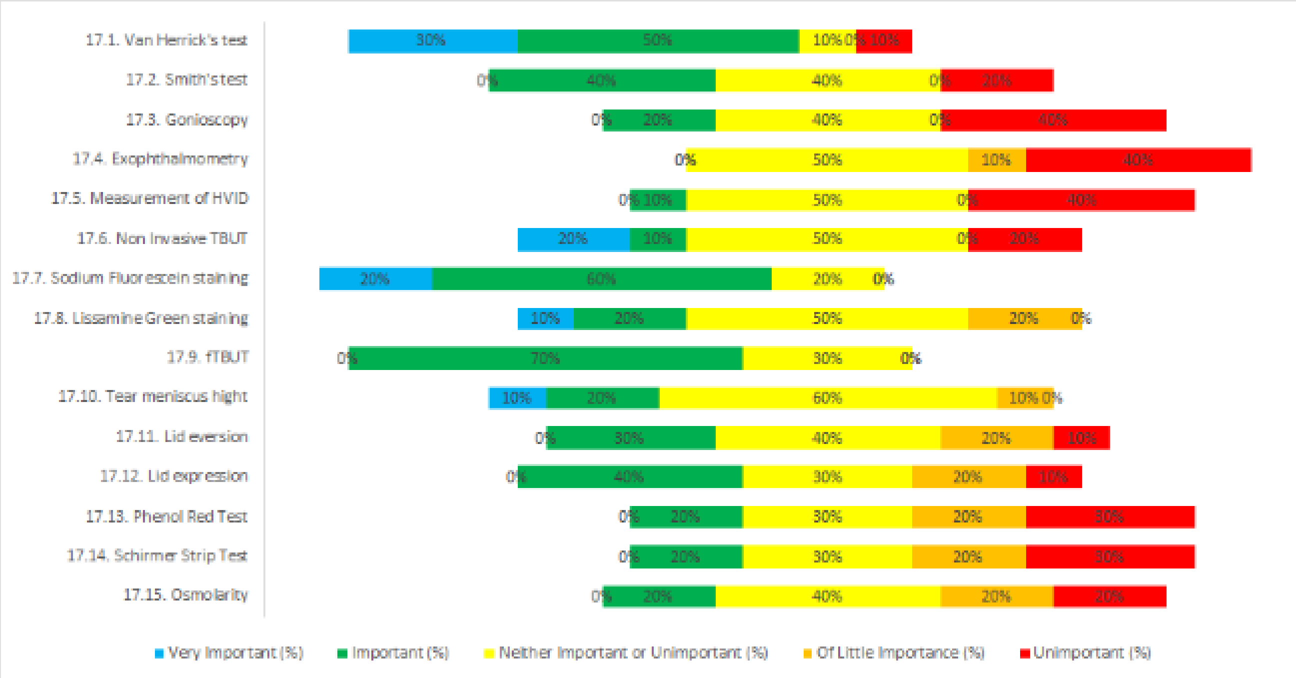
Respondents were universal in their recommendation of the use of the slit lamp biomicroscope to assess the anterior segment.



Respondent's recommended method of anterior eye assessment in a patient presenting with a history of stroke

Question 17: In addition to the basic assessment of the anterior eye and adnexa, which of the following tests should be undertaken?

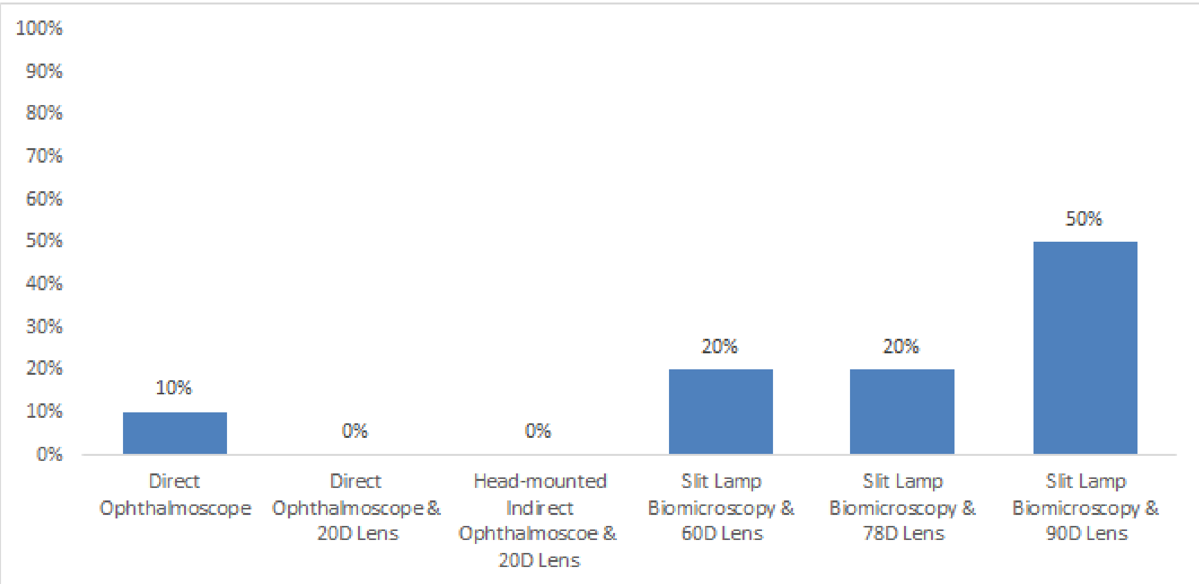
Respondents were mixed in outlining the tests that should be conducted in addition to a basic anterior segment assessment. While many tests received a mixed response, Van Herrick's assessment, and the assessment of the corneal surface and tear film using Sodium fluorescein were recommended by most respondents.



Respondent's recommended tests of the anterior eye in a patient presenting with a history of stroke

Question 18: For examination of the internal eye, which of the following instruments should be used?

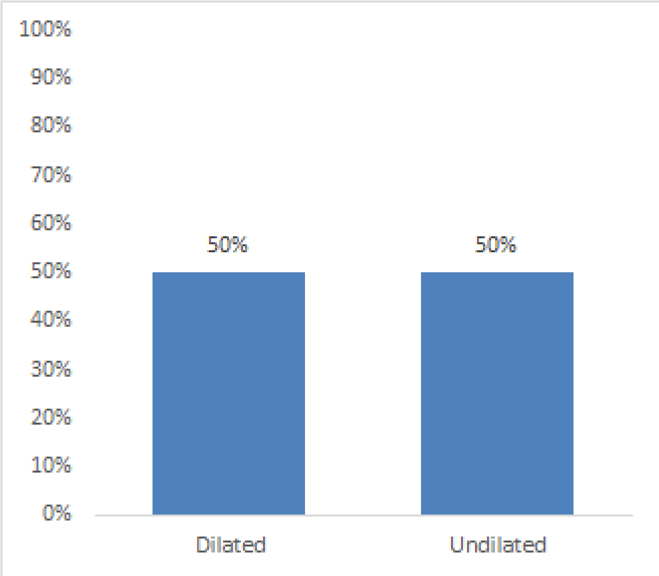
Most respondents indicated a preference for the use of slit lamp indirect ophthalmoscopy when examining the inner eye, with half of respondents demonstrating a preference for a wider field examination using the 90D lens.



Respondent's recommended method of posterior eye assessment in a patient presenting with a history of stroke

Question 19: When undertaking examination of the posterior segment, the patient should be:

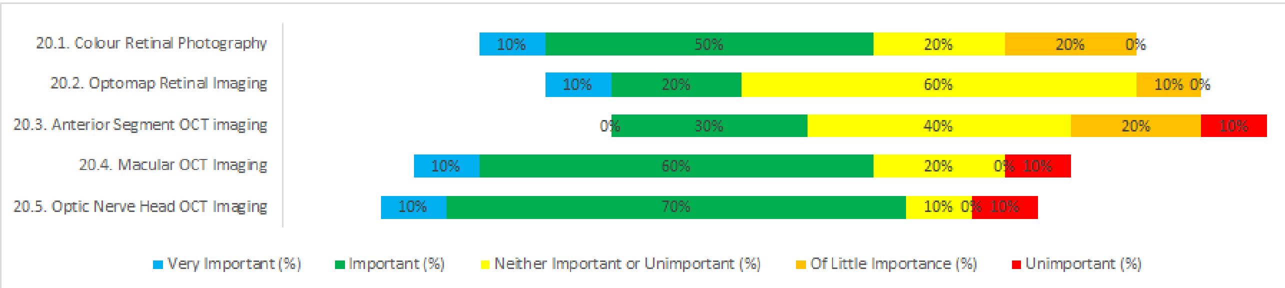
Responses were mixed to this question, with the longer period of exam off-setting the stereo viewing opportunity offered.



Responses to the use of mydriasis in a patient with a history of stroke

Question 20: In addition to a routine examination of the inner eye, which of the following tests should be undertaken in practice?

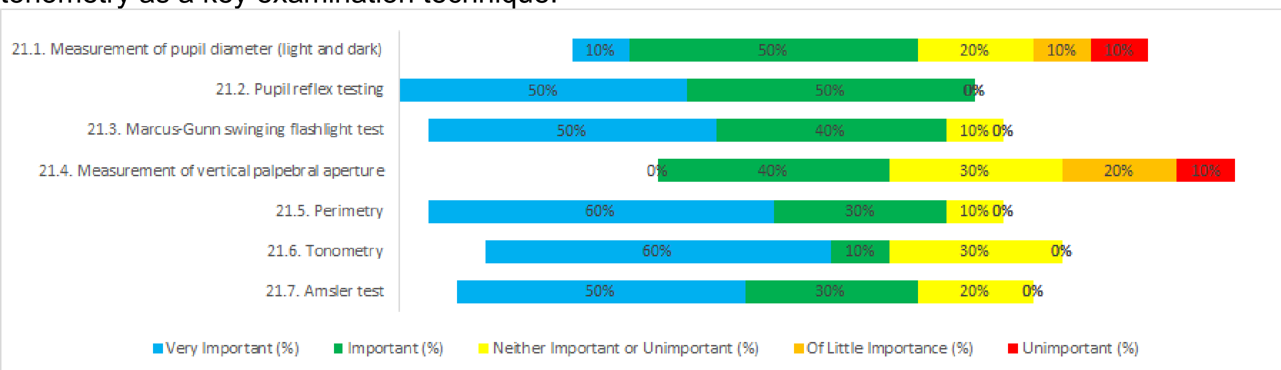
Respondents largely favoured conventional imaging to more modern wide field retinal imaging methods, and showed a preference for posterior OCT examination when reviewing the integrity of the posterior segment.



Additional tests recommended by respondents to be conducted on a patient presenting with a history of stroke

Question 21: What other tests of ocular health should be undertaken?

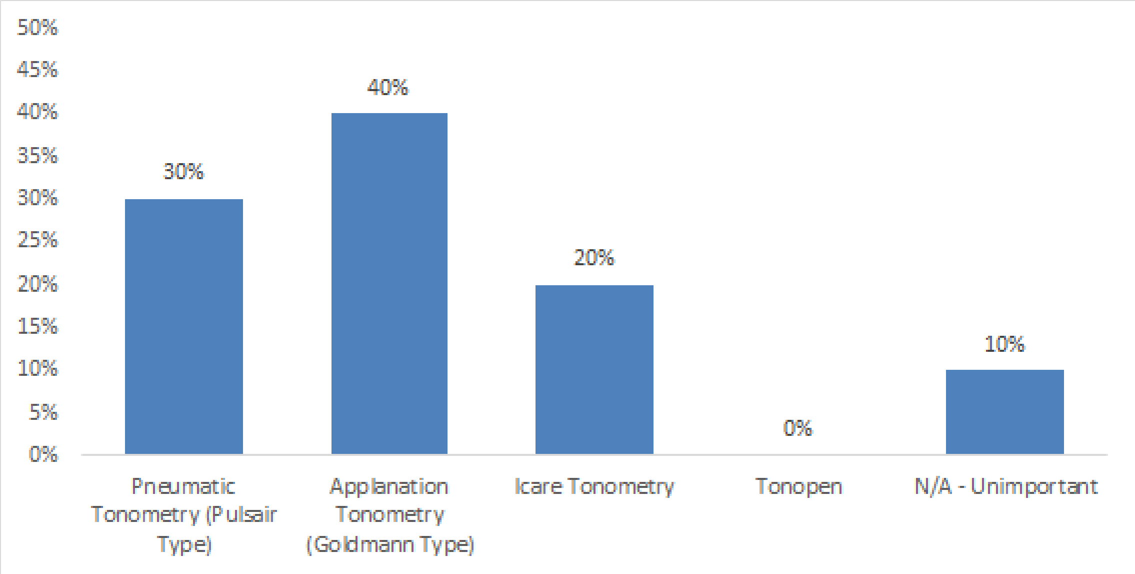
As common text book neurological assessments, it is perhaps unsurprising that pupil assessment, perimetry and Amsler chart testing were identified as key methods. In addition respondents identified tonometry as a key examination technique.



Additional ocular health tests recommended by respondents to be conducted on a patient presenting with a history of stroke

Question 22: Which technique should be used to undertake tonometry?

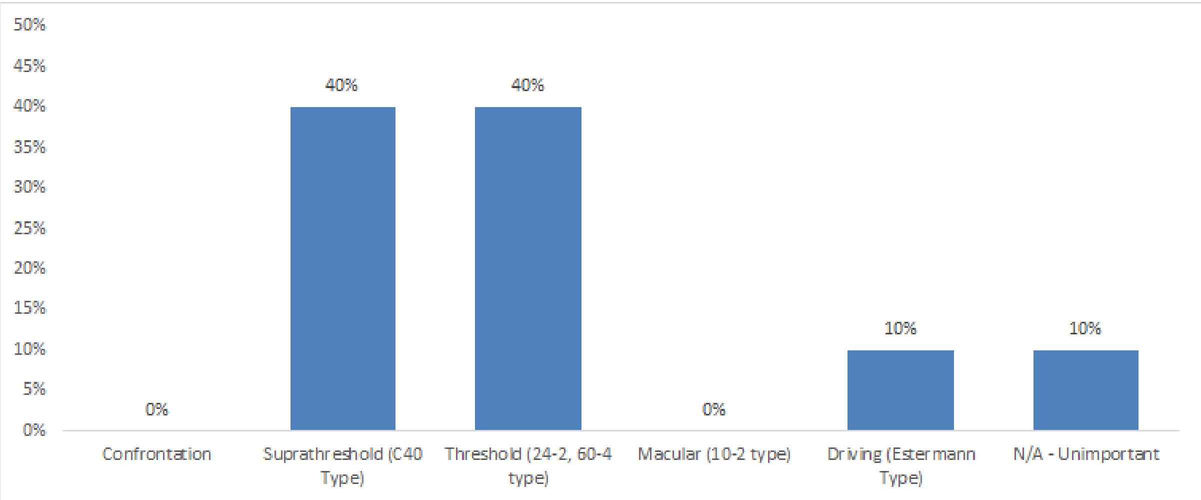
Respondents were split on the optimum method of assessing intra-ocular pressure with the largest proportion of respondents opting for the *gold standard* Goldmann method.



Respondent's recommended method of tonometry in a patient presenting with a history of stroke

Question 23: Which testing strategy should be used when undertaking perimetry?

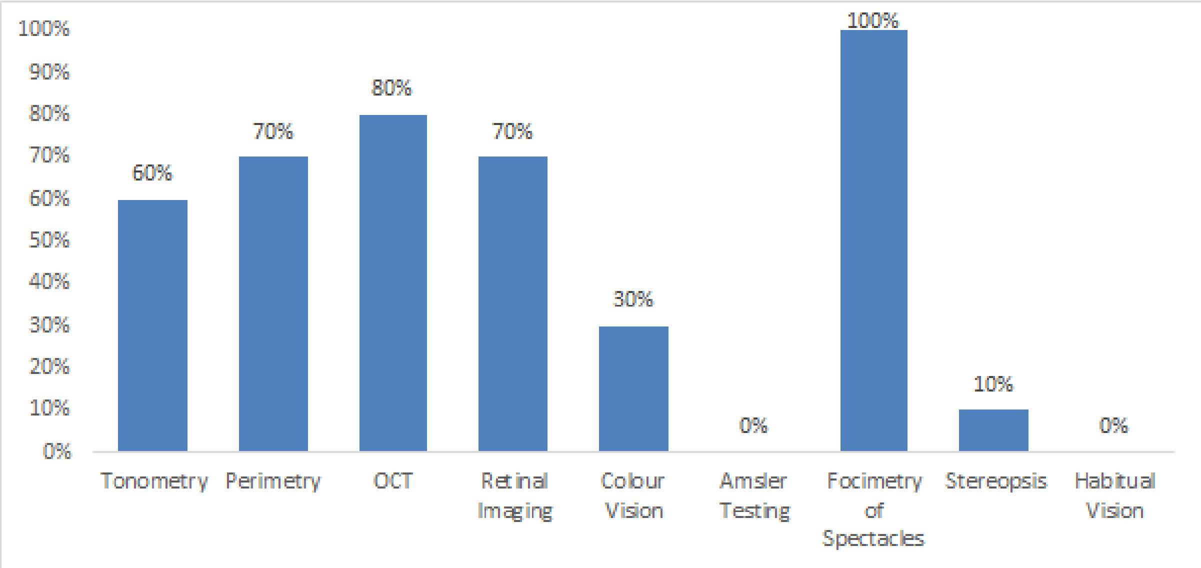
Respondents were split between the use of threshold and supra-threshold methods when examining patients with a history of stroke. This is perhaps unsurprising as while threshold techniques have greater theoretical accuracy they suffer from longer test times, which may lead to inaccuracy with loss of patient attention as the test continues.



Respondent's recommended method of perimetric assessment in a patient presenting with a history of stroke

Question 24: Assuming all staff are thoroughly trained, which of the following tests would you consider delegating to be undertaken with auxillary staff prior to the main examination?

Focimetry was considered universally as a measurement to be undertaken by auxillary staff. With many clinicians recommending other techniques to be assessed prior to the main examination.



Respondent's recommendations for tasks to be delegated to auxillary staff

Question 25: Other comments?

Each patient encounter is unique and those patients who have presented with a history of stroke can have variable sequaele to the episode and may have a range of ocular complications. Such a questionnaire is challenging as it suggests commonality of ophthalmic difficulties between patients with a history of stroke. During the questionnaire respondents identified and outlined the importance of listening to the patient. Indicating that the content of their exam would often be fluid, tailored by the patient's history and stated visual requirements.

This second questionnaire sought to identify the recommendations that experienced clinicians would make to a less experienced and/or confident clinician who was expecting to examine a patient with a history of stroke. This in turn could be used to identify the salient procedures for use by clinicians providing ocular and visual care to patients with a history of stroke.

The third and final round of this study will move to prioritise the procedures recommended to be undertaken in the exam room by an inexperienced / less confident clinician. The next questionnaire will consider the **procedures you would recommend** a less experienced and/or less confident clinician to undertake when they have been informed that a patient with a history of stroke has booked a 25 minute appointment with them. The questions within the third questionnaire will be based on the results summarised above.

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Principal Investigator

Appendix 7: Feedback to Participants – Delphi Round 3

Fractured vision: Optometric examination of patients following stroke Feedback from Round 3

This study was designed to identify a minimum dataset to develop a diagnostic test battery for use by eye care providers when examining patients with a history of stroke.
A review of the literature found a paucity of evidence in the appropriate ophthalmic diagnostic procedures that should be used by clinicians providing vision care to patients with a history of stroke.

The first round of this study sought to establish current clinical practice amongst clinicians with experience of examining and providing ophthalmic health and vision care to patients with a history of stroke. This second round took this information, and used it as a reference base for recommendations that experienced clinicians would make to a less experienced and/or confident clinician who was expecting to examine a patient with a history of stroke. The final round of this study refined this comprehensive test base to a core recommended dataset of tests for use in a *industry standard* 25 minute exam appointment.

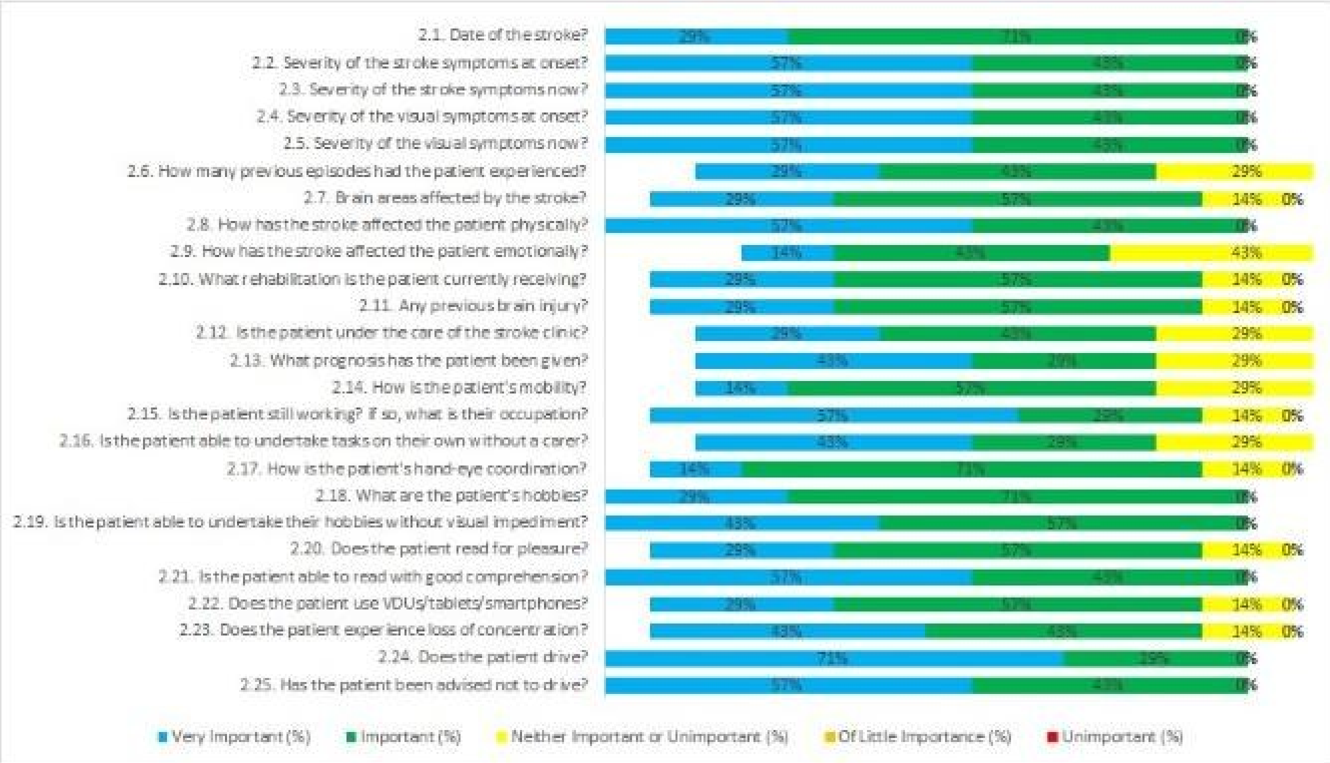
Below is a summary of the results of the data from the final round of this study.

Question 1: Which of the following questions should be prioritised as part of a case history in a 25 minute examination?

Consistent with the first and second round of the study, a comprehensive case history featured as an important factor within the examination. As previously most questions were considered to be of significance for inclusion within the minimum test battery.

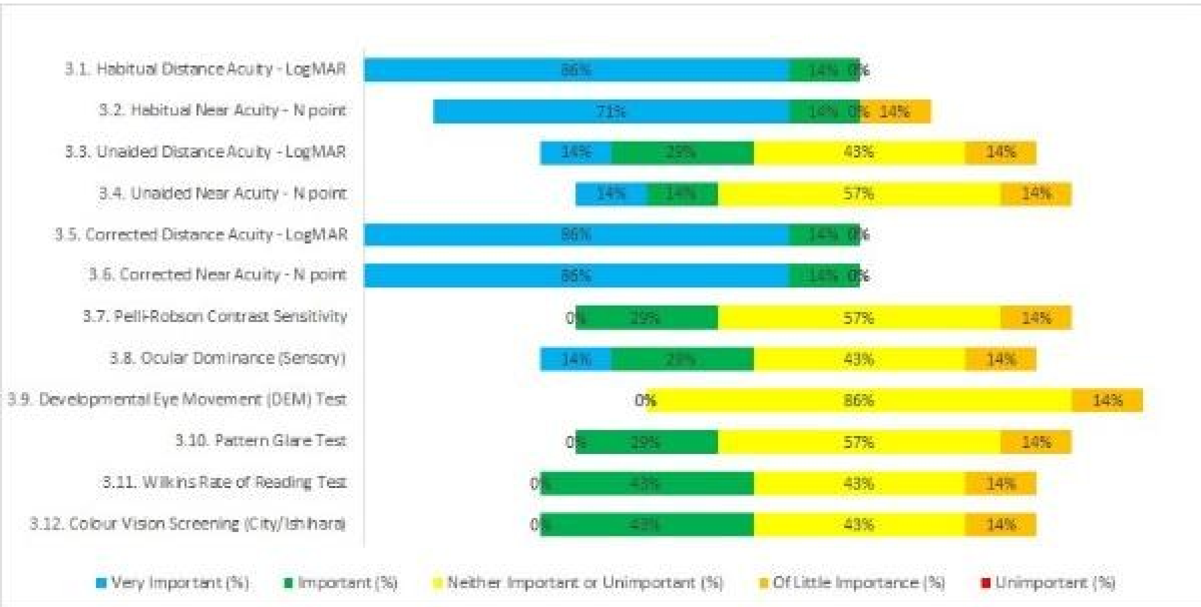
Question 2: In addition, which of the following questions should be prioritised as part of a 25 minute eye examination?

Consistent with the first and second round of the study, a comprehensive case history featured as an important factor within the examination. As previously most questions pertaining to details around the stroke were considered to be of significance for inclusion within the minimum test battery.



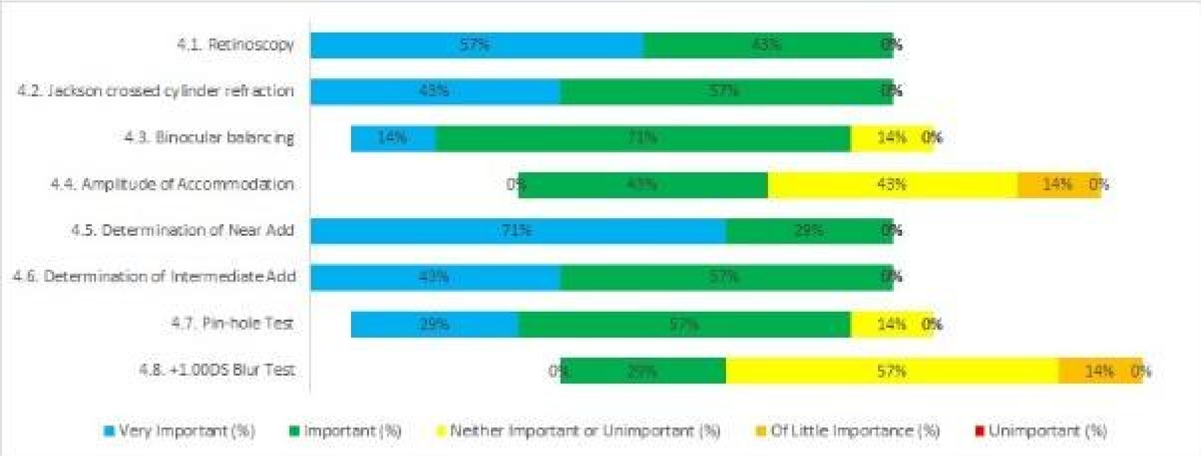
Question 3: Which of the following tests of the visual system should be undertaken as part of the 25 minute examination?

When considering the minimum dataset, participants made a definition between the core constituents of the visual system to be tested, identifying those elements that were of lower priority within the 25 minute examination.



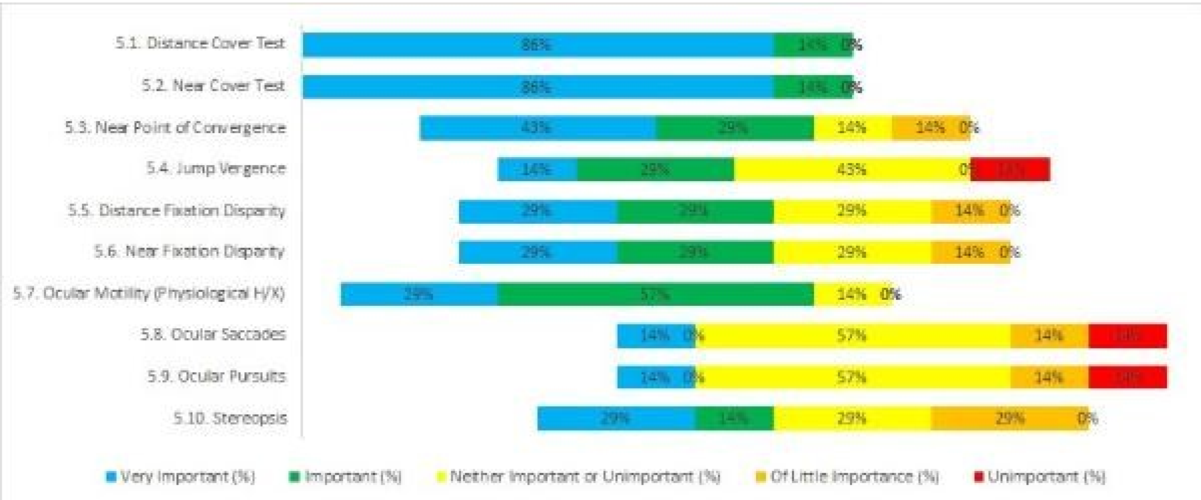
Question 4: Which of the following tests of the refractive system should be undertaken as part of the 25 minute examination?

Tests of the refractive system were largely consistent with the results of round 2 of the study, of note accommodative performance were considered to be of lower priority by participants when constraints were placed on the examination.



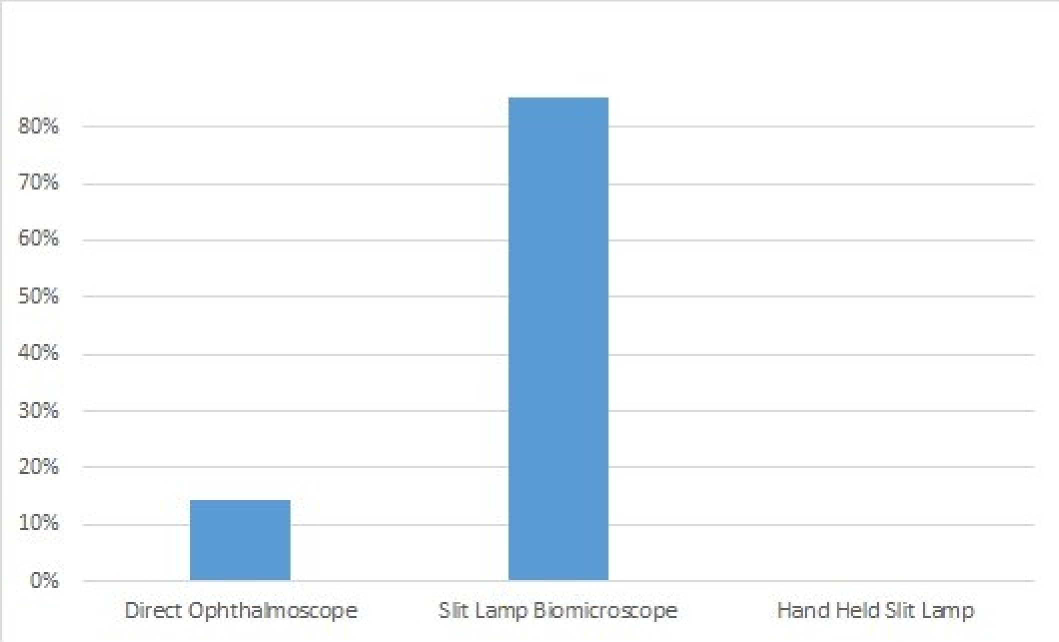
Question 5: Which tests of the binocular vision system would you recommend be undertaken as part of the 25 minute examination?

Key tests identified were objective assessment of heterophoria and oculomotor extension, participants' responses were mixed regarding other tests of the binocular visual system, with no consensus on the use of near point of convergence measurement and assessment of retinal slip.



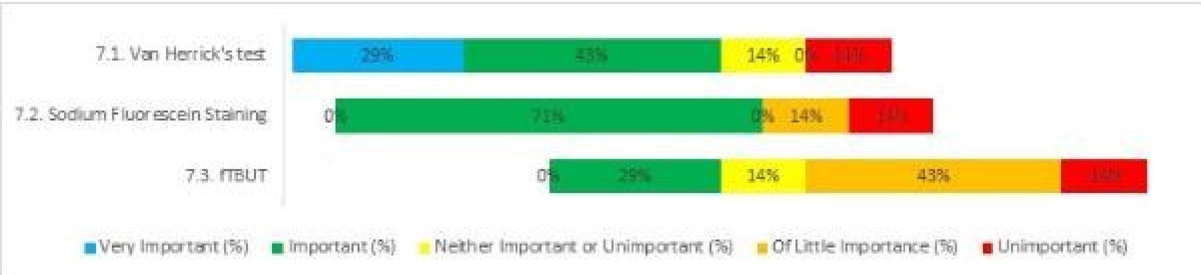
Question 6: Which instrument would you recommend be used to conduct the anterior eye assessment in the 25 minute examination?

For the examination of the anterior segment, most practitioners agreed with the preferred use of the slit lamp biomicroscope. Consistency here was reduced with a minority of responses preferring to use the direct ophthalmoscope to undertake assessment of the anterior eye within the 25 minute examination.



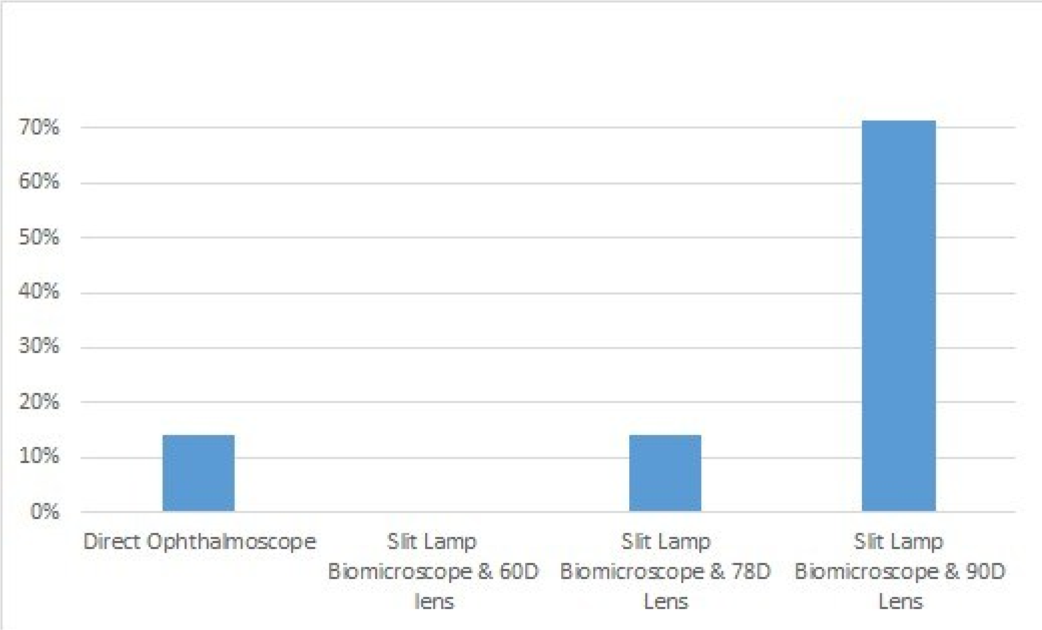
Question 7: Which of the following tests would you recommend as part of the anterior eye assessment in the 25 minute examination?

Participants were in agreement that assessment of the anterior chamber angle and ocular surface were key features of an examination with a patient with a history of stroke. It is worth noting that while corneal integrity was seen as a key feature, assessment of the tear film was seen as a lower priority within the 25 minute examination.



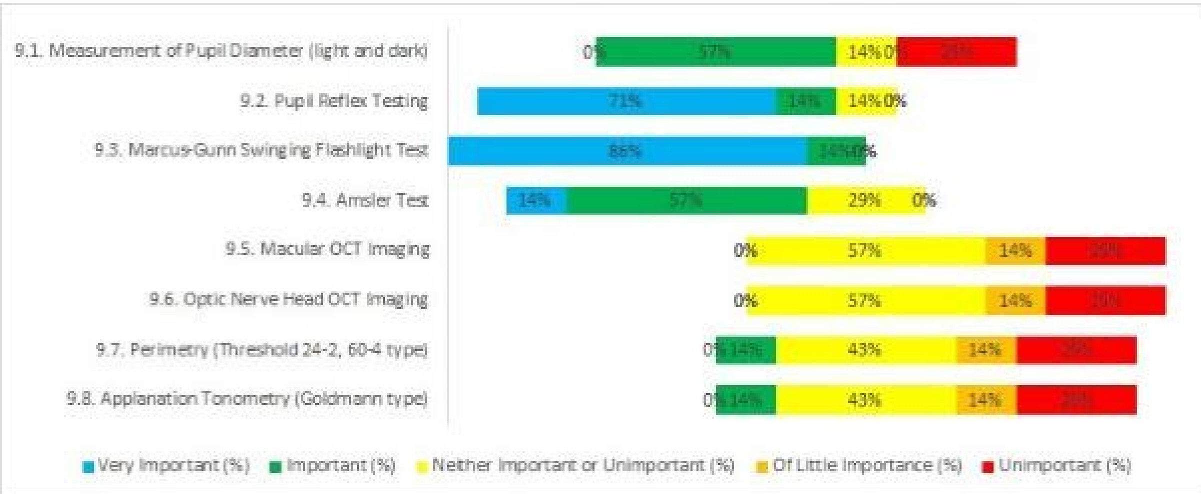
Question 8: Which of the following would you recommend be used to examine the posterior segment (undilated) during the 25 minute examination?

With the reduced examination time, most participants maintained a preference for slit lamp indirect ophthalmoscopy for their posterior segment examination. As indicated in the question sufficient dilation is unlikely to be achieved in a 25 minute examination, so this option was removed. The option was given for a dilated exam to be undertaken as a followup appointment later in the questionnaire.



Question 9: Which other tests of ocular health would you recommend be undertaken as part of the 25 minute examination?

Participants were in agreement that pupil testing remained a key diagnostic measure within the examination, with importance placed on the detection of afferent defects where present. Additionally assessment of macular integrity was considered significant within the primary assessment, with Amsler testing considered as an important component of the 25 minute examination.

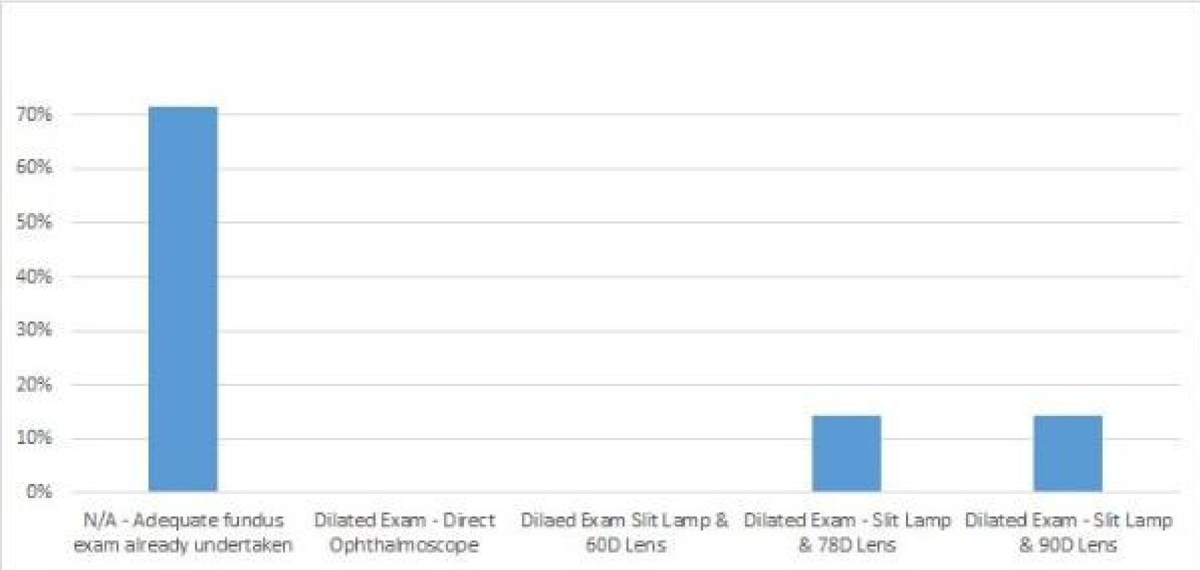


Question 10: Which of the following tests would you recommend be undertaken at a follow-up appointment after the initial examination?

This question gave participants the option to identify important tests to be considered as part of a follow-up appointment following the primary examination undertaken. Of participants who completed this questionnaire, 86% indicated a preference for further diagnostic testing to be undertaken at such a follow-up appointment. Preferences here were mixed, with agreement between participants for further assessment of habitual acuity, Wilkins Rate of Reading Test, and pupil testing. Participant's responses to the use of the Pattern Glare test were inconclusive.

Question 11: Which technique would you recommend be undertaken to examine the posterior eye at a follow-up appointment after the eye examination?

Due to the limitation of the initial examination to 25 minutes, there would be no opportunity to conduct a dilated examination in this initial patient episode. The opportunity to conduct a dilated examination was instead deferred to a follow-up assessment. When recommending further examination on follow-up assessment, the majority of participants were in agreement that further dilated examination following initial assessment was unnecessary.



Question 12: Further comments

Participants indicated the importance of using a problem based approach in examining this patient group. In particular participants linked the necessity of a follow-up appointment with symptoms experienced. One participant identified an alternative follow-up phone call as an alternative to assess the qualitative impact of management & intervention on relieving patient symptoms. Reducing the need for further diagnostic examination unless indicated by symptoms.

This third and final questionnaire was designed to investigate participant's views on the tests that they would recommend that a less experienced and/or confident clinician be prioritised as part of a *standard* 25 minute eye examination appointment.

This study was designed to create a standardised eye examination battery for patients that present with a history of stroke. As previously indicated, many of these patients have difficulty in accessing vision care due to some practitioner's hesitation to conduct examinations on these patients due to their complex visual needs.

The first round of this Delphi study investigated the current practice of experienced clinicians, and their approach to the diagnostic examination of patients who present with a history of stroke. Round two saw participants narrow these diagnostic options to a comprehensive test battery that would be recommended for a less confident and/or experienced clinician to conduct when examining a patient with a history of stroke. This final round refined this to create a minimum dataset of diagnostic tests for the examination of a patient with a history of stroke. This minimum dataset has been identified for the diagnostic ophthalmic examination of patients with a history of stroke, it has been designed to identify the key tests that should be conducted within a *typical* 25 minute examination. This is the first evidence based approach to the diagnostic examination of patients in this demographic, drawing upon expert opinion to develop a diagnostic battery.

The next stage of this study will be to undertake a trial of the diagnostic dataset outlined above, assessing the clinical utility of this battery in the target demographic.

I wish to thank you for the help you have provided in giving your time, experience and consideration when completing these questionnaires. I would envisage that these results may be used in future by clinicians (especially those less experienced with this patient group) to improve the accessibility of patients with a history of stroke to eye and vision care, especially in primary eye care practice. I wish to also thank you for your time in supporting this project from a personal level, as this project forms part of my own doctoral studies and academic development. I hope to be able to feedback further once this has been drafted for publication in an academic journal.

Many thanks again

Malcolm Maciver
Principal Investigator

Appendix 8: Diagnostic Investigation Study – Conditional Approval

Aston Triangle
Birmingham B4 7ET
United Kingdom
Tel +44 (0)121 204 3000

lhs_ethics@aston.ac.uk
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Memo

To : **Prof James Wolffsohn; Malcolm Maciver**
Cc: Tim Batty
Administrator, Life and Health Sciences Ethics Committee

From: Dr Rebecca Knibb
Chair, Health and Life Sciences Ethics Committee

Date: 24/3/2022

Subject: Project #HLS21005 A study to investigate the best tests to evaluate the sight of someone who has had a stroke

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The above proposal has been reviewed by a sub-group of the LHS Research Ethics Committee. The committee is willing to approve the proposal once the amendments below have been made.

Please note:
- The online version of your application itself cannot be modified once submitted. Therefore, all **amendments to the application itself should be uploaded as a PDF document** to the 'Resubmission Form' facility, highlighting any changes.
- Further Documents can be uploaded to the 'Other Documents' in the **Resubmitted Applications** facility.
- **Please ensure that all files are named meaningfully and the filename contains the version number and amended date (e.g. Ethics Application #100 Consent Form v2 17-10-13).**
- **Once the amendments and further documents have been uploaded, please ensure that you change the status of your online application from Resubmit to Final.**

Reviewers' recommendation: Conditional approval

Reviewers' comments: Please consider the following comments from reviewers:

1. C4b – it states that people will not be informed that recording is taking place; I assume this is a typo as this is inconsistent with the broader protocol; please clarify and detail as necessary
2. D5a – A technique referred to as GAT is listed as a potential risk/ethical issue due to 'adverse effects', but these effects are not stated. Please outline the perceived risk/ethical concern with this technique
3. Destruction of personal data is not outlined in section D7d
4. General: it is unclear whether participants will be given any feedback on their performance/eye health.
   Please outline this.
5. General: it is unclear what the control group will comprise –who will the participants be (I assume people who have not had a stroke, matched for age); how will they be recruited?

6. General: The PIS refers to Dr Nicola Logan as part of the research team, but their role is not outlined in the protocol.
7. General: How are the general health data and lifestyle data used, which are collected in the questionnaire? What is the rationale for collecting these data? This isn't clear from the protocol.
8. General: The consent form asks for consent to publish "Direct Quotes". I assume this reflects data from audio recording the questionnaire, but it isn't clear. Also, does this mean that some sort of qualitative analyses are being conducted? This has not been described anywhere.

9. On the PIS:
    a. What will happen to me if I take part? The PIS only describes one of the two sessions. A description should be provided for both.
    b. The PIS does not describe the questionnaire; how this is administered and the nature of the questions. Some of the questions ask about sensitive medical information, e.g., mental health diagnoses, smoking, alcohol, and drug use. The participant should be aware in advance that they will be asked about these and for what purpose.
    c. It is not made clear that audio recordings will take place. This should be stated alongside a rationale.
    d. What are the possible risks and burdens of taking part? An adverse reaction to the drops is implied in two cases, but the potential consequences of such a reaction is not articulated in either case. If there are no longer-term consequences to such a reaction, it would be helpful for the participant to know.
    e. General comments 1)If having a control group, as is outlined in the protocol, the wording in this PIS does not address their role in this research 2)A chaperone was mentioned as possible in the protocol; this should be outlined in the PIS given that the participants may have additional support needs 3)Is it possible to provide the PIS as a Word Document as this has greater accessibility options, which may support people with visual difficulties?
10. The consent form states that confidentiality may need to be breached if a concern is raised, but it's not clear from the submitted documentation how this will be done. If collecting GP information, this should be noted somewhere in the protocol, and the wording on the consent form clear that this is what is meant.
11. The risk assessment has been conducted and appropriate levels applied. The only element which is unclear to me as a non-specialist in the field is whether prior recent exposure needs to be determined.

Action.
Please address the reviewers' comments. In addition:

Comments from the Chair
Please address the following:

1. Please ensure the correct Aston University logo is on all documents (they currently have the old orange logo).

2. Please remove REC/IRAS ID reference in the footer of documents as this is not applicable to this study.

3. The PIS says personal data will be used to arrange study visits or collect data by phone. Is this relevant to your study? If not, please delete.

4. It would be useful to include your exclusion criteria on the PIS

5. Please state Aston University College of Health and Life Sciences Ethics Committee as the committee that has reviewed your application, not Aston University Research Ethics Committee.

6. The Transparency statement is out-of-date. A new one has been available since last year. Please use this one.

7. Please provide a study advert.

Once you have considered these comments please amend your proposal according to the instructions at the start of this letter. Please also include a Response to Reviewers document that refers to the original application number, and explains how you have addressed the reviewers' concerns. It will also facilitate checking of the resubmission if all changes to the amended documents are clearly highlighted. If you have any problems, please contact Tim Batty, Administrator for the HLS REC, or myself.

Yours sincerely,

Dr Rebecca Knibb
Chair, HLS Ethics Committee

Appendix 9: Diagnostic Investigation Study – Ethical Approval

Aston University
Birmingham

Aston Triangle
Birmingham B4 7ET
United Kingdom
Tel +44 (0)121 204 3000

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Memo

Health and Life Sciences Ethics Committee's Decision Letter

To : **Prof James Wolffsohn; Malcolm Maciver**

Cc: Tim Batty
Administrator, Health and Life Sciences Ethics Committee

From: Dr Rebecca Knibb
Chair, Health and Life Sciences Ethics Committee

Date 12/5/22

Subject: **Project #HLS21005** A study to investigate the best tests to evaluate the sight of someone who has had a stroke

---

Thank you for your submission. The additional information for the above proposal has been considered by the Chair of the HLS Ethics Committee.

Please see below for details of the decision and the approved documents.

Reviewer's recommendation: Favourable opinion
Please see the tabled list below of approved documents:

Documentation	Version/s	Date	Approved
Response to reviewers' comments	1	March 2022	✓
Ethics application	2	March 2022	✓
PIS	2	March 2022	✓
Consent form	2	March 2022	✓
Questionnaire	2	March 2022	✓
Risk assessment	1	10/1/21	✓
Poster	1	March 2022	✓

After starting your research please notify the HLS Research Ethics Committee of any of the following:

Substantial amendments. Any amendment should be sent as a Word document, with the amendment highlighted. The amendment request must be accompanied by all amended documents, e.g. protocols, participant information sheets, consent forms etc. Please include a version number and amended date to the file name of any amended documentation (e.g. "Ethics Application #100 Protocol v2 amended 17/02/12.doc").

New Investigators

The end of the study

Please email all notifications and reports to hls_ethics@aston.ac.uk and quote the original project reference number with all correspondence.
Ethics documents can be downloaded from: http://www.ethics.aston.ac.uk/documents-all.
Statement of Compliance
The Committee is constituted in accordance with the Government Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK. In accord with University Regulation REG/11/203(2), this application was considered to have low potential risk and was reviewed by three appropriately qualified members, including the Chair of the Life and Health Sciences Ethics Committee.
Yours sincerely,

Dr Rebecca Knibb
Chair, HLS Ethics Committee

Appendix 10: Diagnostic Investigation Study - Participant Information Sheet

Aston University
BIRMINGHAM UK

A study to identify the best tests to evaluate the sight of someone who has had a stroke.

Participant Information Sheet

Invitation

We would like to invite you to take part in a research study.

Before you decide if you would like to participate, take time to read the following information carefully and, if you wish, discuss it with others such as your family, friends or colleagues.

Please ask a member of the research team, whose contact details can be found at the end of this information sheet, if there is anything that is not clear or if you would like more information before you make your decision.

What is the purpose of the study?

This study is designed to assess a newly developed ophthalmic diagnostic testing routine (test battery) for potential use to examine the eyes and visual system of people with a history of stroke. The results of this test battery will be compared against the results of a more comprehensive set of tests to identify how accurate the new test battery is. It will also be tested on a group of people of similar ages who have not had a stroke (control group).

Why have I been chosen?

You are being invited to take part in this study because you have a medical history of stroke or you are of a similar age to a person who has had a stroke.

Unfortunately you will not be able to take part if you have:

- Had a transient ischaemic attack (TIA – mini-stroke), without a full stroke.
- Another neurological impairment unrelated to stroke.
- Unable to provide consent to participate.

What will happen to me if I take part?

The study consists of two visits; at the first visit you will attend and be issued with a formal consent form to participate in the study. If you would like you can have someone come to the visits with you.

If you choose to proceed a normal, routine sight test will be conducted at both visits, but for one visit (you will be informed at which in advance) you will be issued a comprehensive medical history questionnaire for completion and more time will be spent understanding the visual experiences and impact of the stoke and three drops will be used:

(i) one to dilate (increase the size of) the pupil in order to gain a better view of the inner eye
(ii) one to temporarily numb (anaesthetic) the eye in order to assess the eye pressure (not using the puff of air test)
(iii) one to assess your tear fluid, this also aids in the reading of eye pressure.

During this visit a series of additional scans & photographs will be taken, these are routinely used in ‘enhanced’ eye testing, and further ocular investigations. In order to ensure accuracy, the discussion of visual experiences & impact of the stroke will be audio recorded.

Do I have to take part?

No. It is up to you to decide whether or not you wish to take part. If you do decide to participate, you will be asked to sign and date a consent form. You would still be free to withdraw from the study at any time without giving a reason.

Will my taking part in this study be kept confidential?

Yes. A code will be attached to all the data you provide to maintain confidentiality. Your personal data (name and contact details) will only be used if the researchers need to contact you to arrange study visits. Analysis of your data will be undertaken using coded data.

The data we collect will be stored in a secure document store (paper records) or electronically on a secure encrypted mobile device, password protected computer server or secure cloud storage device.

To ensure the quality of the research, Aston University may need to access your data to check that the data has been recorded accurately. If this is required, your personal data will be treated as confidential by the individuals accessing your data.

In the unlikely event of an ophthalmic issue is identified that requires medical attention, you will be informed of this at the end of the visit where this is identified. A discussion will be had about the best ways of treatment for this and, with your agreement a referral to an appropriate medical practitioner for this can be made. This will require us to share your confidential data and clinical measurements as part of the referral.

What are the possible benefits of taking part?

The study is designed to assess the efficacy of a testing approach that could improve accessibility to primary eye care services for people with a history of stroke.

What are the possible risks and burdens of taking part?

All testing conducted are undertaken in the course of primary eye care practice and have low risk of harm. The greatest burden is likely to be fatigue after the completion of visits (particularly the second visit) secondary to the prolonged concentration during the assessments.
One eye drops used in the study is used to make the pupils larger than normal allowing the investigator to view the inside of the eye more easily. When applied to the eye, they may sting for a few moments. The drops take about 15 to 30 minutes to work and around 6 hours to wear off, off (in some cases up to 24 hours.) The resultant large pupils will make you more sensitive to light, whilst distant and near objects may appear slightly blurred. Consequently,

you shouldn't perform any activities such as driving and/ or cycling for at least 12 hours after the drops have been instilled. On a bright day, sunglasses may be advisable. It is very unlikely, but should you experience any unusual symptoms such as severe pain and/ or blood shot around the eye and cloudy vision during this period please contact one of the investigators whose details are listed below and/ or your optometrist/ GP as you may be experiencing an adverse reaction to the drops.

A moistened strip will be used in the study as a staining agents to aid external examination of your eye. When applied to the eye, they may sting for a few moments. Due to their colouring (orange/ yellow) they may cause the vision to take on a coloured appearance, but this will not last long. As soft contact lenses can absorb the dye, you are advised to refrain from wearing your lenses for at least 15 minutes. Sometimes, the eyelids and the skin around the eyes will be coloured by the stain, but this can be removed with cold water.

Another eye drop used in the study is a mild local anaesthetic used to numb the surface of your eye, which will enable the investigator to measure your eye (intraocular) pressure using a contact technique. The drops take about 60 seconds to work and around 25 minutes to wear off. You should not wear contact lenses for two hours. You should avoid situations where you might get dust or grit into your eye as you will not be able to feel any discomfort straight away. It is very unlikely, but should you experience any unusual symptoms such as pain, soreness or blurred vision during this period please contact one of the investigators whose details are listed below and/ or your optometrist/ GP as you may be experiencing an adverse reaction to the drops.

What will happen to the results of the study?

The results of this study may be published in scientific journals and/or presented at conferences. If the results of the study are published, your identity will remain confidential.

A lay summary of the results of the study will be available for participants when the study has been completed and the researchers will ask if you would like to receive a copy.

Expenses and payments

This is an unfunded study, no expenses are available.

Who is funding the research?

The study is unfunded and is being conducted as part of a PhD study.

Who is organising this study and acting as data controller for the study?

Aston University is organising this study and acting as data controller for the study. You can find out more about how we use your information in Appendix A.

Who has reviewed the study?

This study was given a favorable ethical opinion by Aston University College of Health and Life Sciences Ethics Committee (HLS21005).

What if I have a concern about my participation in the study?

If you have any concerns about your participation in this study, please speak to the research team and they will do their best to answer your questions. Contact details can be found at the end of this information sheet.

If the research team are unable to address your concerns or you wish to make a complaint about how the study is being conducted you should contact the Aston University Research Integrity Office at research_governance@aston.ac.uk or telephone 0121 204 3000.

Research Team

Mr Malcolm Maciver,	07414 552 192	[ID no. removed]@aston.ac.uk
Prof James Wolffsohn,	0121 204 4140	j.s.w.wolffsohn@aston.ac.uk
Dr Nicola Logan,	0121 204 4128	n.s.logan@aston.ac.uk

Thank you for taking time to read this information sheet. If you have any questions regarding the study please don't hesitate to ask one of the research team.

Aston University takes its obligations under data and privacy law seriously and complies with the Data Protection Act 2018 ("DPA") and the General Data Protection Regulation (EU) 2016/679 as retained in UK law by the Data Protection, Privacy and Electronic Communications (Amendments etc) (EU Exit) Regulations 2019 ("the UK GDPR").
Aston University is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study. Aston University will process your personal data in order to register you as a participant and to manage your participation in the study. It will process your personal data on the grounds that it is necessary for the performance of a task carried out in the public interest (GDPR Article 6(1)(e). Aston University may process special categories of data about you which includes details about your health. Aston University will process this data on the grounds that it is necessary for statistical or research purposes (GDPR Article 9(2)(j)). Aston University will keep identifiable information about you for 6 years after the study has finished.
Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.
You can find out more about how we use your information at https://www.aston.ac.uk/about/statutes-ordinances-regulations/publication-scheme/policies-regulations/data-protection or by contacting our Data Protection Officer at dp_officer@aston.ac.uk.
If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Appendix 11: Diagnostic Investigation Study – Participant Questionnaire

Aston University
BIRMINGHAM UK

Vision & Visual Health Questionnaire

Participant Identifier:

This questionnaire is being used as part of a study to investigate the best tests to evaluate the sight of someone who has had a stroke. All information collected below will be used for the purpose of this trial and will remain confidential.
The data collected will not be published in any format, and will be anonymised and securely stored electronically in accordance with Aston University College of Health and Life Sciences Ethics Committee guidance.

Your vision right now

How would you describe the quality of your vision at the moment?

Do you ever experience any of the following?

Fluctuating vision?	Yes / No	Details:............................
Difficulty maintaining focus?	Yes / No	Details:............................
Difficulty changing focus?	Yes / No	Details:............................
Visual difficulty when reading?	Yes / No	Details:............................
Trouble comprehending what you're reading?	Yes / No	Details:............................
Trouble using computers/VDUs?	Yes / No	Details:...........................
Eye strain?	Yes / No	Details:............................
Headaches?	Yes / No	Details:............................
Double vision?	Yes / No	Details:...........................
Flashes of light in your vision?	Yes / No	Details:............................
Shadows in your vision?	Yes / No	Details:............................
Dizziness?	Yes / No	Details:............................
Difficulty in coordination?	Yes / No	Details:............................
Walk / bump into things?	Yes / No	Details:............................
Sensitivity to motion?	Yes / No	Details:............................
Balance issues?	Yes / No	Details:............................
Sensitive to bright light?	Yes / No	Details:............................
Sensitivity to glare?	Yes / No	Details:............................
Pattern related discomfort?	Yes / No	Details:............................
Reduction in peripheral vision?	Yes / No	Details:............................
Leave food on plate when eating?	Yes / No	Details:............................
People's faces appear distorted?	Yes / No	Details:............................
Visual hallucinations?	Yes / No	Details:............................

Your General Health

How would you describe your general health?

Have you been diagnosed with any medical conditions? If so, what are they?

Do you suffer from:

High blood pressure?	Yes / No	Details:............................
High cholesterol?	Yes / No	Details:............................
Diabetes?	Yes / No	Details:............................

Have you been diagnosed with any mental health condition? If so, what?

Do you take any medication? If so, what have you been prescribed?

Do you take any non-prescription drugs? If so, what?

Do you smoke? If so, how much?

Do you drink alcohol? If so how much do you drink in a week?

Your eye health

Do you attend routine appointments with a community optician/optometrist?

Have you ever been diagnosed with any eye conditions? If so what?

Do you use spectacles / contact lenses? If so, what type are they?

Do you take eye drops / medication for your eyes? If so what?

Have you ever had an injury or surgery to the eyes? If so, what happened?

Have you ever been prescribed exercises or patching for your eyes?

Have you experienced any of the following:

Pain when moving your eyes?	Yes / No	Details:............................
Dry gritty eyes?	Yes / No	Details:............................
Itchy eyes?	Yes / No	Details:............................
Eye pain?	Yes / No	Details:............................
Watery eyes?	Yes / No	Details:............................
Flashes of light in your vision?	Yes / No	Details:............................
Changes in colours?	Yes / No	Details:............................
Distortion in vision?	Yes / No	Details:............................

Do you feel that your optician/optometrist has met your visual needs?

Your Neurological episode / brain injury / stroke

What date did the episode (or first episode if multiple) first occur (if known)?

If known, what part of your brain was affected?

What general symptoms were experienced when the episode first occurred?

What general symptoms are still experienced?

What visual symptoms were experienced when the episode first occurred?

What visual symptoms are still experienced?

What emotional symptoms have you experienced since the episode?

What rehabilitation are you receiving, if any?

Are you still under the care of a hospital for this episode?

Your Lifestyle

What is/was your occupation?

What do you like to do in your spare time?

Are you able to do this without visual impediment?

Do you read for pleasure?

When reading are you able to maintain good comprehension?

Do you use a computer/tablet/mobile phone?

Do you ever experience loss of concentration?

Do you drive?

Have you ever been advised not to drive by a medical professional?

How is your mobility?

Are you able to undertake tasks without a carer?

How would you describe your hand-eye coordination?

Appendix 12: Diagnostic Investigation Study – Consent Form

Aston University
BIRMINGHAM UK

A study to investigate the best tests to evaluate the sight of someone who has had a stroke.

Consent Form

Name of Chief Investigator: Malcolm Maciver

Please initial boxes

1.	I confirm that I have read and understand the Participant Information Sheet (V2, March 2022) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my legal rights being affected.	
3.	I agree to my personal data and data relating to me collected during the study being processed as described in the Participant Information Sheet.	
4.	I understand that if during the study I tell the research team something that causes them to have concerns in relation to my ocular health and/or welfare they may need to breach my confidentiality in order to arrange referral to another health professional.	
5.	I agree to my clinical examination being audio recorded and anonymised direct quotes from me being used in publications resulting from the study.	
6.	I agree to my personal data being processed for the purposes of inviting me to participate in future research projects. I understand that I may opt out of receiving these invitations at any time.	
7.	I agree to take part in this study.	

Name of participant	Date	Signature
Name of Person receiving consent.	Date	Signature