The effect of age on binocular functions as measured by stereoacuity, fusion, ocular movements, and ocular alignment

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May 2021

Thesis Summary Aston University

Title of thesis: The effect of age on binocular functions as measured by stereoacuity, motor fusion, ocular movements, and ocular alignment

Geraldine Roseann McBride Doctorate of Ophthalmic Science 2021

Aims: To examine how binocular functions change with increasing age as measured by stereoacuity, motor fusion, ocular movements, near point of convergence (NPC), and ocular alignment.

Methods: A preliminary questionnaire survey to establish the professionals' views on whether age affects distance stereoacuity, fusion and NPC; and what the expected value of stereoacuity was for two age groups using Titmus, TNO and Frisby stereotests. A prospective single-centre cohort study was performed on 77 normal participants aged 10 - 79 years measuring ocular alignment, ocular motility, NPC, motor fusion, and stereoacuity (with Titmus, TNO, Frisby, and Frisby-Davies distance stereotests).

Results: The preliminary study results confirmed there was a gap in knowledge regarding any association between age and fusion, and between age and stereoacuity. From the cohort study, all stereotests showed a statistically significant decline in stereoacuity with increasing age ($p < 0.05$). As age increases NPC declines, this was a statistically significant change ($p < 0.05$); one year increase in age yielded a 0.032 cm decline in NPC. Age-related changes in positive distance fusion were found- as age increases distance positive fusion declines, which was a statistically significant change ($p < 0.05$). Age-related changes in positive near fusion, negative near fusion, negative distance fusion, vertical near fusion, vertical distance fusion, ocular alignment, and ocular motility were not found.

Conclusions: Overall, stereoacuity was affected by age, but this study challenges the view that other aspects of a binocular vision examination are affected by increasing age. The normative data will provide a baseline from which to compare outcomes in clinical situations.

Key words: Age, binocular functions, stereoacuity, fusion.

Dedication

This thesis is dedicated to my parents Ann and Gerry, who I love dearly and appreciate more than I say. To Kirk, who is my 'bumper', and our children.

Acknowledgements

I would like to acknowledge everyone who played a role in my academic accomplishments. Firstly, my family, who supported me with love and understanding, without you I would never have reached my current level of success. Secondly, to Professor Leon Davies and Dr Flors Vineula-Navarro, my supervisors from Aston University who provided advice and guidance throughout the research process; and to Dr Richard Armstrong for his advice and statistical guidance. Thank you to Ms. Deirdre Townley and Miss Orna O Halloran, my colleagues from University Hospital Galway, for their unwavering support. Thank you to Dr Jill Carlton and Dr Kirk Stephenson for reviewing the final thesis.

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List of Abbreviations

AAO	American Academy of Ophthalmology
BA	Black African
BIOS	British and Irish Orthoptic Society
BL	Bailey Lovie
BSV	Binocular single vision
CORU	Health and Social Care Professionals Council Ireland
D	Dioptres
DMFC	Dorsomedial frontal cortex
DC	Dioptres cylinder
DS	Dioptres sphere
EOM	Extraocular muscle
FD2	Frisby Davies 2 stereotest
FEF	Frontal eye field
GOC	General Optical Council
IBM	International Business Machines
IQR	Interquartile range
LE	Left eye
MRI	Magnetic resonance imaging
MT	Middle temporal visual area
NHS	National health service
NPC	Near point of convergence
PIL	Participant information leaflet
RAF	Royal Air Force
RCOphth	Royal College of Ophthalmologists
RE	Right eye
SE	Spherical equivalent
SPSS	Statistical Package for the Social Sciences

List of Abbreviations

TNO	Toegepast Natuurwetenschappelijk Onderzoek stereotest
UHG	University Hospital Galway
VA	Visual acuity
V1	Primary visual cortex
V2	Secondary visual cortex
V3	Visual area 3
V4	Visual area 4
V5	Visual area 5 (also known middle temporal visual area)
WI	White Irish

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Chapter 1:

Introduction, Background, and Purpose of Research

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1.1 Introduction

Binocular functions are the output of the collaborative effort of extraocular muscle (EOM) anatomy and cortical activity. Dysfunction of one or both of these components will result in disrupted conjugate function of the two eyes and thus interfere with normal binocular functions. It has been proposed that up to 10% of patients attending a primary care optometric appointment have symptoms of binocular vision dysfunction (4). The binocular functions are measurable by clinicians using a range of commercially available tests and techniques. Standard guidelines for the measurement and documentation do not exist for particular age cohorts, and the effect of increasing age on binocular functions is ambiguous, both subjects will be addressed in this thesis.

Before discussing binocular functions, it is essential to have a clear understanding of the anatomy and physiology of the EOMs, and relevant central nervous system components, and their actions. There is a complex sensory and motor system of structure and control (i.e. sensory, muscular, neuromuscular junction, motor neuron, inter-neuron and cortical processing) required to achieve the coordinated effort of stereopsis. By dividing this process into its constituent parts, one can more readily comprehend the normal situation and the means by which dysfunction in one or more part(s) of the system may interrupt stereopsis. Following this, the Royal College of Ophthalmologists (RCOphth) (5) recommended clinical tests of stereopsis are discussed, along with the current evidence base for their use. Unclarified areas are then identified and the rationale for this research project laid out to clarify and extend the current knowledge of this area. The aim is to identify the best choice of clinical stereotests for a given age group by means of statistical analysis of comprehensive examination results.

1.2 Extraocular muscles

1.2.1 Anatomy and physiology of EOMS

EOMs are highly specialised and unique skeletal muscles, but gene profiling studies have shown that EOMs are distinct from other skeletal muscles with their own specific allotype (6-9). A gene expression study has shown that even the orbital and global layers of the EOMs have different and unique genetic profiles (10). Skeletal muscle

found elsewhere in the body is developed from mesodermal somites whereas the EOMs develop from prechordal and paraxial head mesoderm (9, 11, 12).

The EOMs and their tendons are composed of parallel fibre bundles having few transverse interconnections (13). There are approximately 20,000 muscles fibres in each recti muscle and 5,000 in each oblique muscle (13, 14). It has been suggested that there are more fibres than each EOM actually requires, supporting the idea that each EOM has multiple functions (13). EOM fibres are separated into a global layer (facing towards the eye) and an orbital layer (facing the bony orbit), with a marginal zone between the layers (12, 15). The global layer contains large muscle fibres and the orbital layer smaller muscle fibres (15). It is believed that the global layer fibres insert into the sclera whilst the orbital layer fibres insert into orbital fascia (10). The horizontal recti further divide into superior and inferior sections (16). Compartmentalisation of fibre bundles may allow different forces to be transmitted to different scleral points via the action of the EOM (13).

Skeletal muscle contains only singly-innervated fibres, whereas EOMs are comprised of singly-innervated fibres and multiply-innervated fibres (15, 17). Both the global and orbital layers of EOMs contain approximately 80% singly-innervated fibres and 20% multiply-innervated fibres (15). The multiply-innervated fibres emerge post-natally and have been shown to develop in the absence of any extrinsic eye movement cues (17). The multiply-innervated fibres produce graded contractions that allow small slow eye movements (18). The singly-innervated fibres are the last of the EOM fibres to mature and do so during the establishment of binocular single vision (BSV) (19). The EOM singly-innervated fibres are unique due to their high mitochondrial content and intense oxidative metabolism; which is proposed to assist in muscle fatigue resistance (6, 19). Approximately 80% of the singly-innervated fibres in the orbital layer of each EOM are fast-twitch generating fibres (19). Fast-twitch fibres use glycolytic metabolism and are specialised for phasic activity, for example, rapid and short activity, whereas the slow-twitch fibres are rich in myoglobin and oxidative enzymes and specialize in slow continuous activity (20). The significance of this division of fibre types facilitates the different eye movement systems (i.e. saccades and smooth pursuits) which will be discussed later in this chapter.

The density of capillaries in the EOMs are five times higher than in somatic skeletal muscle (8). The arterial blood flow to EOMs is greater than in skeletal muscle and appears steady regardless of gaze position (21). There are changes in overall muscle volume during EOM contraction which may be as a result of the increased blood flow to

the EOM, as seen in the larger skeletal muscles (21). Muscle volume changes are greatest for the superior recti, then the medial and inferior recti, and least for the lateral recti (21). Muscle volume then decreases to normal levels on relaxation (21).

Evidence suggests that EOMs have different metabolic profiles/activities than other skeletal muscles (6, 22). This evidence supports the discrepancy in susceptibilities to different pathologies. For example, Duchenne muscular dystrophy spares EOMs while myasthenia gravis has a predilection for EOMs, often presenting with diplopia from a breakdown of binocular functions (8). The glycogen content is reduced and the regulators and inhibitors for glycogen breakdown are downgraded in EOMs (8, 18). It is suggested that unlike other skeletal muscles (for example, limb muscles), EOMs are unlikely to store glycogen as an energy source (6). Evidence supporting the use of an alternative energy metabolism comes from the finding of creatine kinase and adensine monophosphate deaminase-1 in the EOMs (8). Additional support for the theory of oxidative metabolism, i.e. the metabolism of glucose using oxygen via the mitochondrial respiratory chain rather than glycogen pathways, comes from the differential expression of nuclear genes encoding mitochondrial proteins (8, 22). EOMs have the highest mitochondrial content of any skeletal muscle, enabling the EOMs to function continuously (9, 23). Unlike limb skeletal muscle the EOM fibroblasts are uniform in size and shape with a large nucleus and large volume of cytoplasm (24). It has been suggested that these fibre size and subsequent differences in contractile mechanics may contribute to the metabolic demands of EOM muscle fibres (24). It has also been suggested that the EOM singly-innervated fibres may have a capacity for anaerobic metabolism as they have been shown to have a higher lipid content (6, 17). The relevance of these alternate energy pathways are that EOMs do not easily become fatigued under normal circumstances, in stark contrast to skeletal muscles, which rely primarily on the aerobic metabolism of glucose.

1.2.2 Positioning of EOMs relative to the eye

The positioning of the EOMs has implications for the eye coordination and fine motor control required to maintain binocularity. The recti muscles originate from a fibrous ring in the orbital apex, called the annulus of Zinn (10, 25). The annulus of Zinn is attached to the greater and lesser wing of the sphenoid bone. The superior oblique origin is the sphenoid bone at the orbital apex, medial to the optic canal; however, the effective origin is the trochlea, a cartilaginous anchor point and pulley in the anterior

superonasal orbit (see Figure 1.1) (25). The inferior oblique originates from the periorbita of the inferonasal orbital rim adjacent to the anterior lacrimal crest (25).

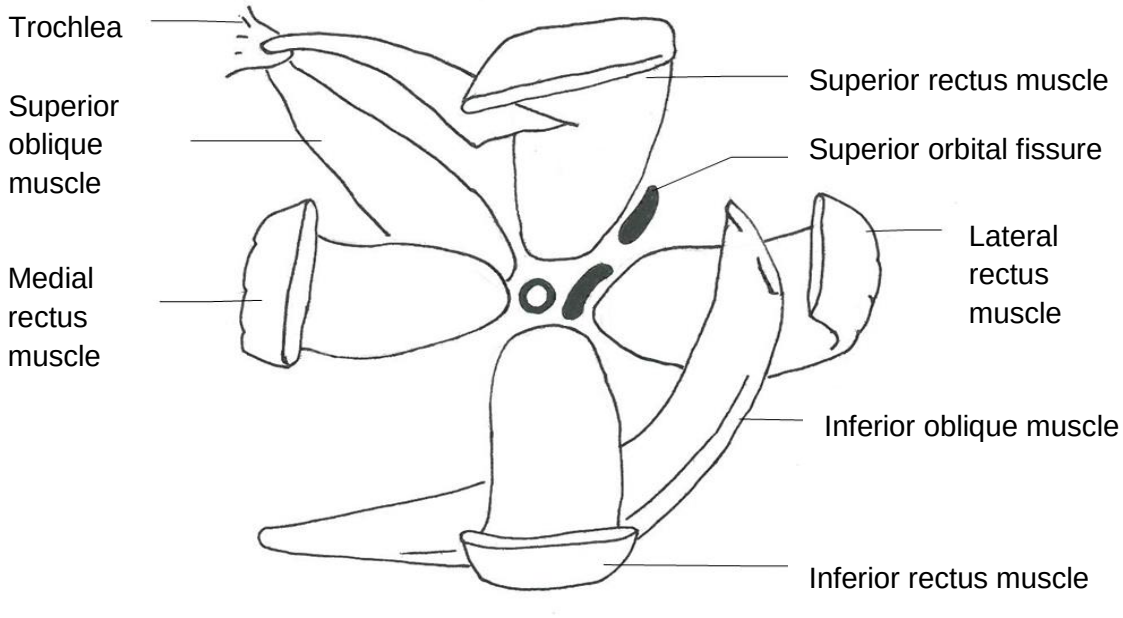

Figure 1.1 EOM positions in the orbit. This figure shows an *en face* coronal view of the structures of the left orbit relevant to EOMs with the globe removed. The annulus of Zinn (not shown) is the common tendinous origin of all four rectus muscles (medial, superior, lateral and inferior) and the superior oblique. The inferior oblique origin is on the anterior medial orbital (maxillary bone). The course and insertions of the muscles are shown relative to the globe (globe not shown).

EOM pulleys

The EOMs do not follow a straight line from their origins to their insertions, but rather have inflections. These inflections are referred to as the "pulleys of Miller". The pulleys change the path of the EOM and, therefore, the vector, during a duction movement (25). It is proposed that the active pulley system provides adjustment in the EOM vector forces in different positions of gaze; this is required as not every eye movement is initiated from primary position (6). The pulleys consist of discrete rings of dense collagen encircling the EOM, transitioning into broader collagenous sleeves (25) (see Figure 1.2). These collagen sleeves form slings coursing in a convex manner anteriorly towards the orbital wall and posteriorly towards the orbital centre (25).

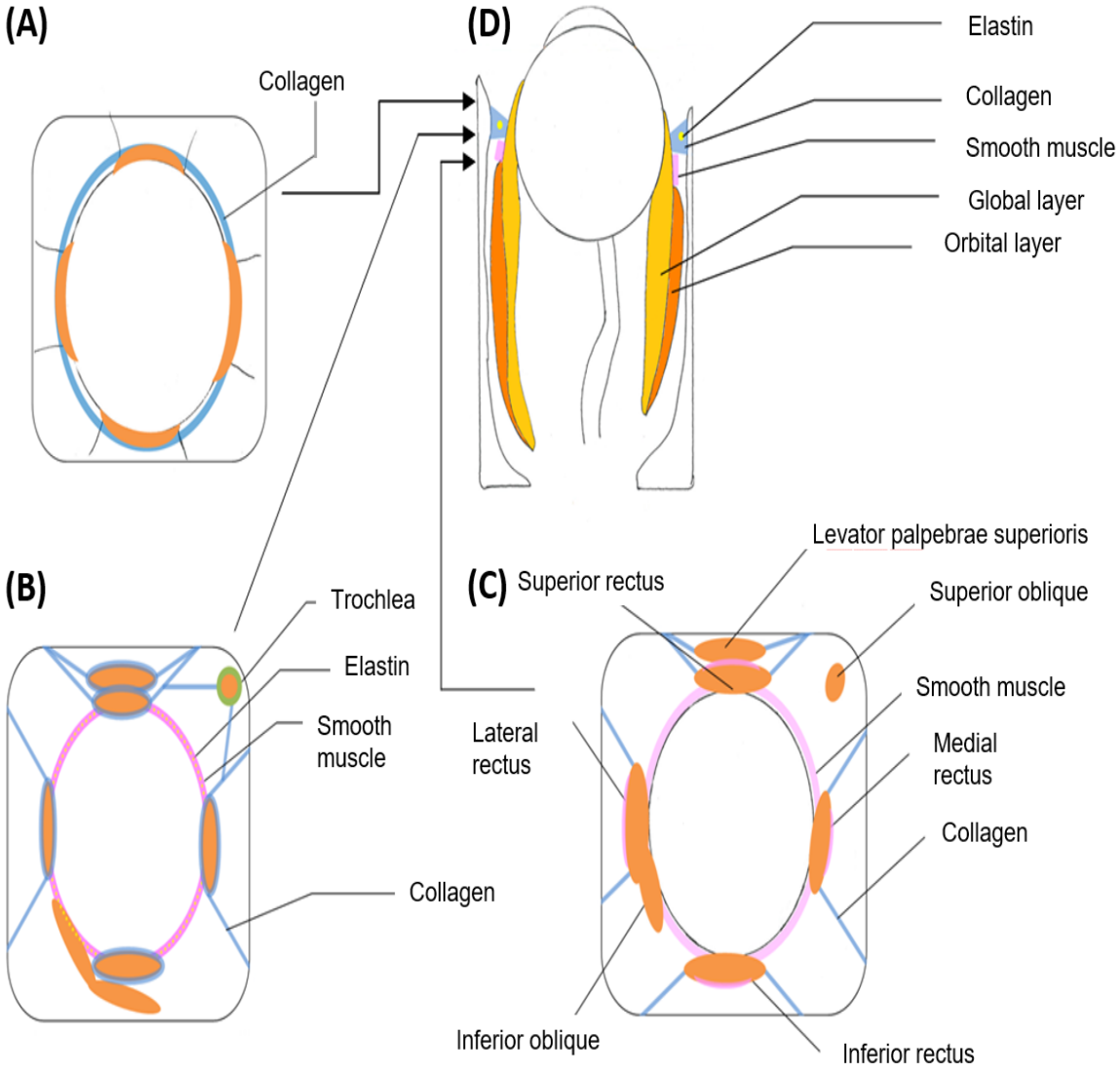

Figure 1.2: Diagram of the EOM pulleys. The components of the orbital pulley system have been divided into (A) the collagen ring/intermuscular septum, (B) the interaction of collagen with smooth muscle and elastin, (C) the incorporation of the recti and oblique muscles within this framework all in a coronal view of the right orbit, and (D) Axial (superior) view of the above orbital pulley components. Collagen is coloured blue, the EOMs and the levator palpebrae superioris are coloured orange, elastic/smooth muscle in pink and the trochlea is in green.

Association between age and EOM pulleys

The horizontal recti pulleys may be displaced as a consequence to orbital connective tissue degeneration with increasing age, initially referred to as “non-myopia heavy eye syndrome” (26), and later as “sagging eye syndrome” (27). It is suggested that this defect in the pulley system could result in disorders of eye movement and/or a strabismus (10). Based on magnetic resonance imaging (MRI) findings of three elderly patients with new onset adult strabismus versus 12 elderly participants without a strabismus, the authors suggested degeneration of the band that connects the lateral and superior recti pulleys was the cause of the strabismus (26). The MRI showed that the lateral recti were displaced inferiorly (26). The authors diagnosed the cause of the diplopia as “non-myopia heavy eye syndrome” (26). In a subsequent publication with 28 patients (mean age of patients 69 years) who presented with acquired diplopia, the authors reported that MRI showed a displacement of the horizontal recti pulleys away from the orbital centre and elongation of the EOM (27). The authors diagnosed the cause of the diplopia as “sagging eye syndrome” (27). More recently the same supervising author, published an audit of 945 patient medical records who presented with binocular diplopia over a three year period to the Stein Eye Institute, in 31% of cases, the cause was identified as sagging eye syndrome (28). The study reported that the mean age of patients diagnosed with sagging eye syndrome was 71 years, and the prevalence increased with each age decade (28). Sagging eye syndrome was more common in females, which was identified as a statistically significant risk factor (28). The authors proposed that waning female sex hormones (progesterone and oestrogen) with increasing age, effects collagen maintenance (28). As the orbital pulley system is comprised of collagen (in addition to elastin and smooth muscle), it was an expected finding that females were more frequently affected than men (28). An audit of 236 elderly Japanese patients medical records who presented with binocular diplopia over a three year period, found 24% of causes related to orbital pulley disorders (29). However, a third of patients did not have an orbital MRI, and therefore the prevalence may have been higher; they did not assess gender as a risk factor in this study (29). In summary the eye has a small, fixed and typically unchanging load for the EOMs pulleys, but the EOM load and pulleys may be altered by disease, trauma, or surgery, as we age, and result in a binocular vision dysfunction (6, 30).

The EOMs are composed of a muscular portion and a tendinous segment, which inserts onto the sclera; each EOM has a differing muscle and tendon length, described here in that order: medial rectus, 40 mm and 4 mm; inferior rectus, 40 mm and 7 mm;

lateral rectus, 40 mm and 8 mm; superior rectus, 40 mm and 6 mm; inferior oblique, 37 mm and 1 mm; superior oblique, 32 mm and 26 mm (31). The distance from the corneoscleral limbus at which the rectus muscle tendons insert is called the spiral of Tillaux, with the medial rectus inserting closest to the limbus at 5.5 mm, followed by inferior recuts at 6.5 mm, lateral rectus at 6.9 mm, and, farthest from the limbus, superior rectus at 7.7 mm (32). The inferior oblique tendon inserts into the sclera between the inferior and lateral recti, while the superior oblique inserts into the posterolateral sclera overlying the posterior pole/macula (33). It is these sites, primarily of the rectus muscles, which are identified and adjusted during strabismus surgery procedures (33).

1.2.3 EOM Innervation and sensory receptors

Cranial nerves

A human has twelve pairs of cranial nerves which control the motor and sensory functions of the head and neck (see Table 1.1) (34). The olfactory and optic nerves arise from the cerebrum (34). The nuclei of remaining cranial nerves arise from the midbrain (oculomotor, trochlear), pons (trigeminal, abducens, facial, vestibulocochlear) and medulla (glossopharyngeal, vagus, accessory, hypoglossal) (34).

Cranial nerve roman numerals	Cranial nerve name	Function
I	Olfactory	Smell (s)
II	Optic	Sight (s)
III	Oculomotor	Eyelid and eye movement (elevation, adduction, depression) (m)
IV	Trochlear	Eye movement (depression, torsion and abduction) (m)
V	Trigeminal	Chewing, face and mouth sensation (s/m)
VI	Abducens	Eye movement (abduction) (m)
VII	Facial	Facial movements, tear and saliva secretion, and taste (s/m)
VIII	Vestibular cochlear	Hearing and balance (s)
IX	Glossopharyngeal	Taste and gag reflex (s/m)
X	Vagus	Taste, stimulate digestive organs and slows heart rate (s/m)
XI	Accessory	Neck and back muscles, controls swallowing (m)
XII	Hypoglossal	Tongue movement (swallowing and speech) (m)

Table 1.1 The cranial nerves and their principal functions (34). The cranial nerves can be identified by their name or by roman numerals. The most applicable to binocular functions are the optic (II), oculomotor (III), trochlear (IV), and abducens (VI) cranial nerves. (s) denotes a sensory nerve, (m) denotes a motor nerve, and (s/m) denotes combined sensory and motor function.

The six EOMs, the iris and the ciliary body are innervated by lower motor neurons of three cranial nerves: the oculomotor nerve (III), trochlear nerve (IV), and abducens nerve (VI) (35). The oculomotor nucleus is located in the midbrain (34); its nerve exits the rostral midbrain near the cerebral peduncle and separates into groups of lower motor neurons which innervate the ipsilateral medial rectus, inferior oblique, inferior rectus, the contralateral superior rectus, and the eyelid levator muscle (35). The oculomotor nerve is the largest of these three cranial nerves and has approximately 15,000 axons supplying the muscle fibres (36). The anterior part of the oculomotor

nucleus contains the Edinger Westphal nucleus which innervates pupil and accommodation responses (37).

The trochlear nucleus is located in the midbrain (34); its nerve exits from the caudal region of the midbrain to innervate the contralateral superior oblique muscle (36). Up to 5% of the motorneurons innervate the ipsilateral superior oblique (36). The trochlear nerve has approximately 2,100 axons supplying the muscle fibres of the superior oblique muscle (36). The trochlear nerve is the smallest of the three cranial nerves (by axon count) involved in eye movements and has the longest intracranial course of all cranial nerves (36).

The abducens nucleus is located in the pons (34); its nerve exits the brainstem from the pontomedullary junction and innervates the ipsilateral lateral rectus (36). The abducens nerve has approximately 3,750 axons supplying the muscle fibres (36).

In order for the eyes to move synchronously, there must be coordination between these three motor neurons. For example, for the eyes to move left, the left abducens nucleus causes contraction of the left lateral rectus (left abduction), while its interneurons stimulate/communicate with the contralateral medial longitudinal fasciculus which activates the oculomotor neurons controlling the right medial rectus (right adduction) (38). For vertical eye movements, messages are transmitted via the tectospinal tract rather than the medial longitudinal fasciculus, connecting the trochlear and oculomotor nuclei (38).

EOM sensory receptors

All skeletal muscles are organised into motor units (meaning one motor neuron innervates a set number of muscle fibres), EOMs have approximately 10 muscle fibres per motorneuron (6, 39). The low muscle fibre to motorneuron ratio allows for recruitment of precise degrees of contraction to control fixation and eye movements (6). Myotendinous nerve terminals were once regarded as the proprioceptors for the EOMs, but now the myotendinous cylinders comprising of fibroblast-like cells are recognised as the only proprioceptive source in the myotendinous region of human EOMs (16). Muscle spindles act as sensory receptors within the belly of a muscle (16).

1.2.4 Actions of EOMs

There are six EOMs per eye which work as antagonist pairs; the vertical EOMs have primary, secondary and tertiary actions and the horizontal EOMs have a primary action only (see Table 1.2). The first antagonist pair is the medial and lateral recti, their only function being horizontal rotation of the eyes. The medial recti are the principal adductors and the lateral recti are the principal abductors for each eye (6, 40). The superior and inferior recti form a vertical antagonist pair, with the primary function to move the eyes up (elevate) or down (depress) respectively. The secondary function of the superior recti is to adduct and intort the eye. The superior rectus will only act as a pure elevator when the eye is abducted by 23^{o}, because of the nature and orientation of its insertion into the sclera (41). The secondary function of the inferior recti is to adduct and extort the eye (6, 40). The superior and inferior obliques are not antagonists. The primary function of the superior oblique is to intort the eye, with secondary functions of depression and abduction (6, 40). The primary function of the inferior oblique is to extort the eye, with secondary function of elevation and abduction (6, 40) (see Table 1.2).

Muscle	Primary Action	Secondary Action	Tertiary Action
Medial Rectus	Adduction	/	/
Lateral Rectus	Abduction	/	/
Superior Rectus	Elevation	Intorsion	Adduction
Inferior Rectus	Depression	Extorsion	Adduction
Superior Oblique	Intorsion	Depression	Abduction
Inferior Oblique	Extorsion	Elevation	Abduction

Table 1.2 The primary, secondary and tertiary actions of each EOM from the primary position.

1.2.5 EOM laws of innervation

There are EOM innervation ‘laws’ which explain how EOMs communicate with their contralateral yoke muscles and ipsilateral antagonists to achieve coordination of binocular gaze. These are:

Hering's law of equal innervation- when a nerve impulse causes an EOM to contract, an equal signal is sent to contralateral synergist EOM (i.e. yoke muscle) to contract (41). Thus Hering's law applies to EOMs in both eyes, for example, the left medial rectus and right lateral rectus both contract to elicit dextroversion (right gaze).

Sherrington's law of reciprocal innervation- when a nerve impulse causes an EOM to contract, an equal signal is sent to its direct ipsilateral antagonist to relax (41). Thus Sherrington's law applies to EOMs of one eye, for example, the right medial rectus contracts while the right lateral rectus relaxes resulting in adduction of the right eye.

For every binocular horizontal eye movement (i.e. version), two muscles are activated and two muscles are inhibited (see Table 1.3). As obliques are not antagonist pairs only three muscles are involved in vertical movements.

Direction of gaze	**EOM RE activated**	**EOM RE inhibited**	**EOM LE activated**	**EOM LE inhibited**
Left	Medial rectus	Lateral rectus	Lateral rectus	Medial rectus
Right	Lateral rectus	Medial rectus	Medial rectus	Lateral rectus
Leavo elevation	Inferior oblique	/	Superior rectus	Inferior rectus
Leavo depression	Superior oblique	/	Inferior rectus	Superior rectus
Dextro elevation	Superior rectus	Inferior rectus	Inferior oblique	/
Dextro depression	Inferior rectus	Superior rectus	Superior oblique	/

Table 1.3 The cardinal positions of gaze and the yoked EOM pairs which facilitate the direction of eye movement. The obliques are not antagonist pairs, so an oblique muscle is not inhibited when another oblique muscle is activated. Right eye (RE) and left eye (LE).

1.3 Eye movement systems

1.3.1 Description of the six eye movement systems

EOMs control both the voluntary and reflexive movements of the eyes (12, 42). There are six eye movement systems: saccades, smooth pursuits, vestibular, optokinetic, vergence and fixation (43).

Voluntary eye movements include smooth pursuit, vergences and saccades. Voluntary eye movements are initiated by a small cortical region in the brain's frontal lobe called the 'eye field' (44). In fact there are two eye fields, the frontal eye field (FEF) which generates eye movements and the dorsomedial frontal cortex (DMFC) (also known as the supplementary eye field) which integrates eye movements with skeletomotor movements (i.e. hand-eye movements) (44). The eye fields are located anterior to the motor cortex on the dorsal surface of the hemisphere, bounded by the precentral sulcus, the superior frontal sulcus and the cingulate cortex (44). The FEF receives its nerve fibres from ventrolaterally located nuclei (44). EOMs can produce slow, smooth, tracking movements of the eyeball (called smooth pursuits), or execute fast movements to fix on a new visual stimulus (called saccades) (8).

Saccades

To achieve normal vision, the EOMs must provide quick foveal localisation of a target (42). Saccades are the fast eye movements which bring new visual information to the foveal region (45). The FEF and posterior parietal cortex will give the instruction to initiate a saccade (46). The initiation signal is then generated from stimulation of either eye field (44). The superior colliculus receives this initiation signal and in turn signals generators in the brainstem (46). The brainstem circuit generators signal the motorneurons of the III, IV or VI cranial nerves to move the eyes (46). The brainstem circuit includes the paramedian pontine reticular formation, the rostral interstitial nucleus of the medial longitudinal fasciculus and the nucleus raphe interpositus (47). Where the brainstem generates commands for saccades, the cerebellar cortex and nuclei support the accuracy of the voluntary eye movements (47). It is reported to take 200 milliseconds for saccade movement to begin after instruction to initiate (40). If during this 200 milliseconds the target moves, then a second instruction to initiate a saccade will be initiated (40). In the FEF, the saccadic eye movements have constant vectors, with ongoing stimulation producing a staircase of equal size saccades (44).

Whereas the DMFC stimulates saccades to move the eye to a specific orbital position following presentation of a visual stimuli (44). Ongoing DMFC stimulation holds the eye in that position (44). During saccadic eye movements, there is a rapid shift in gaze and so visual processing is suppressed (45). The peak velocity of the saccade is 30 - 700 degrees/second and the duration of the movement between 30 - 100 milliseconds (36).

Whilst saccadic eye movements can be demonstrated in toddlers, a study of 93 children aged 7 - 42 months found that the saccades amplitude were shorter when compared to a control cohort of adults (26 adults aged 20 - 31 years), and that the amplitudes demonstrated by the children were variable (48). The authors concluded that as toddlers developmentally improve with increasing cortical functions, there was a corresponding improvement in their saccadic reaction time (48). A study of 72 children aged 6 - 15 years, with five age cohorts, found that, as age increased, that the latency to initiate saccadic eye movements decreased (49). However, there was no statistical difference between children aged 12 - 13 and children aged 14 - 15 years, and so the authors concluded that the saccadic eye movement system was mature from age 12 years (49). The authors linked the maturation in the saccadic eye movement to the maturation of cortical circuits (49).

A study of 90 participants, with 30 participants in each age cohort (cohorts were < 30 years, 30 - 50 years and > 50 years), found that aspects of saccadic eye movements were affected by increasing age (50). The authors found no statistically significant relationship between the duration of the saccade and age (50). However, they found that peak velocity had a statistically significant relationship with age, when the saccade was initiated by a visual stimuli and not when an auditory instruction to commence the saccade (50). The study found that there was a statistically significant increase in the latency of saccade initiation in the eldest cohort, and concluded that this reflected age related degeneration of the central nervous system (50).

Smooth pursuits

Smooth pursuit movements are slower eye movements used to track a moving object (40, 51). Smooth pursuits are designed to keep a moving stimulus on the fovea (40, 51). There is overlap in the neural pathways for saccades and smooth pursuits (47), but a detailed pathway for the smooth pursuit system is not as clearly understood as it is for saccades (35). It has been suggested that the DMFC is involved in smooth

pursuit stimulation based on past stimulus memories (47, 52). The medial temporal and the medial superior temporal areas of the cerebral cortex are critical for guiding the direction of the smooth pursuit (47). The initiation signal when received by the cerebellum sends a message to the vestibular nuclei to generate an activation signal, which is sent to the oculomotor nerves (35). It is reported to take 100 - 160 milliseconds for the smooth pursuit movement to begin after instruction to initiate (51). The eyes will track an object using smooth pursuit providing the object velocity is < 50 degrees/second (36).

Research on smooth pursuit eye movements indicated that it matures later than saccadic eye movements, but again in the 2nd decade of life (53, 54). Whilst a study on 71 infants aged 1 - 18 months found a rapid improvement in smooth pursuit gain in the first six months of life (to near adult levels) (55), a number of studies have shown that the latency of the smooth pursuit system is not mature until adolescence (53, 54). One study of 40 participants (four cohorts of 10 participants), aged 4 - 6 years, 8 - 10 years, 12 - 16 years and 20 - 36 years, who had their smooth pursuit tracked using a video based pupil/cornea tracking system, found that smooth pursuits matured between age 6 - 12 years (53). The authors postulated that the smooth pursuit eye movements matured in co-ordination with maturity of the frontal cortex and maturity of the cortical pathway projections (53). In addition, another study found that whilst average smooth pursuit latency was adult like at 8 - 9 years, there was variability in the measurements until age 15 years (54). In this later study, the experiment consisted of 58 participants aged 5 - 16 years who watched a stimulus on a screen move for 600, 700 and 800 seconds, with each participant undergoing the trial 18 times (54).

It has been suggested that smooth pursuit eye movements are an age dependent eye movement system, and subject to nervous system degeneration with increasing age (56). In their experiment, 10 adults aged 65 - 77 years, with a normal neuro-ophthalmology and mental history and examination, had prolonged latency for initiation when compared to the control cohort (15 adults aged 19 - 32 years) (56). The authors also found that the delayed latency was not dependent on the velocity of the target used (56). This was supported by a later study of 15 adults aged 64 - 81 years with normal vision and without a history of any conditions which affect eye movements; the later study found that whilst full eye movement was achieved, that there was a statistically significant delay in the latency of initiating the movement when the cohort was compared to the control cohort (10 adults aged 19 - 26 years) (57).

Clinically, the latency of the smooth pursuit eye movements is not measured, but rather the extent of the movement is qualitatively assessed whilst the patient follows a slowly moving target (usually a light). This will be discussed further in Chapter 1.3.2.

Vestibular and Optokinetic

There are two gaze stabilising eye movements, the vestibular and the optokinetic systems. Vestibular eye movements compensate for head and body movements to allow for maintained fixations on an object, for example, during head movements (41). The vestibular system detects the head movements and produces corrective eye movements (40). Sensory information from the semi-circular canals in the inner ear, instruct the eyes to move in the opposite direction to the head movement (40). Optokinetic eye movements stabilise fixation on a single object when the visual world is moving (40). Vestibular and optokinetic eye movements are conjugate movements, i.e., both eyes will move in same direction (38). The vestibular and the optokinetic movements are often combined and referred to as the vestibulo-ocular reflex (35). It is reported to take 15 milliseconds for a vestibulo-ocular eye movement to begin after instruction to initiate (58). The vestibular nuclei (cranial nerve VIII) send messages to the oculomotor, trochlear and abducens nuclei via the medial longitudinal fasciculus (38).

Vergence

Vergence movements align the fovea of both eyes with an object at near or distance fixation (40). Unlike the other eye movements described earlier, vergence movements are disconjugate horizontal eye movements, with the two eyes moving in different directions, for example the eyes will converge or diverge (40). During vergence movements the medial and lateral recti motorneurons are reciprocally innervated (35). The stimulus for a vergence movement is retinal blur or retinal disparity, with a reported latency of 160 - 200 milliseconds for retinal blur stimulus and 80 - 160 milliseconds for retinal disparity stimulus, with a maximal velocity of a vergence movement is 20 degrees/second (35, 36, 58). Neurons for vergence movements are found in the mesencephalic reticular formation and transmit generation signals to medial recti nuclei and the abducens nuclei (35). Vergence movements facilitate stereopsis by aligning foveal images for near or distance as appropriate (36).

Fixation eye movements

Fixation eye movements are the micro-movements unseen to the naked eye. They maintain steady fixation through a combination of microsaccades, microtremors, and microdrifts (36). Microsaccades are miniature saccades < 1 degree of visual angle, microtremors are rapid oscillations, and microdrifts are smooth eye movements of slow velocity (59). Fixation movements occur in horizontal, vertical and torsional directions (36). Fixation movements prevent 'slippage' of the target, i.e. the target remains on the fovea despite head or body movements (58). Several cerebral areas may be involved with fixation movements, in particular the parietal lobe (36).

1.3.2 The clinical examination of eye movements

Typically only smooth pursuits and convergence are assessed clinically (the remaining eye movement systems form part of the neuro-ophthalmology examination and were not included in the study, and so their method of assessment is not described) (see Chapter 1.6.2 for the clinical measurement of convergence). Whilst there are no specific guidelines on how to assess and document ocular movements from the major eye care professional bodies (for example, Irish College of Ophthalmologists, College of Optometrists or American Academy of Ophthalmology), there are clinical guidelines available to British and Irish Orthoptic Society (BIOS) members, which recommend a diagrammatic representation of ocular movements (60).

The actions of the EOMs are assessed via movements of the eyes together (i.e. versions), and by movements of the eyes individually (i.e. ductions) (41). Ductions and versions should be assessed in the eight positions of gaze (41) (see Table 1.4). It is reported that some subtle EOM paresis can be seen with a version and not with a duction movement (41). Clinically, the version movements of the eyes are tested binocularly using a spotlight. Without wearing any spectacle correction, the patient follows a spotlight held at 40 cm from primary position into each of the eight cardinal positions of gaze. The corneal reflections are observed to ensure that they remain central and symmetrical in both eyes (61). The head is kept immobile and erect throughout testing. In each cardinal position, an alternating cover test is performed to assess for the presence or change in amplitude of any phoria. The clinician observes the behaviour of the eyes, looking for underactions, overactions, or limitations/restrictions, whether the movement is jerky or smooth, nystagmus, change

in lid or globe position, signs of fatigue, any torsional movements, any discomfort on movement, and/or any abnormal head movements (35).

The direct elevation and depression positions are assessed to confirm the presence or absence of an alphabet pattern strabismus, for example, a V-pattern esotropia (61). Movements can be quantified/graded - 4 to + 4, with -4 indicating maximum limitation or underaction (no movement of the eye past the midline) and +4 indicating maximum overaction (62, 63); zero representing a normal movement, and - 3, - 2 and - 1 corresponding to a 75%, 50% and 25% limitation or underaction, (60). The BIOS recommended method (60), is in line with standard clinical practice of UK and Irish orthoptists.

A study performed on 29 orthoptic students (mean age 20.3 ± 1.7 years) by a UK qualified orthoptist, found that, when using the BIOS recommended method (60), 23/29 participants had some degree of superior rectus underaction in either one or both eyes, with 19 participants having - 1 underaction (64). There was no statistically significant difference between right and left eye underactions (64). The authors concluded that this clinical method of examining ocular movements, discovers clinically normal small degrees of superior rectus weakness (64). Therefore, raising the concern that studies concluding associations between age and limitations of upgaze may have measurement methodology errors.

Dextro-elevation Right superior rectus Left inferior oblique	**Elevation** Right superior rectus Left superior rectus	**Laevo-elevation** Right inferior oblique Left superior rectus
Dextro-version Right lateral rectus Left medial rectus	**Primary position**	**Laevo-version** Right medial rectus Left lateral rectus
Dextro-depression Right inferior rectus Left superior oblique	**Depression** Right inferior rectus Left inferior rectus	**Laevo-depression** Right superior oblique Left inferior rectus

Table 1.4 The eight positions of gaze with the eye muscles that are contracting.

(NB: Direction of eye movement in bold with the muscles involved in the movement named). Diagram is in anatomical position.

1.4 Effect of ageing and disease on EOMs and eye movements

The EOMs are distinct from other skeletal muscle by their response to disease and age. Ageing can be defined as the "process of becoming older" (65). EOMs can either be affected or spared in a range of metabolic, mitochondrial and neuromuscular disorders (8, 11). It has been demonstrated that there is an increase in gene expressions for growth, development and regeneration in EOMs (9), and thereby, ageing may not have the same effect on EOMs as it does on other muscles. Fibroblasts are known to have a critical role in wound healing and tissue repair (24). It is suggested that the unique EOM phenotype produces the distinct properties of EOM fibroblasts (i.e., morphologically distinct to skeletal muscle fibroblasts, as they are uniform in size, with copious cytoplasm, and a large central nucleus) (24). These differences, combined with the altered nuclear gene expression may explain their differential response to disease compared with other skeletal muscles (24).

In skeletal muscle, ageing causes a decrease in muscle power through the loss of muscle mass and a loss of the muscle fibres that generate the force (66). In the quadriceps skeletal muscle the fast-twitch-generating muscle fibres size are reduced with increasing age (66). As mentioned in Chapter 1.2.1, approximately 80% of the singly-innervated fibres in the orbital layer of each EOM are fast-twitch-generating (19), which could suggest that increasing age may affect EOM power and in the context of this study it would reduce the fusional reserves in the older population. However, unlike other skeletal muscles in the body which may not be actively used in an older population, EOMs may be spared as they are in lifelong continual usage throughout every waking hour and during the REM phase of sleep. A study of mice EOM showed that EOMs have a robust growth and renewal capabilities which suggests that age may not effect EOMs like other skeletal muscles (11).

A study of 124 participants aged 23 - 84 years (six cohorts based on age decades, with 20 or 21 participants in each cohort), found that elevation was most affected by increasing age, and depression was least affected (67). The authors reported a decline in EOM function of 0.5 - 1% per year of life in their age profile (67). They proposed that because elevation is the least used eye movement in adult life, that there could be more atrophy of the superior recti, compared with the other EOMs (67); this was supported by their finding that depression was the least affected movement. The authors in this study did not use the BIOS recommended standard clinical method of studying EOM movements, they used a standardized lateral version light reflex measurement, which was then converted into degrees of eye rotation and based on the

assumption that all the eyes in the study has a standard global size (67); a method reported to be affected by standardisation and parallax errors (68). Additionally, the authors measured upgaze in direct elevation only, whilst clinically, elevation is assessed in laevo-elevation and dextro-elevation positions in addition to direct elevation.

Another study found a statistically significant relationship between age and decreasing horizontal eye movements, and a statistically significant relationship between age and decreasing upgaze eye movements (68). The authors reported no statistically significant relationship between age and downgaze eye movements (68). This study undertaken in Korea on 261 subjects aged 5 - 91 years, and for the purposes of analysis participants were divided into two cohorts based on median age (cohort sizes were not provided) (68). Again, the authors did not use a standardised clinical method, but used photographs taken in primary position and in each extreme gaze position; with the aid of imaging software, they overlapped the photographs to establish the amount the eyes had moved (68). For their software-based calculation, a number of assumptions were made to facilitate the software functions, one example, the shape of the eye was a perfect sphere (68); this assumption was made without any calculation or comment of auto-refraction. The authors did not comment on whether any participant had astigmatism, but merely stated that the axial length was between 21 and 26.5 mm for inclusion in the study (68). This method is not easily applicable to standard clinical practice, unlike the BIOS method which requires limited equipment (for example, a pen torch and a Romaine occluder) to replicate.

1.5 Visual cortex

There are six visual cortical areas (V1 to V5, and inferior temporal cortex) within the occipital cortex that are interconnected, visual information is transmitted between these areas to be analysed and interpreted (58, 69) (see Figure 1.3). Visual information is received by the retina (photoreceptor, bipolar and ganglion cells), synapses in the lateral geniculate body and is then processed in the contralateral hemisphere primary visual cortex (V1) (i.e. information seen by the right eye is processed by the left V1) (69). V1 (Brodmann area 17) receives, assimilates and processes visual information (69). V1 is situated in the occipital lobe (69); it is comprised of cell nuclei and myelinated fibres and is thinner than other cortical areas (58). V1 is only excited or inhibited by specific psychophysical stimuli in the visual field, often referred to as the ‘receptive field’ (58). V2 is the secondary visual cortex and it transfers information to

and from V1 to the other visual cortical areas; V3 is visual area 3, it processes motion and colour (V3A and VP are subdivisions of visual area 3); V4 is visual area 4, it processes colour; V5 is visual area 5 (also referred to as middle temporal visual area MT), it processes motion; inferior temporal cortex processes shapes (69, 70).

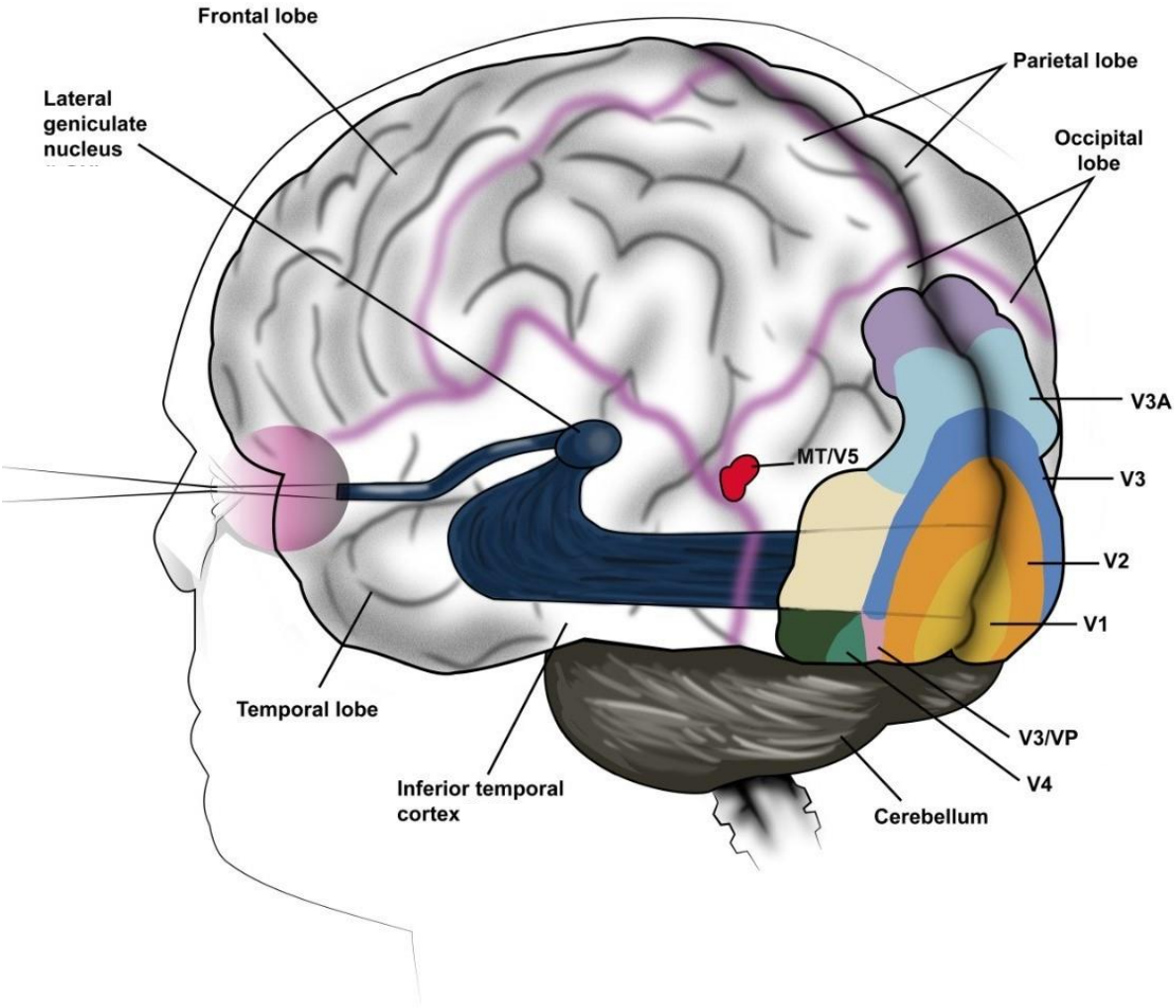

Figure 1.3 The location of the six visual cortical areas (V1, V2, V3, V4, V5, and the inferior temporal cortex) in relation to the cerebral lobes and left eye (69, 70).

The visual information from each eye remains separated until arriving in V1 (71, 72), where monocular and binocular neurons in V1 receive the sensory input (71). It is

proposed that the binocular integration of the visual information in these V1 binocular neurons generates binocular functions (72-74). While in 2021, binocular vision is still being described as an incompletely understood pathway (75), binocular vision research on animals has been performed since the seminal studies of Wiesel and Hubel in the 1950s and 1960s (76, 77). Wiesel and Hubel's collaborative efforts on how the brain processes the visual signals received from the eyes, led to their joint receipt of a Nobel Prize for Physiology or Medicine in 1981 (78).

Wiesel and Hubel's animal studies have shown that binocular integration occurs in V1, and when binocular integration is disrupted, binocular neurons in the visual cortex disappear (79-81). One study on four kittens with a surgically induced exotropia at birth (medial rectus severed), showed that this disruption of binocular integration caused a severe decline in the number of binocular neurons in V1 area 17 (79). After 30 days of an induced strabismus, the number of binocular neurons in the primary visual cortex had dropped to 50%, and to only 10% after 60 days. compared with non-strabismic age-matched controls (79). This experiment suggested that binocular neurons will degenerate or fail to develop if binocular functions are impaired in infancy due to a defective/dysfunctional EOM.

A separate experiment by Hubel and Wiesel assessed the impact on the visual system of occlusion (i.e. sensory deprivation) early in life, including four kittens (kitten A, B, C, D) having their right eye occluded from birth for three months, and one kitten (kitten E) having both eyes occluded from birth (right eye three months, left eye seventeen months) (80). In this experiment, kitten A was dissected age three months and kitten E was dissected age seventeen months. At three months, kitten A (without any recovery period) showed that 27% of binocular neurons were unresponsive to stimuli, 32% were abnormally functioning, and only 41% were functioning normally (80). In contrast, kitten E (binocularly occluded for three months and monocularly occluded for further 14 months), had 10% binocular neurons unresponsive to stimuli, 60% were abnormally functioning, and only 30% functioning normally (80). This experiment demonstrated that the visual cortex needed to receive bilateral visual stimulation for binocular neurons in the brain to develop normally, as the number of normally functioning cells was lower in the kitten with a three month period of binocular occlusion than the kitten with monocular occlusion.

In another experiment with five kittens comparing unilateral and bilateral eye lid closure, the kitten occluded between the age of 30 days and 60 days and then immediately dissected for histological examination, had less than 40% of their binocular

neurons still functioning on day 60 (81). This experiment also found that the level of binocular neurons remained unchanged after 90 days of non-occlusion; indicating no restoration of normal neuron function levels despite returning to binocular viewing (81). Early life / infantile visual stimulation was clearly shown to be significant in the development of binocular functions on a central nervous system level.

Hubel and Wiesel later performed their experiments on Macaque monkeys. Three monkeys had monocular occlusion of different durations and commenced at different ages in their infancy; the impact of the monocular occlusion was more severe when deprivation occurred at a younger age, for example, there was more cell shrinkage in the lateral geniculate body when deprivation was commenced in the second week of life, compared to deprivation from the third week of life (82). Another monkey, aged 2.5 years, had induced monocular occlusion for six months; when the eyelids were unsutured the vision was reported as normal; thus suggesting that occlusion after visual maturation has no impact on vision (82).

In conclusion from these Hubel and Wiesel animal experiments, normally functioning EOMs, normal ocular alignment, and visual input from both eyes are required to develop binocular functions.

1.6 Binocular Functions

1.6.1 The grades of binocular functions

Originally described by Claud Worth in 1903, there are three grades of binocular functions - simultaneous perception, fusion, and stereopsis (83, 84). Simultaneous perception is the ability to concurrently resolve two similar images, one from each eye (62). Sensory fusion is an open loop perceptual phenomenon with cortical processing; it requires small retinal image disparities from each eye which can be blended to perceive a single image (62, 74, 83). Motor fusion is the ability to maintain sensory fusion through a range of vergences: horizontal, vertical and torsional (i.e. cyclovergence) (62, 74). Motor fusion is the mechanism that allows fine tuning of eye position to maintain alignment on a target, for example as a locking mechanism to keep the eyes aligned on a moving target (74). Motor fusion has been described as a closed loop oculomotor reflex requiring larger retinal images disparities (83). Fusion can occur because optic nerve fibres from the nasal retinal cross in the optic chiasm to join the uncrossed temporal retinal nerve fibres from the fellow eye (74). The combined nerve fibres project to the lateral geniculate body and then to the visual cortex (74). Within

the visual cortex, afferent pathways connect these fibres to the binocular neurons (74). It is thought that motor fusion develops from age 3 - 6 months, and can be clinically detected at age 6 - 8 months (62). Research relating to the impact of age on fusion and convergence will be discussed later in this chapter.

The third grade of binocular functions is the ability to perceive stereopsis. Stereoacuity is the measurement of stereopsis and is the smallest threshold disparity that can be discriminated between two adjacent surfaces (1). Stereopsis arises from horizontal retinal image disparity (85); with the disparate retinal images falling within Panum's fusional area (1, 74, 86) (see Figure 1.4). Panum, a Danish physiologist, in the mid-1800s discovered with the use of stereograms that two vertical lines separated by 15 to 25 minutes of arc could be fused to see one vertical line; however when the separation was greater than 25 minutes of arc then three lines were seen (87). From his experiments, Panum suggested that a given retinal point in one eye could correspond to a number of retinal points in the fellow eye (87, 88). Panum called this the "circle of correspondence", now referred to as Panum's fusional area (87). While Panum's fusional area refers to the displacement on the retina, Panum's fusional space refers to the separation possible in actual space (89).

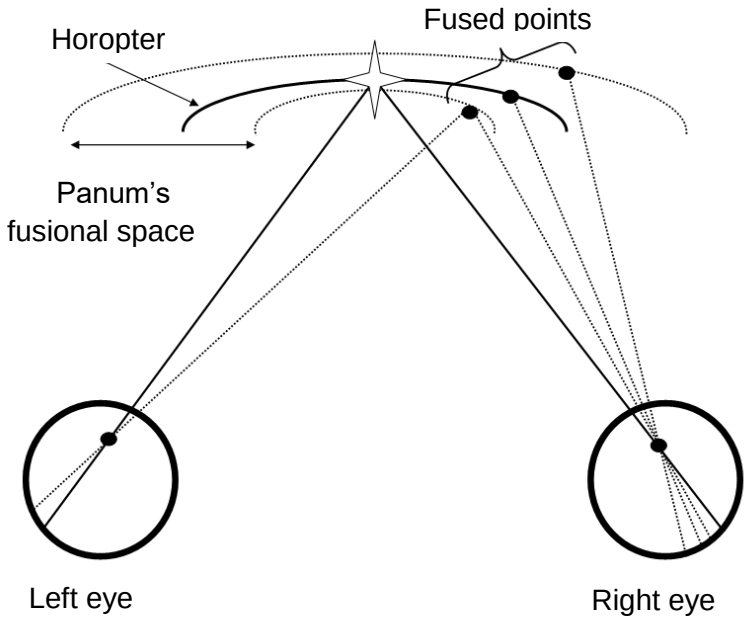

Figure 1.4 Panum's fusional area and Panum's fusional space. The horopter is a curve of points in space that project on corresponding points in the two retinas. The star represents a fused image, which will lead to stereopsis. This figure shows how one retinal point in the left eye could correspond to three retinal points (or a retinal area) in

the right eye, as the three points fall within Panum's fusional area. Points viewed outside Panum's fusional space will not be fused and diplopia will be appreciated (88).

It has been reported that stereopsis develops from age three to six months (1, 86, 90, 91). A study involving 95 infants using a random dot pattern visual evoked potential (VEP), found no stereoacuity at two months of age, 80% of 'normal' levels at four months of age and "adult-like" VEP responses at five to seven months of age (90). The studies that have used commercially available stereotests show variability as to when stereoacuity reaches adult level, but it is reported to occur before age nine years (1, 92-95). It is for this reason that the research participants in this thesis study will be aged 10 years and over. The Mount Sinai study of 120 participants aged 20 - 79 years, found a linear relationship between increasing age and decreasing stereoacuity, with a marked deterioration from age > 60 years and the regression line crossing the demarcating 'abnormal stereoacuity' line at age 65 years (96). The commercially available stereotests used for this research study will be discussed later in this chapter, along with publications investigating the effect of age on stereoacuity as measured by commercially available stereotests.

1.6.2 Convergence

Convergence is a disconjugate eye movement (97). Convergence is driven by several cues including- accommodation, retinal image disparity and target proximity (98), resulting in an eye movement which is the combination of tonic convergence, accommodative convergence, fusional convergence and proximal convergence (99-102). Tonic convergence is brought about from EOM muscle tone, bringing the eyes into a physiologic position of rest (i.e. being parallel at infinity, or 6 metres in clinical practice) (99, 100). Accommodative convergence occurs when accommodation is exerted, being a synkinetic response (99, 100); it is measured when the two eyes are dissociated, thus eliminating some of the other types of convergence (102). Accommodative convergence is reported to only provide gross adjustment in the position of the eyes and does not provide binocular fixation (99). It is fusional convergence that allows for fine adjustment in the position of the eyes to aid binocular fixation (99), and correct any near misalignment (100). Proximal convergence is induced by the awareness of a near object (99, 102).

The NPC is a point in space located directly in front of the person's face in the median plane were there is an intersection of the visual axes (103). Simply, it is the nearest point in which binocular fixation can be maintained.

It has been reported that there is little consensus as to what the most appropriate test target is to use when assessing convergence, or how many times it should be repeated (104, 105). RCOphth "Guidelines for the Management of Strabismus in Childhood" has recommended the measurement of NPC with a RAF rule (106). It is normal practice for UK and Irish based orthoptists to follow guidelines issued by the RCOphth; however, it has been suggested that there is little or no research to validate RAF rule use (107). It has been found that NPC recorded using the RAF rule will be reduced (i.e. further away from the nose) in comparison to a free space target (107).

The measurement of NPC using the RAF rule

The RAF rule (RAF binocular Gauge, Clement Clarke, Essex, UK), consists of a sliding four-sided drum mounted onto a measuring gauge approximately 50 cm long. On one end of the RAF rule is a handle for the clinician to hold the apparatus, on the other end is a 6 cm V-shaped bridge which rests onto the patient/participant's maxilla (cheek) bones. There are four differing images on the drum faces, the dot and line is used when measuring NPC (see Figure 1.5). The RAF rule states that NPC < 10 cm is normal, 10 - 15 cm is reduced and > 15 cm is defective. The author was unable to identify any publications giving the specificity and sensitivity of the RAF rule at detecting a disease/condition (for example, convergence insufficiency).

Figure 1.5 Left: Image of RAF binocular Gauge. Right: Image of the convergence dot and line target (Clement Clarke, Essex, UK).

A study which used the RAF rule on 51 children and young adults noted that the use of the RAF rule created a larger standard deviation, and recommended that NPC should be measured by same method (either free space or RAF rule) between successive eye

examinations (107). The authors proposed that the larger standard deviation was a reflection of their participants being novices at using a RAF rule (107). The authors also commented that proximal accommodation, proximal convergence, and proprioceptive feedback from the RAF being placed on the face may create an impression to the patient/participant that the object is closer than it is, and stimulate a better NPC response (107). The authors also identified a testing error with using the RAF rule, because the RAF rule sits on the face, the 'best' response for NPC is 5 cm, whereas when tested in free space NPC may be a value better than 5 cm (i.e. closer to the nose) (107).

Association between age and convergence

Convergence is reported to develop in conjunction with stereopsis (98). A study of 34 healthy full-term infants using an illuminated toy in a dark room to measure convergence, found that no infant under six weeks of age had full convergence (full convergence was defined as a NPC of less than 12 cm) (98). Although, the authors did not state the age when 100% of the infants had full convergence, they noted that at 11.9 weeks 50% exhibited full convergence and at 18 weeks > 90% had full convergence (98). The study found that the time interval between no convergence and full convergence was less than two weeks (98). The study also noted that the onset of fusion occurred only one week before full convergence, with a highly statistically significant correlation between the presence of fusion and full convergence (98). A study of 59 infants found 50% of the infants had full convergence by 12 weeks of age (98); the authors suggested that retinal disparity may be involved in the development of accurate convergence (98). Another study on 307 newborns, showed that infants from nine weeks of age were demonstrating convergence, with improvements in the accuracy of convergence between age 9 - 16 weeks; the authors believed this was an indication of the infants responding more accurately to retinal disparity cues (108). The same sample of infants showed accommodation from 8 weeks of age, which improved between age 9 - 26 weeks, with the authors commenting that accommodation had a longer period of development in infancy, and its development may be linked to contrast sensitivity rather than retinal disparity (108).

A study of 3628 children aged 4 - 6 years who found the mean NPC was 5.1 cm (109). A study of 217 10-year-old children found the mean NPC using a fixation stick was 6.2 cm (110). A study of 1056 secondary school children, aged 13 - 18 years, using the RAF rule found adult like levels for NPC, with mean NPC 6.88 ± 2.88 cm, with 6.25% (n

= 66) having NPC ≥ 10 cm. A study of 150 participants in their second, third and fourth decade of life (50 participants per cohort), found that the NPC was 7.17 cm, 8.59 cm and 9.52 cm for the respective cohorts (111). A study using RAF rule on 51 participants aged 6 - 30 years, found the mean NPC for 6 - 9 year olds was 9.9 cm, 11 - 13 year olds was 8.6 cm and 20 - 30 year olds was 8.8 cm, there was no statistically significance difference between the cohorts (107). Therefore, these studies would suggest there is a normal range of NPC values in children and young healthy adults of 5 - 10 cm.

A study using the RAF rule compared 14 optometry students (mean age 25.1 years) to 14 older adults (mean age 75.6 years) found the mean break point declined from 5.3 cm to 14.8 cm between the cohorts (104). A study comparing 10 orthoptic students (mean age 20.2 years) to 12 older adults (mean age 72.73 years) also reported a statistically significant decline in NPC with ungrouped age (112); however, the median NPC for both cohorts was still 7 cm (112). However, the authors did note that the weakest NPC values were in the three oldest participants (112).

This is in contrast to the Moorfields study which found no significant change in NPC with age (113). In the Moorfields study 60 participants aged 17 - 83 years in four age cohorts, had no statistically significant relationship between increasing age and NPC (mean NPC was 6 cm across all cohorts) (113). However, their method of testing was not described, so comparability to this thesis is compromised (113). A large population based study performed in Iran on 2433 participants aged 10 - 86 years, found the NPC for the total population was 8.6 ± 4.8 cm, 7 ± 3.9 cm in the youngest cohort (10 - 19 years) an 13.1 ± 5.2 cm in the eldest cohort (≥ 70 years) (114). There was a statistically significant relationship between increasing age and a decline in NPC ($P < 0.001$) (114). A second large population-based cross-sectional study performed in Iran on 1784 participants aged over 60 years (mean age 65.9 ± 4.6 years) was published in 2021 (115). For the total population, the mean NPC was 7.84 cm; there was no statistically significant change in NPC with increasing age ($p = 0.148$) (115). NPC did decline from 7.8 cm in cohort 60 - 64 years, to 8.8 cm in cohort ≥ 80 years, but this was not a statistically significant change (115). As these two large population studies are based on participants with similar ethnic and racial compositions and their method was consistent (single letter fixation target and a ruler to measure NPC), it would suggest that the effect of age on NPC is more notable when the study also includes participants under 60 years.

In conclusion, there are conflicting reports as to whether NPC is associated with age. Whilst the Moorfields study used four age cohorts, this research will use seven age cohorts and aims to identify whether there is an association between age and NPC, and whether this is clinically as well as statistically significant.

1.6.3 Motor Fusion

Fusion is the ability to combine two similar images from corresponding retinal points (sensory fusion) and maintain binocularity through vergence movements (motor fusion) (88, 116). Fusion is a psycho-optical reflex (99) (meaning it is a corrective reflex dependent on visual stimuli, for example, diplopia), its sensory stimulus being disparate retinal images (88). Orthoptists regularly measure the horizontal and vertical fusion range using a synoptophore or with prism bars (see Figure 1.6) (86, 117), and less frequently with loose prisms; these measurement methods form part of the British undergraduate orthoptic course skills framework (118). Other machines/methods not commonly used by orthoptists include a phoropter, aligning prism within a Mallet unit and a rotary prism (116, 119). A prism bar allows for a smooth and natural viewing method at any distance (120); and allows the researcher to view the eye movements throughout the test to ensure the participant is maintaining fusion. When a prism is placed in front of an eye there is a change in the fixation disparity, this stimulates actions from the EOMs, and results in a fusion modification. When the prism is removed, the eyes return to their original position. Positive fusion is a measurement of the person's ability to maintain single vision whilst the eye converge using prisms held in a base out direction (35, 74, 121). Negative fusion is a measurement of the person's ability to maintain single vision whilst the eye diverge using prisms held in a base in direction (35, 74, 121). The prism fusion range provides important information regarding the ability to maintain binocularity and control any heterophoria (119).

The measurement of fusion using a prism bar is undertaken whilst the patient fixates on an appropriate target (further discussed in Chapter 3). The prism bar is then placed in front of one eye and moved up (i.e. increasing the magnitude of the prism power), to produce the desired fusional movement (99). The subject is instructed to state when the fixation target appears double. The prism strength is increased slowly until diplopia is reported. The point at which diplopia is reported is known as the break point. The prism power is then reduced and the point at which the patient regains single vision is noted, this is the recovery point. Some clinicians also measure the blur point. The blur point indicates when accommodation is no longer activated on the target (99, 119).

When measuring near fusional reserves the patient will normally report blurring of the fixation target (i.e. the blur point), before complaining of diplopia (i.e. the break point) (119).

Whilst there are studies comparing methods of assessment motor fusion to each other (119, 122), there is limited information published on studies which compared the same method on the same participants over multiple visits to elicit the reliability and repeatability of the prism bar method. The only study identified was published in 2006, and was performed on three participants (optometry academic department staff aged 26, 31 and 57 years); it measured motor fusion weekly over a 10 week period (at the same time of the day, using a prism bar), and found that the mean base in and mean base out values showed little variation over the 10 weeks, and concluded it was a consistent and repeatable method of measuring motor fusion (123). The intercession mean variability for near positive fusion for each participant was 0^{Δ}, 0.5^{Δ} and 2.7^{Δ} base out (123) ($^{\Delta}$ = prism dioptres). The intercession mean difference for near negative fusion for each participant was 1.2^{Δ}, 0.6^{Δ}, 1.7^{Δ} base in (123).

Figure 1.6 Photograph of the Clement Clarke Prism Bars used for measuring ocular alignment and all fusion measurements. The prism bar increments (steps) are 1 - 2 - 4 - 6 - 8 - 10 - 12 - 14 - 16 - 18 - 20 - 25 - 30 - 35 - 40 - 45^{Δ}. ($^{\Delta}$ denoting prism dioptres).

Normal fusion range

Whilst orthoptic textbooks may provide values of expected normal fusion ranges (35, 124); it has also been suggested that it is not possible to specify what the normal fusional ranges should or should not be (99). Probably, reflecting the lack of a national or international specific procedure protocol for the measurement of fusion. In general, (in the absence of an intermittent strabismus or a large latent strabismus), the near fusion range is usually greater than the distance fusion range, the positive fusion values are usually greater than the negative fusion values, and the vertical fusion range is the smallest (99).

The variability in the accepted 'norm' may be related to the state of alertness, visual activity prior to measurement and methodology (i.e. the use of naive/non naive participants, presence of heterophoria, target size and single versus double prism technique) (99, 125) (see section *Factors influencing the measurement of motor fusion* for further detail).

A collection of fusional values that have been reported in previous publications are presented in Table 1.5.

	Berens *et al.* (1927) in von Noorden (1996) (99)	Mellick (1949) in von Noorden (1996) (99)	Melville and Firth (2002) (126)	Jimenez *et al.* (2004) (127)	Rowe (2010) (125)	Ludden and Codina (2013) (128)	Schultinga *et al.* (2013) (129)	Fray (2013) (130)	Godts *et al.* (2016) (131)
Mean Age (years)	Not provided	Not provided	19	Not provided	20	20	21	Not specified for control cohort, only total population (37).	38
Age range (years)	Not provided	Not provided	18 - 23	10 – 12	19 - 23	18 - 32	17 - 28	20 - 65	21 - 54
Number of subjects	218	561	28	390	22	26	52	50	41
Median/Mean positive fusion near	Mean = 38^{Δ} base out	Mean = 26^{Δ} base out	Mean = 45^{Δ} base out	Mean = 17^{Δ} base out	Median = 25^{Δ} base out	Mean = 39^{Δ} base out	Median = 38^{Δ} base out	Median = 40^{Δ} base out Mean= 37^{Δ} base out	Median = 35^{Δ} base out Mean = 31^{Δ} base out
Median/ Mean negative fusion near	Mean = 16^{Δ} base in	Mean = 14^{Δ} base in	Mean = 14^{Δ} base in	Mean = 10^{Δ} base in	Median = 10^{Δ} base in	Mean = 16^{Δ} base in	Median = 13^{Δ} base in	Median = 14^{Δ} base in Mean= 15^{Δ} base in	Median = 12^{Δ} base in Mean= 13^{Δ} base in
Median/Mean positive fusion distance	Mean = 14^{Δ} base out	Mean = 18^{Δ} base out	Not studied	Mean = 18^{Δ} base out	Median = 16^{Δ} base out	Mean = 21^{Δ} base out	Median = 33^{Δ} base out	Median = 26^{Δ} base out Mean= 27^{Δ} base out	Median = 20^{Δ} base out Mean= 21^{Δ} base out
Median/Mean negative fusion distance	Mean = 6^{Δ} base in	Mean = 8^{Δ} base in	Not studied	Mean = 7^{Δ} base in	Median = 6^{Δ} base in	Mean = 10^{Δ} base in	Median = 8^{Δ} base in	Median = 4^{Δ} base in Mean = 5^{Δ} base in	Median = 8^{Δ} base in Mean = 8^{Δ} base in
Additional comments	Men only	None	Orthoptic students	None	None	Orthoptic students Results for 2 second viewing time	None	None	None

Table 1.5 The median and mean fusional ranges obtained from published studies which measured horizontal fusion, along with participant descriptions, study specific features and details of any confounding bias (for example, the use of orthoptic students).

Fusion recovery

Whilst the motor fusion break point gives a value of the person's positive or negative fusional reserves, it is the fusion recovery point that provides information about the person's ability to regain fusion after it is disrupted (119). The fusion recovery point is of clinical importance as an indicator of a patient's heterophoria control; some patients with an intermittent strabismus may have difficulty regaining fusion (99). A study with 22 university students (age range 19 - 23 years) found the median recovery point was 5^{Δ} base out less than the break point for near, 4^{Δ} base out less than the break point for distance, and 2^{Δ} base in less than the break point for near and distance (125). It is important to remember that the prism bar increases in 2^{Δ} incremental steps from 2 - 20^{Δ}, then jumps in 5^{Δ} steps from 20 - 45^{Δ}. As a result, the largest amount of change of '5^{Δ} base out' for near positive fusion was actually only one prism bar step, like the 2^{Δ} base in measurements for near and distance. A study of 50 participants aged 20 - 65 years found the median recovery point was 5^{Δ} base out less than the break point for near, 10^{Δ} base out less than the break point for distance and 2^{Δ} base in less than the break point for near and distance (130). This corresponded to a three step reduction in prism to regain fusion for distance positive fusion and only a one step reduction in prism for near positive fusion and the negative fusion (near and distance).

Vertical fusion range

The vertical fusion range is known to be the smallest fusional range. The total vertical range has been given as 3 - 9^{Δ} (to the nearest whole prism) (130, 132-136); with 2 - 5^{Δ} in one direction (124, 125, 135). It is reported that there is no statistically significant difference between the fusion value obtained for near compared with distance (133). The vertical fusional range is known to increase in the presence of vertical heterophoria, as occurs in cases of long standing/congenital superior oblique palsy (99). A study comparing 14 orthophoric participants aged 13 - 83 years, to 14 participants with an congenital superior oblique palsy (aged 12 - 60 years), and 14 participants with an acquired oblique palsy (aged 13 - 83 years), found the total mean vertical fusion values where $4.85^{\Delta} \pm 1.2^{\Delta}$ (control cohort), $3.86^{\Delta} \pm 0.63^{\Delta}$ (acquired cohort) and $15.93^{\Delta} \pm 6.1^{\Delta}$ (congenital cohort) (135). The congenital superior oblique palsy cohort had a statistically significant difference, and a clinically significant difference from both the control and acquired superior oblique palsy cohorts, concluding that the vertical fusion range gives an indication of whether the superior oblique palsy is acquired or congenital/longstanding (135). A study using MRI of 14

'normal' adults concluded that the vertical fusion was primarily executed by superior oblique, in conjunction with inferior oblique and inferior rectus contraction (137).

Association between age and motor fusion

Large cross-sectional studies assessing fusion are difficult to perform with a wide age range. There have been a few larger studies of primary school-aged children, where the researchers attended a number of bigger primary schools and screened all the children. However, when researchers require recruitment from participants from outside schools/universities the numbers available to participate dramatically decrease. A study of 79 participants aged 4 - 70 years did not find any significant change in motor fusion with increasing age (120). They grouped their participants per decade with unequal participant numbers in each cohort. Unfortunately, the author did not present the mean positive and distance fusion values, despite reporting that they were measured for near and distance. The author also did not confirm whether they performed any statistical analysis to come to this conclusion.

- Near negative fusion

The mean near negative fusion in primary school children showed a normal range of 10 - 16$^{\Delta}$ (127, 138-141); the studies showing little variability between them. A cross-sectional study of 1016 children aged 6 - 12 years found mean near negative fusion 11$^{\Delta}$ base in (127). Another cross-sectional study of 530 children aged 6 - 14 years found mean near negative fusion 10$^{\Delta}$ base in (141). A third cross-sectional study of 386 children aged 6 - 12 years found mean near negative fusion 12$^{\Delta}$ base in (138). A fourth cross-sectional study of 879 children aged 6 - 11 years found mean near negative fusion 16$^{\Delta}$ base in (139). A cohort study of 114 children aged 7 - 13 years found mean near negative fusion 13$^{\Delta}$ base in (140).

The mean near negative fusion in younger adults (teenagers to presbyopia (≤ 42 years)) showed a wider normative range of 10 - 19$^{\Delta}$ base in (126, 142). A cross-sectional study of 28 adults aged 18 - 23 years, found mean near negative fusion 14$^{\Delta}$ base in (126), and another cross-sectional study of 20 adults aged 18 - 35 years found 19$^{\Delta}$ base in (143). The control cohort of 33 participants in a case-control study aged 6 - 42 years found the smallest mean near negative fusion with 10$^{\Delta}$ base in (142). A significantly sized cross-sectional study of 500 adults aged 18 - 59 years (mean 42

years) found the mean negative fusion measured using the Mallet unit was 13^{Δ} base in (116).

There are limited studies with a wide range of ages with the participants equally subdivided into age cohorts. A study of 60 participants aged 17 - 83 years with four age cohorts, reported that the overall mean near negative fusion was 14^{Δ} base in (113). The study found no difference in the mean near negative fusion for age cohorts 17 - 70 years, and then a slight increase to 16^{Δ} base in for age cohort 70 - 83 years (113). The authors stated that there was no statistically significant correlation between age and the near negative fusion (113); however there were unequal numbers of participants in their cohorts. Therefore, it appears there are stable values of near negative fusion from childhood to adulthood, but it remains unclear as to what association age in older adults has with near negative fusion.

- Distance negative fusion

The studies mentioned in the above section also measured mean distance negative fusion in primary school children (127, 139-141). A cross-sectional study of 1016 children aged 6 - 12 years found mean distance negative fusion 6^{Δ} base in (127), and a second cross-sectional study of 879 children aged 6 - 11 years found mean distance negative fusion 7^{Δ} base in (139). A smaller cross-sectional study of 530 children aged 6 - 14 years (141), and a cohort study of 114 children aged 7 - 13 years additionally found mean distance negative fusion 7^{Δ} base in (140). Therefore these studies indicated a normative range of 6 - 7^{Δ} base in.

In the studies with 'young adult' cohorts (teenagers and pre-presbyopic adults), the mean distance negative fusion had a slightly stronger normative range of 8 - 10^{Δ} base in (116, 142-144). A cross sectional study of 20 adults aged 18 - 35 years found mean distance negative fusion 10^{Δ} base in (143). The control cohort of 33 participants in a case-control study aged 6 - 42 years found the least mean distance negative fusion with 8^{Δ} base in (142). A cross-sectional study of 500 adults aged 18 - 59 years (mean 42 years) found the mean negative fusion measured using the Mallet unit was 9^{Δ} base in (116).

There are limited studies with a wide range of ages with the participants subdivided into age cohorts. A study of 60 participants aged 17 - 83 years, with four unequal age cohorts, reported that the overall population median distance negative fusion was 4^{Δ} base in, finding no difference in the median distance negative fusion for the age

cohorts, and stating that there was no statistically significant correlation between age and the distance negative fusion (113). However, on reviewing their figures it can be seen that the oldest cohort had a significant outlier who achieved 16$^{\Delta}$ base in, and this will have influenced the median for cohort 70 - 83 years, by increasing it (113); there were also unequal numbers of participants in their cohorts. A study of 271 adults (21 - 80 years) found a mean of 10$^{\Delta}$ for the three younger age cohorts (21 - 50 years) and a mean distance negative fusion of 9$^{\Delta}$ base in for the three older age cohorts (51 - >70 years), they reported that this was not a statistically significant change with age (144). However, there were an unequal amount of participants in each age cohort, with 57 participants in the 21 - 30 years, reducing numbers in each cohort, to only 27 participants in cohort > 70 years (144). Therefore, it appears whilst there may be stable values for distance negative fusion from childhood to adulthood, it remains unclear as to what association age in older adults has with distance negative fusion.

- Near positive fusion

The mean near positive fusion in primary school children shows a wide range of values 18 - 30$^{\Delta}$ base out (127, 138-141). A cross-sectional study of 1016 children aged 6 - 12 years found mean near positive fusion 18$^{\Delta}$ base out (127). A second cross-sectional study of 530 children aged 6 - 14 years found mean near positive fusion 20$^{\Delta}$ base out (141). A third cross-sectional study of 341 children aged 7 - 12 years found mean near positive fusion 23$^{\Delta}$ base out (138). A fourth cross-sectional study of 879 children aged 6 - 11 years found mean near positive fusion 21$^{\Delta}$ base out (139). A cohort study of 114 children aged 7 - 13 years found the highest mean near positive fusion of 30$^{\Delta}$ base out (140).

Compared to the school aged children, the mean near positive fusion in younger adults (teenagers to presbyopia) appears to be higher and wider range, 27 - 57$^{\Delta}$ base out (116, 126, 142, 143). A cross-sectional study of 28 adults aged 19 - 23 years found mean near positive fusion 46$^{\Delta}$ base out (126), and another cross-sectional study of 20 adults aged 18 - 35 years found mean near positive fusion 57$^{\Delta}$ base out (143) (in this study two prism bars were used to give measurements greater than 45$^{\Delta}$ base out). The control cohort of 33 participants in a cohort study aged 6 - 42 years found the smallest mean near positive fusion with 28$^{\Delta}$ base out (142). A cross-sectional study of 500 adults aged 18 - 59 years (mean 42 years) found the mean near positive fusion measured using the Mallet unit was 27$^{\Delta}$ base out (116).

There are limited studies with a wide range of ages with the participants subdivided into age cohorts. A study of 60 participants aged 17 - 83 years with four age cohorts reported that the overall mean fusion was 40^{Δ} base out, finding no difference in the median near positive fusion for age cohorts 17 - 70 years, and then a decrease to 32^{Δ} base out for age cohort 70 - 83 years (113). The authors stated that despite the obvious decrease, there was no statistically significant correlation between age and the near positive fusion (113). However, there were unequal numbers of participants in their cohorts, and some of the participants in cohort 70 - 83 years did reach the maximum obtainable fusion 45^{Δ} base out (113). If the authors had been able to measure values of fusion > 45^{Δ} base out, it would have very likely increased the overall mean for the cohort 70 - 83 years. Therefore, it appears there is an improvement in near positive fusion from childhood to adulthood, but it remains unclear as to what association increasing age in older adults has with near positive fusion.

- Distance positive fusion

The mean distance positive fusion in primary school children shows a wide range of values from 13 - 30^{Δ} base out (127, 138-141). A cross-sectional study of 1016 children aged 6 - 12 years found mean distance positive fusion 17^{Δ} base out (127). A second cross-sectional study of 530 children aged 6 - 14 years found mean distance positive fusion 13^{Δ} base out (141). A third cross-sectional study of 341 children aged 7 - 12 years found mean distance positive fusion 23^{Δ} base out (138). A fourth cross-sectional study of 879 children aged 6 - 11 years found mean distance positive fusion 21^{Δ} base out (139). A cohort study of 114 children aged 7 - 13 years found the highest mean distance positive fusion of 30^{Δ} base out (140).

Compared to the school age children, the mean distance positive fusion in younger adults (teenagers to presbyopia) appears to have a similar range, 17 - 33^{Δ} base out (116, 142-144). A cross-sectional study of 20 adults aged 18 - 35 years found mean distance positive fusion 33^{Δ} base out (143), and the control cohort of 33 participants in a cohort study aged 6 - 42 years found 21^{Δ} base out (142). A cross-sectional study of 500 adults aged 18 - 59 years (mean 42 years) found the mean distance positive fusion measured using the Mallet unit was 21^{Δ} base out (116).

There are limited studies with a wide range of ages with the participants subdivided into age cohorts. A study of 60 participants aged 17 - 83 years with four age cohorts reported that the overall median fusion was 19^{Δ} base out, stating that there was

decrease in the median value, and a statistical significant correlation between increasing age and decreasing mean distance positive fusion (113); although, there were unequal cohort numbers, and the median distance positive fusion value for cohort 70 - 83 years was actually slightly higher than cohort 50 - 69 years. A study of 271 adults (21 - 80 years) found a mean of 19^{Δ} base out for cohort (21 - 30 years), a mean of 17^{Δ} base out for the oldest age cohort (>70 years), the authors reported that there was not a statistically significant change with age (144). The best mean distance positive fusion of 20^{Δ} base out was reported in cohort 41 - 50 years (144). However, there were unequal participant numbers in each age cohort, with 57 participants in the 21 - 30 years, waning numbers in each cohort, to 27 participants in cohort > 70 years (144). Therefore, it appears there is a stable value in distance positive fusion from childhood to adulthood, but it remains unclear as to what association age in older adults has with distance positive fusion.

- Fusion recovery

A study of 271 adults (21 - 80 years) reported a statistically significant association between distance horizontal fusion recovery point (positive and negative values) and age (144). The change for positive recovery was 11.1^{Δ} base out for cohort 21 - 30 years, and 11.8^{Δ} base out for cohort > 70 years (144); which would not appear to be clinically significant, despite the statistically significant finding. The change for negative recovery was 3.3^{Δ} base in for cohort 21 - 30 years, and 5.9^{Δ} base in for cohort > 70 years, and this was also a statistically significant difference (144). Using linear regression modelling on their raw data there was a reduction in negative recovery of approximately 0.05^{Δ} base in/year, and a reduction in positive recovery of approximately 0.07^{Δ} base out/year (144). The accuracy of this method seems questionable because they used actual recovery prism power rather than the difference between break and recovery points. As there is not a study that measured recovery point with an equal number of participants in each cohort, it remains unclear as to what association age has with fusion recovery.

In conclusion, there is a lack of evidence to establish whether older adults have the same horizontal motor fusion as pre-presbyopic adults and children, and whether there is an association between age and fusion recovery. To the author's knowledge, there are no studies which investigated the effect of age on vertical fusion. The present study will use cohorts based on age decades, and use the same number of participants in each cohort, to improve the clinical application of this present study (see Chapter 3).

Factors influencing the measurement of motor fusion

A 1948 study recommended the use of a 6/9 (0.2 LogMAR) size target, and this has become the standard in orthoptic clinical practice (99). A study which compared the fusional ranges obtained for a central target (6/6), paracentral target (6/9) and a peripheral target (6/60) on 22 university students (age range 19 to 23 years), found that the negative fusional reserves for near and distance were unaffected by target size (125). However, using a peripheral size target produced a statistically higher near and distance positive fusion value (125). For example, for near, the mean was 25^{Δ} base out with a central target versus 35^{Δ} base out with a peripheral target, and for distance, the mean was 16^{Δ} base out with a central target versus 25^{Δ} base out with a peripheral target (125).

When both vertical and horizontal fusion ranges are being tested, one standard routine (often used by orthoptists) is base out, base up, base in, and base down (99), whereas others suggest testing base in before base out (121). The order of testing has been reported to potentially influence the fusion range (130, 145). A study of 50 participants aged 20 - 65 years (mean 37 years) found that the order of testing had no effect on the positive fusion break and recovery points (130); but the negative fusion break and recovery points were affected by testing the negative range after the positive range, and this was a statistically significant finding (130). The difference in mean fusion range value was 0.5^{Δ} for both positive and negative break points, 0.6^{Δ} for positive recovery and 0.5^{Δ} for negative break points (130). Therefore, the effect of testing ordering would not be clinically significant, despite the potential for a statistically significant influence on measurements. A study of 10 participants aged 21 - 58 years (mean 32 years) found the testing order had a statistically significant effect on negative recovery point when the negative range was tested first (145). There was a difference in mean recovery by 1^{Δ} base in (145). Testing order had no effect on positive break and recovery points or negative break point (145). A study of 30 participants aged 18 - 30 years (mean 24.5 years) measured fusion at 40 cm; they found that when positive fusion was tested first it influenced negative fusion, negative fusion was reduced by 6^{Δ} base in, and this was a statistically significant finding (146). Whereas, when negative fusion was tested first, there was no effect on the positive fusion break (146). In contrast, a study of 79 participants aged 4 - 70 years, found testing order had no statistically significant effect on fusional values (120). In summary, the evidence is conflicting, but it appears that when positive fusion is tested before negative fusion, there may be an effect on the negative fusion (reducing the break point value and increasing the reduction in the number of prisms required to regain fusion).

There is dispute as to whether the laterality of the eye (i.e. right or left) which the prism is held in front of affects the fusion range. For example, it is reported that when the prism is held in front of the non-dominant eye, that a larger positive fusion range could be obtained (147). However, in a study using university orthoptic students (n = 23), ocular dominance did not have any effect on the fusional ranges (128). A survey of 90 international orthoptists from 17 countries, found 61 respondents (68%) reported that they placed the prism bar in front of the fixing eye (130). The orthoptists chose the fixing eye via cover test, dominance testing, visual acuity or by asking the patient their preference (130). Whereas, 29 respondents (32%) who habitually held the prism bar over the right eye (130).

It is reported that testing speed (the time in which each prism is held in front of the eye), affects the results. One study of 27 university students aged 18 - 32 years (mean 21 years), showed that there was no statistically significant difference in fusional ranges when a one second or two second testing speed was used (128). However, the positive fusion distance results showed a statistically significant improvement when testing speed was increased to three seconds (128). However, the participants reported that the three second testing speed was tedious and resulted in discomfort (128). Only three participants (12%) preferring the three second testing speed, compared with 18 participants (69%) who preferred a two second testing speed (128). It should be noted that all the participants were orthoptic university students; it is currently not known what testing speed is preferred by novice participants, and whether appropriateness of testing speed varies with age, (particularly those in an elderly population). Studies have shown that encouragement from the researcher may impact the results (148). One study, showed encouragement improved both negative and positive fusion range by both a clinically significant and statistically significant amount (148). In this study of 10 naive university students (mean age 20 years), the near positive fusion range increased from 24^{Δ} to 30^{Δ} base out ($p < 0.005$), and the near negative fusion range increased from 10^{Δ} to 12.6^{Δ} base in ($p < 0.05$) (148). Another study of 50 participants (mean age 37), found that encouragement would increase the mean distance positive fusion by 2.4^{Δ} base out, which was a statistically significant change ($p < 0.005$) (130). Whereas, the mean distance negative fusion value was unchanged by encouragement, and the values were not statistically significant ($p = 0.78$) (130).

It is reported that ocular alignment may influence the size of the fusional reserve. In a study of 14 university students, there was a tendency for esophoric participants to have a larger positive fusion range and for exophoric participants to have a larger negative

fusion range (125). In this study, the ocular alignment ranged from 8^{Δ} exophoria to 10^{Δ} esophoria for near, and 10^{Δ} exophoria to 2^{Δ} esophoria for distance (125).

The two studies which used orthoptic students as participants showed fusional reserves in the higher end of the range (126, 128). In a comparison study, the significance of knowledge/previous experience was assessed by comparing orthoptic students to age-matched naive participants (148). The study compared naive participants to orthoptic students in year one, year two and year three of their studies and, found that the mean fusion range values increased from naive to year 1, and continued to increase from year one to year two, and from year two to year three (148). However, there was only a statistically significant difference in positive fusional values when naive and year one students were combined and compared to the combined year two and year three mean values (148). With > 20^{Δ} difference in base out range, the authors concluded that this was of clinical significance as well as statistical significance (148). The negative fusional reserves were unaffected by level of experience with orthoptic measurements (148).

Whilst it is possible for a participant to still maintain fusion at the highest prism strength on the prism bar (i.e. 45^{Δ}), it is reported that adding an additional prism either in front of the first prism or in front of the fellow fixating eye does not allow accurate assessment of fusion at prism powers >45^{Δ} (149). The use of multiple stacked prisms in the same orientation, for example, two prisms both aligned based out, does not create an additive effect (149). For example, a 5^{Δ} glass prism in front of a 40^{Δ} glass prism, both oriented base out, produced 59^{Δ} base out, not 45^{Δ} base out (149).

1.6.4 Commercially available stereotests for the measurement of stereopsis

The RCOphth “Guidelines for the Management of Strabismus in Childhood” recommends the measurement of stereoacuity via TNO stereotest, Frisby stereotest, Titmus stereotest, or Lang stereotest or via the synoptophore (106). It is normal practice for UK and Irish based orthoptists to follow guidelines issued by the RCOphth; as such orthoptists would have access to all stereotests listed in the guideline. However, Lang is considered for use mainly in younger children and the synoptophore only measures gross levels of stereopsis, and therefore neither where included in this research study.

Frisby Stereotest

The Frisby stereotest is manufactured by Haag Streit UK Ltd (Clement Clarke International Ltd, Harlow, Essex). It is easily understood by patients from a young age. The Frisby stereotest is made from two thin transparent perspex sheets. One sheet has four boxes of printed geometric shapes and on the second sheet, over-lapping in the centre of one box is a printed circle; the circle also contains a pattern of geometric shapes (see Figure 1.7). The angular disparity depends on the distance between the Perspex sheets (plate thickness) and the viewing distance (see Table 1.6). It can measure both crossed (circle protruding towards the patient) and uncrossed disparities (circle protruding away from patient). It is a real depth free space stereotest, it does not require the use of polarised or coloured spectacles.

Monocular clues are present with the Frisby stereotest, one study reported that a participant with an alternating vertical strabismus achieved mean 54 arcsec with Frisby (150). The manufacturers have warned that head movement parallax may be a cause for monocular clues (151). A study of 1035 children aged 12 - 13 years from four schools in Mexico reported the sensitivity of Frisby for detecting strabismus as 33% (n = 24), for detecting amblyopia as 12% (n = 50) (152). Unfortunately, the authors did not provide exact details of the values of specificity but merely stated that it was high (152). A study on 365 participants aged 5 - 82 years, reported when using Frisby stereoacuity as an indication of a general visual problem there was a 51% sensitivity and 66% specificity (1). The same study reported that when using Frisby stereoacuity as an indication of a binocular vision problem, the sensitivity increased to 62% and the specificity was 65% (1).

Figure 1.7 Photograph showing of the Frisby stereotest (box and 6 mm plate). Note the four squares with geometric shapes, and the instructions for interpreting the value of stereoacuity to be documented based on testing distance and plate thickness.

Test distance, cm	6 mm plate	3 mm plate	1.5 mm plate
30	600	300	150
40	340	170	85
50	215	110	55
60	150	75	40
70	110	55	30
80	85	40	20
90	25	10	5

Table 1.6 Frisby stereotest scores in arcsec at each testing distance. ©Haag Streit UK Ltd

The clinical assessment of stereoacuity using Frisby

When using the Frisby stereotest in clinic, the patient is shown both the forward projection of the circle (crossed) and the backward projection of the circle (uncrossed) before commencing, and asked which is easier for them to appreciate. The 6 mm, 3 mm, and then 1 mm plate is shown to the patient against the white background of the Frisby box at a distance of 40 cm (corresponding to 340, 170, 55 arcsec respectively). The patient is asked to locate the position of the circle in one of the four boxes. This test is continued until the patient reaches their maximum level of stereopsis. When the patient fails to identify the circle at a particular distance, the plate is brought forward by 10 cm and the patient asked to identify the circle at that position again. If correctly identified (for a second time), the stereoacuity is recorded for this plate and testing distance (see Table 1.6). The test is performed with the patient's distance spectacles unless normally removed for near tasks. If the patient requires a presbyopic correction for near tasks then those spectacles are used to perform the Frisby stereotest.

Association between age and Frisby tested stereoacuity

There is a lack of published peer reviewed data on the normative values of Frisby stereoacuity in pre-school aged children. One study published as an abstract from a conference poster measured Frisby stereoacuity on 100 children aged 37 - 52 months without amblyopia or strabismus; they reported that stereoacuity could be measured on

89 children (153). The median stereoacuity was 75 arcsec (IQR 40 - 85) (153). Six children did not comprehend the test; five children appeared to understand the test, and yet were stereo-negative, despite normal vision and demonstrable motor fusion (153). A study of 186 children aged 6 - 16 years, assessed in primary and post-primary (secondary) schools in Northern Ireland, found that the 97 primary school aged children (6 - 11 years) has a median stereoacuity of 20 arcsec for crossed disparity and 25 arcsec for uncrossed disparity (94). There was an improvement in the median stereoacuity for the 89 post-primary school children (12 - 16 years) to 10 arcsec (crossed and uncrossed disparity), which was a statistically significant finding (94).

A study of 206 participants aged 16 - 40 years (qualified eye care clinicians and undergraduate eye care students from two UK universities), found the median stereoacuity was 20 arcsec (154). Supporting an earlier study (referred to as the Newcastle study in this thesis) of 196 participants aged 11 - 49 years, who also found a median stereoacuity of 20 arcsec for their total population, which had similarly aged participants (1).

There are three studies which have looked at the effect of age on stereopsis using the Frisby stereotest. One study found a decline in stereoacuity after the age of 35 years; using crossed disparity they found that cohort 15 - 24 years achieved a mean value of 7.5 arcsec, cohort 25 - 34 years achieved a mean value of 6.7 arcsec and cohort 35 - 60 years achieved a mean value of 19.5 arcsec; however in this study there was an uneven number of participants in each cohort (3). The results were slightly better with uncrossed disparities, 6.8 arcsec, 5.2 arcsec and 13.6 arcsec for the three age cohorts respectively (3). Unfortunately the authors did not state whether this was statistically significant difference (3). The Newcastle study comparing 196 participants aged 11 - 49 years to 16 participants aged 50 - 82 years, they found that the mean stereoacuity dropped from 20 to 80 arcsec between the younger and older cohorts (1). In the third study undertaken at Moorfields Hospital based on 60 participants, there was no difference in the mean stereoacuity between cohorts 17 - 29 and 30 - 49 years, but a decrease in cohort 50 - 69 years, and a further decrease in cohort 70 - 83 years was noted when using the Frisby stereotest (113). Currently, with regard to the Frisby stereotest, there are no published studies which have compared the effect of age on stereoacuity using the same number of participants in each cohort and used a more regular division of age for the cohorts (for example, decades).

Toegepast Natuurwetenschappelijk Onderzoek Stereotest

The Toegepast Natuurwetenschappelijk Onderzoek (TNO) stereotest (155), is reported as the only stereotest to be free from monocular clues (156). It is manufactured by Lameris Ootech BV, Nieuwegein, Netherlands (see Figure 1.8). The test was developed for the Dutch military as a screening test for stereopsis (155). TNO is an anaglyph test based on chromatic random dot stereograms which are displaced horizontally (35, 132). The green and red dots are displaced from one another to allow stereopsis to be created through fusion of disparate images. The TNO book contains some non-quantitative pages which are used clinically to screen the patient for the presence of stereopsis (plates I, II, III) and a suppression plate (plate IV) (132). To determine the level of stereoacuity, plates V, VI, and VII are used; these correspond to ranges from 480 to 15 arcsec (35, 132). Plates V, VI, and VII consist of circles with a 60-degree sector missing from each in one of four possible positions (see Figure 1.9).

Figure 1.8 Photograph on left shows the TNO stereotest book and accompanying red/green glasses (Lameris Ootech BV, Nieuwegein, Netherlands). The right eye views the stereotest through the green filter, and the image appears green, while the left eye views the stereotest through the red filter, and image appears red. The two images should then be fused to see the image in 3-D, and hence measure stereoacuity. Photograph on right shows the pages inside the book demonstating “cake with missing piece” or “PAC-MAN”, and the stereotest page where the patient must locate the “PAC-MAN” in each of the four squares.

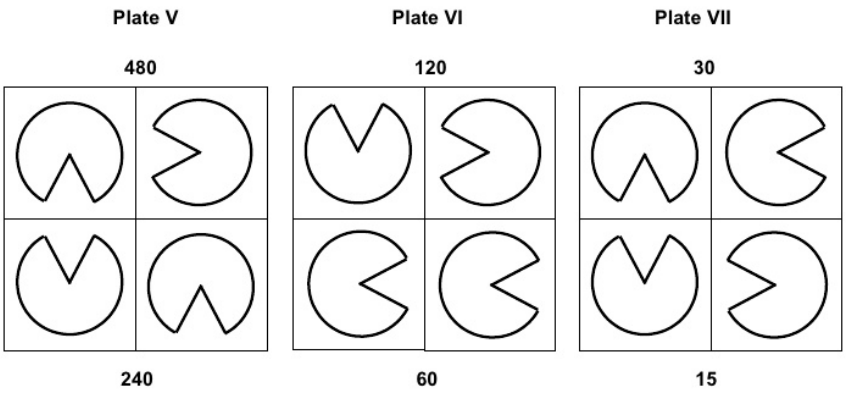

Figure 1.9 Schematic showing the position of 60 degrees segment missing in each square. The missing segment can only be seen whilst wearing the red/green glasses. There are two “PAC-MAN” plates for each level of stereoacuity. After the patient has reached their maximum stereoacuity the “cake” will disappear and the patient will only see a pattern of red and green dots.

The clinical assessment of stereoacuity using TNO

The patient wears the red/green glasses over any habitually worn distance or presbyopic spectacles. The book is held at 40 cm from the patient in a slightly depressed position (i.e. chin down). The patient is shown the screening plates, to familiarise themselves with the images created by the test, before moving to the graded section of the test. With each level of stereoacuity, there are two circles with a segment missing in each circle, patients are asked to identify where in each circle the segment is missing. Patients are required to identify both missing segments correctly to attain that level of stereoacuity. The stereoacuity is recorded as the last level/value were both circle segments are correctly identified (see Figure 1.9).

It has been reported that the chances of getting one correct response through guessing is 1 in 16, whilst the chances of getting an entire plate correct through guessing is 1 in 256 (156). A study using 31 participants with a strabismus aged 3 - 18 years, found the sensitivity of the TNO stereotest in detecting an abnormality to be 94%; this was based on no stereopsis recorded on 29 participants and 2 participants with a micro-esotropia detecting stereoacuity (157). Unfortunately, the authors did not detail the level of stereoacuity achieved by the two participants diagnosed with micro-esotropia, to comment on whether this was a clinically significant ‘normal’ value of stereoacuity. The same study, reported the specificity for achieving a stereoacuity value of 120 arcsec in children aged 3 - 18 years as 98%, based on 275/281 children achieving this

level (157). In comparison, a study based on 59 participants with a strabismus aged 4 - 78 years reported only 80% sensitivity, and a specificity of 87% based on 84 participants without a strabismus (158). However, the study with the lower sensitivity and specificity scores, used only the TNO screening plates, which scores 1,900 arcsec (158); this would not be normal clinical practice, nor does it adhere to the manufacturer's instructions. A study of 1035 children aged 12 - 13 years from four schools in Mexico reported the sensitivity of TNO as 71% for detecting strabismus (n = 24), and 46% for detecting amblyopia (n = 50) (152). Unfortunately, the authors did not provide exact details of the values of specificity but merely stated it was high (152). It has been reported that a difference of 30 arcsec may occur between different editions of TNO stereotest used (159).

The association between age and stereoacuity measured with TNO

It was stated that the TNO stereotest is an unreliable method to assess stereoacuity in children aged under three years (157), as they may lack the communication skills to understand the complexity of the instructions. A study of 186 children aged 6 - 16 years, reported the median stereoacuity was 60 arcsec (94). Whereas, a study of 97 children aged 4 - 16 years found mean stereoacuity was clinically significantly weaker, at 118 arcsec (159). A large population based study of 1060 adults aged 16 - 40 years from Cambridge UK, found median stereoacuity with TNO was 60 arcsec in pre-presbyopic adults (160). A study of 206 participants aged 16 - 40 years, who were optometry and orthoptic qualified clinicians and undergraduate students from two UK universities, also found the median stereoacuity with TNO was 60 arcsec (154). Therefore prior experience with orthoptic practice did not influence stereoacuity.

In the Moorfields study there was no difference in median stereoacuity between cohorts 17 - 29 years and 30 - 49 years, but then a decrease in stereoacuity for cohort 50 - 69 years, and a further decrease in stereoacuity for cohort 70 - 83 years when using TNO (113). The authors discussed how the decrease in stereoacuity could be a related to a decline in cortical disparity detectors function with age (113). A second study comparing stereoacuity with age using TNO was undertaken in Keimyung, Korea (n = 79) (2). In the Keimyung study, stereoacuity remained stable until cohort 51 - 60 years and then decreased, continuing to decrease with cohorts 61 - 70 years and 71 - 80 years (2). There was a statistically significant change with each age cohort (2). The Keimyung study had a regimented approach in terms of regular age progression cohorts, and a consistent number of participants in each cohort (2). The Keimyung

study will be the main antecedent comparator to this research study in terms of TNO stereoacuity change with age.

Titmus Stereotest

The Titmus stereotest (Stereo Optical Company, Chicago) is a vectograph test in which two targets are polarised at 90 degrees to each other (see Figure 1.10). The targets are then viewed through polarised filter glasses. The polarised filters induce retinal disparity thus creating the perception of depth. This is a two-page book design, on the right side is a Titmus stereo fly (3000 arcsec), and on the left side nine boxes (with four circles in each box) and three rows containing five animals (see Figure 1.10). The circles have a disparity of 800 to 40 arcsec (see Table 1.7).

Figure 1.10 The Titmus Stereotest. When wearing the accompanying polarised spectacles, the fly's wings will appear to protrude from the book towards the viewer. One animal will appear in 3D in rows A - C, and one circle in boxes 1 - 9. When the patient has reached their maximum stereoacuity, all four circles in the subsequent boxes will appear flat and identical. (Stereo Optical Company, Inc. Chicago, IL USA).

Stereotest- box	***Stereoacuity level (*arcsec*)***
1	800
2	400
3	200
4	140
5	100
6	80
7	60
8	50
9	40

Table 1.7 Stereoacuity level documented with correct identification of circle in stereotest box using the Titmus Stereotest.

The clinical assessment of stereoacuity using Titmus stereotest

The patient wears polarised filter glasses over any habitually worn distance or presbyopic spectacles. The book is held at 40 cm from the patient in a slightly depressed position (i.e. chin down). The patient is shown how the fly's wings appear to be coming out from the book; the patient is then shown the nine Wirt boxes, and asked to identify which of the four circles in the box appears to protrude forwards. With each correct response the patient moves to the next box of circles. If an incorrect response is given the previous box is rechecked. The stereoacuity is documented according to the number of correctly identified circles (see Table 1.7).

The concern with the Titmus stereotest is that monocular clues may invalidate the results; in fact, with the first four boxes, the protruding circle can be seen monocularly, giving 140 arcsec. It has been suggested that a reason why stereo-blind strabismus patients achieve artificially good stereoacuity is by observing image jump through alternating fixation, or possibly through monocular displacement in the first four circles (161, 162). A study of 23 participants with small angled strabismus aged 8 - 82 years, versus 10 participants without a strabismus aged 8 - 60 years, indicated that the sensitivity of for detecting strabismus with the Titmus stereotest was 79%, and the specificity was 26% (163). This study assessed the sensitivity and specificity for the presence of stereoacuity using only the Titmus fly stereogram image (see Figure 1.10).

A study based on 59 participants with a strabismus aged 4 - 78 years, compared with 84 participants without strabismus, reported only 83% sensitivity, and a specificity of 83% for detecting strabismus with the Titmus stereotest (158). This was based on box number 5 (100 arcsec) taken as the 'normal' level of stereoacuity (see Figure 1.10 for a photograph depicting the size of the fly in comparison to the circles). A study of 1035 children aged 12 - 13 years from four schools in Mexico reported the sensitivity of the Titmus stereotest as 62% in detecting strabismus (n = 24), and 38% in detecting amblyopia (n = 50) (152). Unfortunately the authors did not provide exact details of the values of specificity but merely stated it was high (152).

The association between age and stereoacuity measured with Titmus Stereotest

A study of 344 children aged 1.5 - 13 years found a gradual improvement in stereoacuity using the Titmus stereotest up to the age of 9 years, with a consistent value of 40 arcsec (the maximum achievable stereoacuity value with the Titmus stereotest), recorded for participants older than 9 years (n = 56) (95). However, in this study the non-verbal children were included with the authors interpreting their responses; and the non-verbal children could hold the stereotest book at any testing distance rather than the manufacturer's recommended 40 cm testing distance (95). Whilst the authors presented a scatter graph of the stereoacuity values for every participant, and provided the lower limit of stereoacuity achieved, they did not detail mean stereoacuity for the total population or the cohorts (95). The scatter graph showed that the children < 2 years achieved 3000 arcsec or no stereoacuity, and that children in cohorts 2 - 3 years and 3 - 4 years achieved 40 arcsec to no stereoacuity (95). The authors did detail that only 5/87 children under four years could achieve ≤ 100 arcsec (95). A large cross-sectional study of 5,780 children aged 4 - 18 years performed in Shandong, China found the mean stereoacuity with Titmus stereotest was 50 arcsec (164). The authors reported that 89/94 (95%) of their four-year-olds achieved equal to or worse than 100 arcsec (164). There was a statistically significant improvement in stereoacuity between cohort 4 years and cohort 6 - 7 years (164). The authors found that individual factors such as lower visual acuity, the presence of anisometropia and a rural region habitation, had a statistically significant impact on lowering stereoacuity (164). The authors reported that 4,384 children (76%) could achieve the maximum recordable stereoacuity value of 40 arcsec (164).

The Moorfields study of 60 participants aged 17 - 83 years found a mean stereoacuity of 40 arcsec for their total population (113). There was a decrease in mean

stereoacuity only in the cohort 70 - 83 years when using Titmus stereotest, and this was a statistically significant finding (113). The Keimyung study supported the findings of the Moorfields study; they found in cohorts 7 - 10 years, 11 - 20 years, 21 - 30 years, 31 – 40 years, and 41 - 50 years that the mean stereoacuity in every cohort was 40 arcsec (2). Whilst there was a reduction in mean stereoacuity for cohorts 51 - 60 and 61 - 70 years, there was only a statistically significant reduction in mean stereoacuity found in cohort 71 - 80 years (2).

Frisby Davies 2 (FD2) Stereotest

The FD2 (Stereotest Ltd, Sheffield, UK) is a free space distance stereo-acuity test, performed at 6 m (see Figure 1.11). The FD2 test comprises of a white illuminated box (900cd/m^2) containing four green coloured differently shaped plastic objects mounted on rods (shapes projecting toward viewer with rods behind into the back wall). There are four geometric shapes (half-moon, star, arrow and cross) and four animal shapes (fish, cat, duck and pig). The rods are translucent with faint markings along them indicating the seconds of arc (arcsec). By changing the distance between the protruding rod and the three accompanying rods range of stereoacuity values can be assessed. With a 6 m testing distance the disparities are 50, 40, 20, 10 and 5 arcsec. There is a recognised potential for monocular clues with the FD2, with one study suggesting shadows from the backlight as a potential cause (1). Another study showed that 37% of their 95 participants were able to see the largest disparity monocularly (165). The designers recommend monocular testing after binocular testing, if the patient is able to appreciate stereoacuity monocularly, then the test is documented as invalid. Unlike the Frisby near stereotest, this test may be difficult for children under seven years to understand, and potentially produce false stereo-negative results (1).

Figure 1.11 Photographs of the FD2 stereotest illuminated with the star protruding forwards (Stereotest Ltd, Sheffield, UK).

The clinical assessment of distance stereoacuity using FD2

Full details for how FD2 stereotest was performed can be found in Chapter 3.8. The stereoacuity disparity for the FD2 is found on the rods inside the FD2 box (see Figure 1.11). The clinician moves one of the four rods forward whilst the box front door is closed, then asks the patient to correctly identify which of the four shapes appears closer to them. If the patient is able to correctly identify the shape which is closer to them, the FD2's front door is closed and the procedure repeated with a smaller disparity distance. If the patient reports that all four shapes are now in the same position the test is recorded as a negative result.

After identifying the patient's level of stereoacuity the monocular threshold test is performed. If the monocular stereoacuity level is equal or better to the binocular stereoacuity level, the test is deemed invalid and recorded as inconclusive. If the monocular stereoacuity level is worse than the binocular stereoacuity level the test is deemed valid and level of stereoacuity recorded. The results are recorded as either the minimum stereoacuity achieved, as an invalid result or as a negative result, and the last correctly viewed level is recorded as their stereoacuity.

A study on 365 participants aged 5 - 82 years, reported when using FD2 stereoacuity to detect a general visual problem there was a 31% sensitivity and 87% specificity (1). When using the FD2 to detect a binocular vision problem, the sensitivity increased to 44%, and the specificity was 86% (1).

The association between age and stereoacuity measured with FD2 Stereotest

A study of 59 children aged 3 - 6 years, found four children (6.8%) who reportedly understood the test, but were unable to identify disparity (classed stereo-negative), 13 children (22.0%) who were only able to complete the test when testing distance was reduced to 3 m, and a mean stereoacuity of 29.6 arcsec based on 42 children (71.2%) who completed the test when testing distance was 6 m (166). Age was a statistically significant influencing feature, with younger children less likely to complete the test successfully at 6 m (166). A study of 109 participants aged 16 - 40 years (qualified and undergraduate eye care students from two UK universities) found that median stereoacuity was 10 arcsec (154). These findings support an earlier study (Newcastle Study) of 195 participants aged 11 – 49 years which found the median was 10 arcsec as measured by FD2 stereotest, for the total population (1). Another smaller study on

46 adults aged 20 - 49 years (mean 29.61 years) found the mean stereoacuity on FD2 was 12.5 arcsec (167).

There have been two studies comparing age to the level of stereoacuity on FD2 (1, 113). The Newcastle study compared 195 participants aged 11 - 49 years to 16 participants aged 50 - 82 years; the study reported that the level of stereo-acuity was 10 arcsec and 12.5 arcsec respectively for the cohorts, but this was not statistically significant (1). In the Moorfields study, there was a reduction in stereoacuity in the third cohort (50 - 69 years), which was a statistically significant change from second cohort (30 - 49 years) (113). Distance stereoacuity measured by the FD2 stereotest then remained unchanged between the third cohort (50 - 69 years) and fourth cohort (70 - 83 years) (113). Currently, there are no published studies which compare and statistically analyse the level of stereoacuity on FD2 for each decade of life.

1.6.5 Ocular alignment

The association between age and ocular alignment

Most infants are orthophoric or exophoric (98). A study of 1016 children aged 6 - 12 years measured ocular alignment using the Maddox rod and reported a mean near exophoria of 0.4^{Δ} and a mean distance esophoria of 0.6^{Δ}, there was no statistically significant change between the seven age cohorts (127). A study of 271 adults aged 21 - 80 years, found that the mean distance heterophoria was minimal exophoria for all adults except cohort 71 - 80 years, which had minimal esophoria (0.2^{Δ}) (144).

A study of 753 adults aged 19 - 100 years found a statistically significant increase in the incidence adult onset strabismus with the peak incidence from ≥ 70 years (168). It is reported that an adult onset strabismus can occur for reasons unrelated to neurological diseases, mechanical diseases, infection or trauma from age 50+ years (168). The authors reported that three common subtypes of adult onset strabismus were: convergence insufficiency (median onset age 69 years), vertical strabismus (median onset age 72 years) and divergence insufficiency (median onset age 74 years) (168). Convergence insufficiency is classified by an exophoria/exotropia for near and orthophoria or smaller angle exophoria/exotropia in distance (168). Divergence insufficiency is classified by an esophoria/esotropia for distance and orthophoria/exophoria or smaller angle esophoria/esotropia at near (168).

A large cross-sectional study of 663 participants aged 5 - 85 years measured the distance heterophoria using the Maddox groove (rod), found a minimal increase in esophoria over the total age range from the youngest to the eldest (<1$^{\Delta}$) (169). The authors reports that this was not of clinical or statistical significance (169). The study found that the near heterophoria, measured with the Maddox wing, changed towards exophoria with increasing age (approximately 5$^{\Delta}$) (169). From age ≥ 25 years, and most notable from age ≥ 60 years, the change in ocular alignment for near was statistically significant (169). The authors concluded that they did not attribute this change to presbyopia (169). A retrospective analysis of an university optometry clinic charts (500 patients aged ≥ 60 years), reported no significant change in the heterophoria with increasing age in the three age cohorts (60 - 69 years, 70 - 79 years and 80+ years) (170).

Therefore, although two large studies have reported significant associations between age and ocular alignment, this is not a conclusive and further evidence from this thesis will add to the existing knowledge on the association between increasing age and ocular alignment. The current study will establish whether an association is also present when using the standard orthoptic method of measuring a heterophoria with a prism bar.

1.7 Problems with the Existing Data / Knowledge Base

The existing literature has shown that binocular functions are not present at birth, but develop in early childhood, and mature in the pre-teenage/early-teenage years. A number of studies have provided normative data for children and younger adults. However, there is a lack of evidence to guide the clinician as to what is a normal binocular response when the patient is an older adult, what studies are available, having varying methodologies (for example, differences in study populations or potentially biased participants), and lack of uniformity/standardization as to what test types were used to measure data for these normative data.

Despite the fact that larger population studies have been published, these were performed on school aged children, university students, or used methods that did not control visual acuity to set inclusion criteria (94, 171-173); and so have little applicability to the older age range of patients. Whilst a large sample size can be easily obtained by researchers attending a few large schools or universities, it becomes increasingly difficult to achieve adequate numbers in the older age strata in a non-

reimbursement research study; a potential reason for the lack of published research using older populations. Additionally, within the older population, there are a greater proportion of ineligible individuals, due to acquired eye diseases and the treatment thereof.

The researcher acknowledges that values obtained under experimental conditions may not be exactly applicable in clinical settings, when there are time constraints, variances in noise and lighting, distractions e.g. younger siblings, or external stressors influencing the patient or clinician. However, by having normative data appropriate to the age of the patient, it aids clinicians in their diagnosis and management strategies of binocular vision disorders. Therefore, this present study aims to be beneficial to optometrists and orthoptists in making appropriate choices about what type of stereotest is most useful in clinical practice, and in establishing whether their patients of varying ages have normal or abnormal assessments of ocular alignment, ocular motility, NPC, motor fusion and stereoacuity.

Therefore, the problem identified with the existing data / knowledge base was the lack of information available for clinicians on the association between increasing age and binocular functions for the delivery of evidence based practice. For that reason, the researcher designed a study to investigate this association and address the question *what is the effect of age on binocular functions?*

1.8 Objectives

The objectives of the preliminary study were firstly, to ascertain practicing optometrists' and orthoptists' opinions on the association between age and binocular functions, and secondly, to identify if there was a gap in current knowledge on the association between age and binocular functions among professionals. The objectives of the main study were to measure and analyse the binocular functions in a population of participants aged 10 years to 79 years, and to determine if there were any associations between increasing age and binocular functions.

1.9 Summary and thesis structure

Chapter 1 has introduced the background of this present study, and literature relevant to the main study research. This included a description of EOMs anatomy, physiology, neurological control, as well as an overview of eye movements. The visual cortex and

its role in delivering binocular functions was described. Binocular functions and the clinical tests of binocular functions were discussed, along with a review of the publications relating to the effect of age on these clinical tests.

Chapter 2 will describe the preliminary research investigation and analysis. This preliminary research was undertaken to obtain a better understanding of the level of knowledge of optometrists and orthoptists regarding the association between age and binocular functions. The purpose of the preliminary research was to identify whether there are any gaps in the knowledge of practicing clinicians.

Chapter 3 will describe the main study research methodology along with details of the clinical assessments (equipment and procedure) that were conducted. There will be a description of the research ethics, the recruitment of participants, the consent process and how the sample size was calculated. The inclusion and exclusion criteria will be specified. There will be a discussion on the statistical analysis methods employed to analyse the main study investigation.

Chapter 4 will describe the findings of the investigation into the association between age and stereoacuity as measured by four commercially available stereotests. There will be a discussion on how the findings support or conflict with existing publications, and how the findings from this present study can be applied to clinical practice. There will be a reflection of the strengths and limitations of the present study's investigation into the association between age and stereoacuity.

Chapter 5 will describe the findings of the investigation into the association between age and the other aspects of binocular functions (for example, motor fusion, ocular alignment, ocular motility, NPC). There will be a discussion on how the findings support or conflict with existing publications, and how the findings from this present study can be applied to clinical practice. There will be a reflection of the strengths and limitations of present study's investigation into the association between age and binocular functions.

Chapter 6 will provide a general conclusion to this Doctorate in Ophthalmic Science thesis. In chapter 6, the clinical applications of chapters 4 and 5 will be discussed and contextualised. The overall strength and limitations of the complete thesis work discussed, along with suggestions for future research.

Chapter 2:

Preliminary Research

Chapter 2: Preliminary Research

2.1 Introduction, background and purpose of preliminary research

This chapter describes the preliminary research untaken to guide the direction of the research thesis. The preliminary research evaluated the opinions of practicing optometrists and orthoptists in relation to what were considered to be the normal values of stereoacuity for two age groups. Secondly, the preliminary research investigated whether practicing optometrists and orthoptists considered increasing age to be associated with changes in fusion, convergence, near stereoacuity and distance stereoacuity.

Binocular functions are assessed by clinicians to give information for the diagnosis and management of amblyopia and strabismus, and in the monitoring of monovision contact lens wearing (174). The results from different near stereotests are not comparable because of the design and execution of each stereotest (94, 175). The range of stereoacuity values measured by each test is completely different (1, 174). It has been recommended that near stereotests are not interchanged between assessments on the same patient (94). The similarly designed free-space stereotests (Frisby near stereotest and FD2 distance stereotest), are also not directly comparable, as a result of differing testing distances, differing ranges of stereoacuity measured, and the effects of accommodation and vergence with near stereoacuity measurements (1). The choice of stereotest is often guided by which stereotest is available in clinic, clinic setting (for example, a hospital eye department or a university clinical skills unit, versus a high street optometry practice), the individual preference of the clinician, and the age/comprehension abilities of the patient (for example, a child versus an adult).

There are no specific clinical management guidelines on how to assess binocular functions published by the Irish College of Ophthalmologists, BIOS, or the College of Optometrists. However, the RCOphth “Guidelines for the Management of Strabismus in Childhood” has recommended the measurement of NPC with a RAF rule, and the measurement of stereoacuity via TNO, Frisby, Randot, Lang or the synoptophore (106). It is normal practice for UK and Irish based orthoptists to follow guidelines issued by the RCOphth; as such orthoptists would have access to all stereotests listed in the guideline. To the author’s knowledge, there is no research published on which stereotests are predominantly used in clinical practice by optometrists, or which stereotests are typically available in high street practices, where the majority of optometrists deliver their service. A hospital-based optometrist will work in conjunction with an orthoptist, and therefore, should have access to all stereoacuity tests;

approximately 6% of optometrists work in a hospital clinical environment (176). The College of Optometrists does recommend that the patient's binocular vision is tested, stating it is "an integral part of sight test" (177). The College of Optometrists also recommends that when examining children, ocular muscle balance and stereopsis are to be tested, but does not specify or recommend an explicit assessment method (177).

To the researcher's knowledge there is only one published survey comparing the use of stereotests among UK and Irish orthoptists to North American eye care professionals (175). Therefore, there is a lack of published research which describes the opinions or usage of stereotests among eye professionals. The study reported on the views of 289 UK and Ireland orthoptists and orthoptic assistants and 167 North American professionals (62 ophthalmologists, 50 optometrists, 52 orthoptists and 3 undefined) (175). The questionnaire was only distributed through BIOS to UK participants, but via four professional associations in North America representing the three eye care professions. Despite, the authors additionally using personal links and social media to assist recruitment, the lack of distribution via the College of Optometrists and the RCOphth is probably a reason why the authors were only able to recruit orthoptists and orthoptic assistants, and not optometrists and ophthalmologists to the UK and Irish cohort. Despite this recruitment flaw, the study found that when assessing children aged 3 - 12 years, UK and Irish orthoptists predominantly used Frisby stereotest, followed by Lang stereotest in younger children and TNO stereotest in older children (175). Whereas, among North American eye care professionals, Titmus stereotest was predominantly the only stereotest used (175). Thus, indicating an intercontinental difference in the preferred test of stereoacuity.

The study reported that the choice of stereotest reflected what the clinician considered to be 'best practice' (175). This international difference in opinion may be guided by the intercontinental disparity in ophthalmology colleges' guidelines: the American Academy of Ophthalmology (AAO) recommends using a Randot stereotest (for example, Titmus stereotest) (178) whereas the RCOphth recommends the measurement of stereoacuity via TNO, Frisby, Randot, Lang or the synoptophore (106). The RCOphth guidelines offer the UK-based orthoptist a wider range of stereoacuity tests to choose from in comparison to the AAO guidelines. Despite this endorsed available choice, there is little guidance as to which stereotests are most appropriate in particular age categories.

The intercontinental difference in clinicians' opinions may also be influenced by commercial interests or availability of each stereotest. Frisby and TNO stereotests

were designed in Europe, and the Randot stereotests (for example, Titmus stereotest), were designed and sold via an American company (Stereo Optical Company, Chicago) (94, 175). The FD2 distance stereotest was co-designed by a Professor of Orthoptics and an Emeritus Professor of Physiology based at the University of Sheffield (166). All UK university-trained orthoptists are trained and examined in the use of all commercially available stereoacuity measurement tests (for example, Lang stereotest, Titmus stereotest, TNO stereotest, Frisby stereotest, FD2 distance stereotest and synoptophore) as undergraduates. All UK university-trained optometrists have experience in the use of stereotests as undergraduates, although, they have less exposure than orthoptic students to some stereoacuity tests (for example, FD2 stereotest and the synoptophore). These differences likely represent the difference in the scope of practice between the two professions, with the orthoptists primary role being assessment of ocular motility and binocular functions (including stereopsis), with the optometrists having wider scope of practice, including refractive correction and assessment of ocular health.

This research did not receive any financial support; it was undertaken at the ophthalmology department of University Hospital Galway, where the researcher was in full time employment as a senior orthoptist, using existing resources and hospital equipment. As the research would be performed during the hospital eye departments normal opening hours, there were time costs of the research being performed in lieu of patient examinations. Clinically-based research should benefit patients and clinicians, as the evidence base underpins the appropriate assessment and management outcomes for patients. Therefore, it is important to establish the appropriate research question before a study is designed and ethically approved. A scoping exercise (the preliminary research), was carried out to assess the current understanding of the impact of increasing age on binocular functions by optometrists and orthoptists, and if there was a knowledge deficit requiring further investigation in this field. The preliminary research then aided the design of the main study, so as to answer the set research questions. In the context of this thesis, the research had to be suitable to be performed in a hospital clinic setting, as the researcher is based in a country (Ireland) separate to the university (England).

2.2 Aims of the preliminary research

- To ascertain practicing optometrists and orthoptists' opinions on the association between age and binocular functions.

- To identify whether there is a gap in current knowledge on the association between age and binocular functions.

2.3 Methods of preliminary study

Ethics

Ethical approval was obtained from Aston University Ethics Committee for a questionnaire study (see Appendix 1). The method and process adhered to the tenets of the Declaration of Helsinki. The collection and storage of data followed appropriate data protection regulations as outlined in the Data Protection Act 2018. No personally identifiable information was recorded; only participants' professional background was recorded. Participation in the research was voluntary; there was no payment, nor reimbursement for partaking in the survey. The study purpose was described in the participant information leaflet (PIL) (see Appendix 2), and provided by email along with the survey for those who responded online, and in hard copy for those who responded in person. The PIL stated that by returning the online survey, consent was given. Written consent forms were returned along with the paper version questionnaire.

Participants

An online questionnaire was sent to the orthoptists and optometrists who were professionally known to the primary researcher and for whom the researcher had previously received or sent a work-related email communication. This represented a diverse geographic coverage of Ireland and UK. Previous professional interactions with the researcher included: referrals, education, conferences, professional body representations or other professional roles. The questionnaire was also advertised at a clinical training event for optometrists at Aston University; interested optometrists were provided with a paper version of the questionnaire, the PIL and the consent form. The questionnaires were returned to the researcher along with signed consent forms (see Appendix 3).

Survey

The questionnaire consisted of 10 questions with fixed response options to establish the clinician's opinions of the impact of increasing age on fusion, convergence and

stereoacuity. For the electronic version of the questionnaire, the participant had to select an answer to a question to in order to view the next question. There were two fusion questions, one convergence question and seven stereoacuity questions (based on four stereotests: Titmus, Frisby, TNO and FD2). The questionnaire was designed for the purpose of this study by the researcher, and had not been used in previous research. The questionnaire was approved by the research supervisor, and beta tested for content, clarity and language by the researcher's co- workers in advance of distribution to the target audience. The survey content can be seen below.

****

Survey of Knowledge of Binocular Functions for Optometrists and Orthoptists

Q1 Do you think positive fusion deteriorates with age?

- ☐ Yes
- ☐ No
- ☐ Don't know

Q2 Do you think negative fusion deteriorates with age?

- ☐ Yes
- ☐ No
- ☐ Don't know

Q3 Do you think the near point of convergence deteriorates with increasing age?

- ☐ Yes
- ☐ No
- ☐ Don't know

Q4 What do you think is the 'normal' stereoacuity on Titmus for a 20-year-old?

- ☐ 80 arcsec
- ☐ 60 arcsec
- ☐ 40 arcsec
- ☐ Don't know

Q5 What do you think is the ‘normal’ stereoacuity on Titmus for a 60-year-old?

- ☐ 80 arcsec
- ☐ 60 arcsec
- ☐ 40 arcsec
- ☐ Don’t know

Q6 What do you think is the ‘normal’ stereoacuity on Frisby for a 20-year-old?

- ☐ 85 arcsec
- ☐ 55 arcsec
- ☐ 20 arcsec
- ☐ Don’t know

Q7 What do you think is the ‘normal’ stereoacuity on Frisby for a 60-year-old?

- ☐ 85 arcsec
- ☐ 55 arcsec
- ☐ 20 arcsec
- ☐ Don’t know

Q8 What do you think is the ‘normal’ stereoacuity on TNO for a 20-year-old?

- ☐ 60 arcsec
- ☐ 30 arcsec
- ☐ 15 arcsec
- ☐ Don’t know

Q9 What do you think is the ‘normal’ stereoacuity on TNO for a 60-year-old?

- ☐ 60 arcsec
- ☐ 30 arcsec
- ☐ 15 arcsec
- ☐ Don’t know

Q10 Do you think the distance stereoacuity deteriorates with increasing age?

- ☐ Yes
- ☐ No
- ☐ Don't know

-End of Survey-

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Statistical Analysis

The Chi-square test for association between responses and profession was performed. The Chi-square test aims to establish whether two scenarios are associated, in essence, if one scenario is dependent on another. In this preliminary research it would 'test' if responses were dependent on the profession of the person completing the survey. In cases where the assumptions (see below) of Chi-square test are not met, a Fisher's exact test was performed instead. This analysis was done to determine if the orthoptists and optometrists gave similar responses, and to document where there were any significant differences in responses between the two respondent cohorts. Both the Chi-square test and Fisher's exact test were performed using International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Statistics for Windows Version 23.0 (IBM Corp., NY, USA).

A Chi-square test is an analytical method used to compare the distribution of variable in one cohort with the distribution of the same variable in another cohort (179). If the distribution of a variable is not different between cohorts then it can be concluded that the distribution of variables are not related (179).

The Chi-square test is a 'distribution-free' statistical test that can be used when (180):

- The variable values are nominal or ordinal
- The sample sizes in the study cohorts are unequal
- Data is non-parametric

The following assumptions must be met for a Chi-square test to be an appropriate analysis method (180):

- The data should be numbers rather than percentages or transformed data
- The data is exclusive to one variable, for example, data applied to orthoptist
- Each participant can only give one answer per question
- The cohorts are independent, for example, optometrist versus orthoptist. There is no paired data (does not apply in this situation).
- When there are two variables they are measured in nominal values, however, the data can be interval or ratio data (does not apply in this situation)

Data assumptions were met to allow a Chi-square test to be performed on the difference in responses between the two professional cohorts in relation to positive fusion question and the expected level of distance stereoacuity, where the responses "yes", "no" and "don't know" were the potential answers.

A Fisher's exact test is a method of analysing small samples (179). The following assumptions are required for a Fischer's test to be applied (181):

- The data are in a contingency table 2 x 2
- The variables are independent of each other
- The participants are independent of each other
- Each participant can only give one answer per question
- The row and column totals are given and not random

When the Chi-square assumptions were not met the Fisher's exact test was employed, this was performed on the difference in responses between the two professional cohorts in relation to negative fusion question and NPC question, where the responses "yes", "no" and "don't know" were the potential answers; and the expected level of near stereoacuity using Titmus, Frisby and TNO, this was three numerical values appropriate to the stereotest and "don't know" as fourth option to select.

2.4 Results

Response rate, response time, completion rate

The questionnaire survey was distributed to 92 optometrists (67 via email and 25 in person) and 88 orthoptists (all via email). The email with the link to the SurveyMonkey® site was sent on 30th October 2017. By 19th December 2017 there

had been 44 professionals who had opened the questionnaire link, all orthoptists, 39 orthoptists completed the online survey, and 5 opened the survey but did not complete any of the questions or consent to enrolment. The average response time reported by SurveyMonkey® was 74 seconds. There was then a leave of absence approved by Aston University, and the research activity paused for 19 months. Following this leave of absence it was decided that the questionnaire would be also advertised at an educational event day for optometrists at Aston University in September 2019. The survey and PIL were distributed in person to 25 optometrists at the beginning of the day event, and optometrists were advised to leave their completed responses with the University lecturer. By the end of the event day, all 25 optometrists had returned the paper version of the survey and the consent forms. The time to complete the paper version of the survey was unknown. All questions in the paper questionnaire had been answered by all 25 respondents.

Therefore, preliminary research results were based on 25 optometrist responses and 39 orthoptist responses. Overall the response rate was 36%, the response rate was 27% optometrists (100% response from in person recruitment versus 0% from email recruitment) and 44% orthoptists (from email recruitment only). There was a 100% completion rate; all respondents completed all 10 questions.

Based on the 2021 registrants of the General Optical Council (GOC) UK, Health and Social Care Professionals Council (CORU) Ireland there are 17, 394 registered optometrists. Whilst the number of registrants may have changed minimally over the last 3 years, the researcher estimates that this survey represents 0.14% of the total population of registered optometrists. Similarly, in 2021 BIOS had 1421 active members, therefore the researcher estimates that this survey represents 2.74% of the total population of practicing orthoptists (Nota Bene: orthoptists in Ireland are not state registered, therefore, the professional body membership gives a better estimate of the number of practicing orthoptists, as insurance for orthoptic practice is exclusively provided by BIOS).

Fusion

The respondents were asked whether positive and negative fusion deteriorates with increasing age. The majority of orthoptists responded that there was an association between increasing age and positive fusion, and between increasing age and negative fusion (21/39 (54%) and 16/39 (41%), respectively). Therefore, the prevailing opinion

was that, as age increases motor fusion deteriorates. However, the majority of optometrists responded 'don't know' to the fusion questions (15/25 (60%) for both positive and negative fusion questions) (see Figure 2.1).

Regarding the association between positive fusion and age, there was a statistically significant difference in the responses from orthoptists and optometrists (Chi-square $p \leq 0.001$). With regard to the association between negative fusion and age there was again a statistically significant difference in the responses from orthoptists and optometrists (Fisher's test $p < 0.05$).

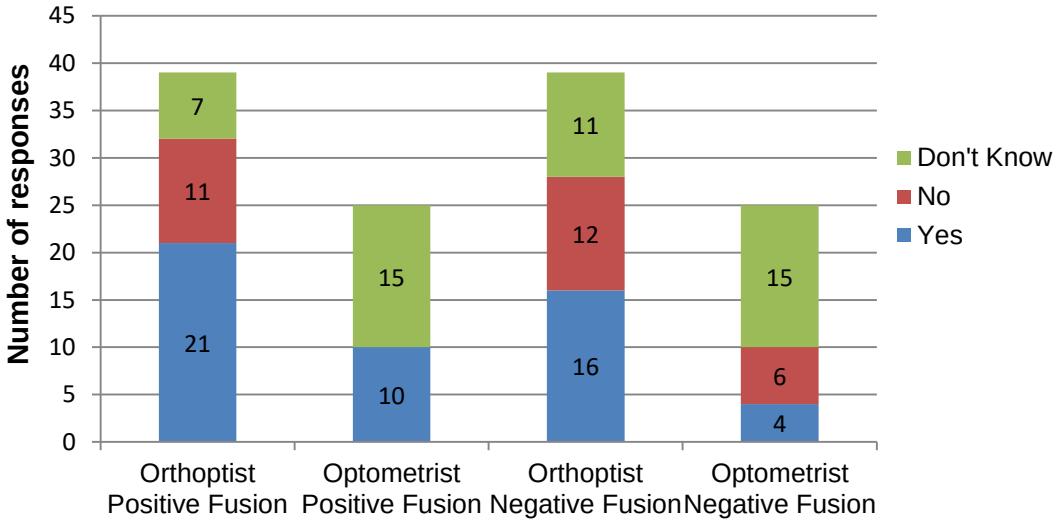


Figure 2.1 Responses to the survey questions on the association between age and motor fusion. Questions set were:

Q1 Do you think positive fusion deteriorates with increasing age?

Q2 Do you think negative fusion deteriorates with increasing age?

Convergence

The respondents were asked whether NPC deteriorates with increasing age. The results from both professional cohorts, indicated a strong preference to the view that there was deterioration in the NPC with increasing age (total population 45/64 (70%), orthoptists 25/39 (64%), optometrists 20/25 (80%)). However, 13/39 (33%) orthoptists responded that there was not a decline in NPC with increasing age versus 2/25 (8%) of

optometrists (see Figure 2.2); this finding lead to a statistically significant difference in the responses from orthoptists and optometrists (Fisher's test $p < 0.05$).

The survey question relating to NPC had the least number of 'don't know' responses when compared to the other survey questions. Only 1/39 (2%) of orthoptists and 3/25 (12%) of optometrists responded that they 'don't know' the effect of age on NPC (see Figure 2.2). Indicating that both professions were confident in their opinions on NPC.

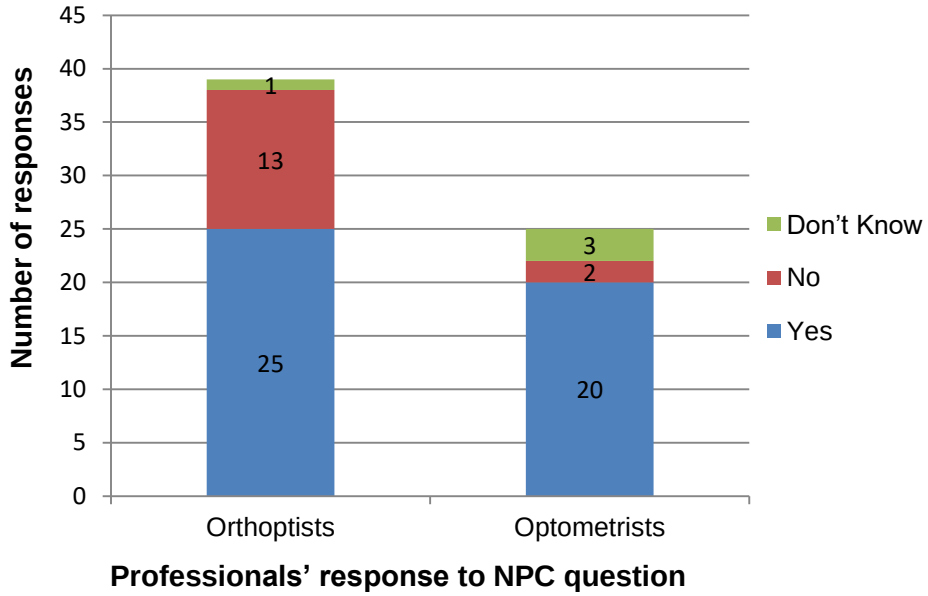


Figure 2.2 Responses to the survey questions on the association between age and NPC. Question set: *Do you think the near point of convergence deteriorates with increasing age?*

Distance Stereoacuity

The respondents were asked whether distance stereoacuity decreases with increasing age, both professions showed a high number of participants responded with 'don't know' (total population 31/64 (48%), orthoptists 23/39 (59%), optometrists 8/25 (32%)). Additionally, the responses from the optometry profession were nearly equally split (yes = 10, no = 7, don't know = 8), indicating a greater distribution in responses (see Figure 2.3). There was no statistically significant difference in the responses from orthoptists and optometrists for this survey question (chi-square $p = 0.11$).

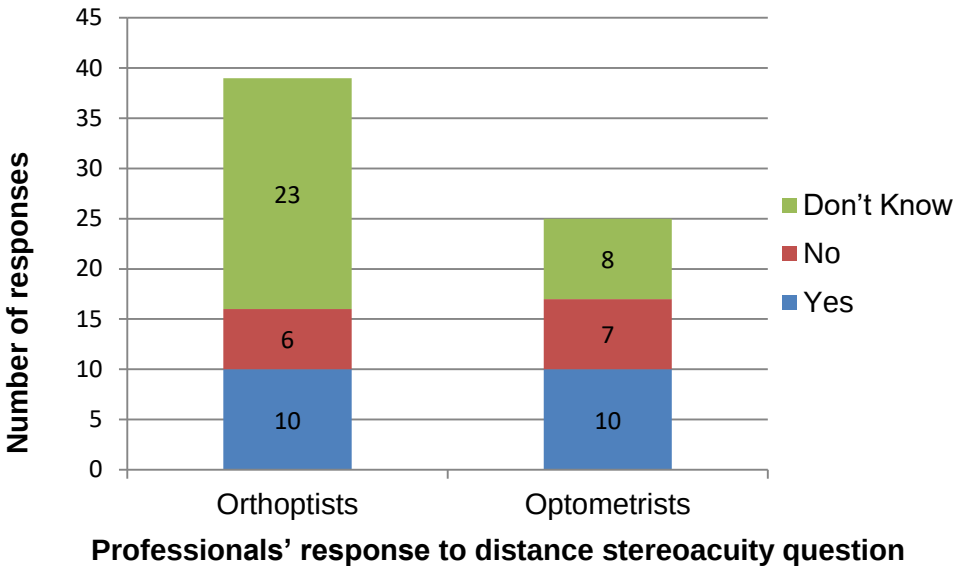


Figure 2.3 Responses to the survey questions on the association between age and distance stereoacuity. Question set: *Do you think distance stereoacuity deteriorates with increasing age?*

Near Stereoacuity

The respondents were asked about the expected near stereoacuity value using different stereotests (Titmus, Frisby and TNO) in a 20-year-old and a 60-year-old. The results, when both professions are considered together, did not indicate that professionals consistently responded that near stereoacuity was expected to be better in a 20-year-old than in a 60-year-old.

Titmus stereotest

The results showed that 20/39 (51%) orthoptists believed a 20-year-old should achieve the maximum stereoacuity on Titmus stereotest (40 arcsec). Whereas, only 9/39 (23%) orthoptists believed a 60-year-old would achieve this level of stereoacuity, and instead the majority 17/39 (44%) believed it would be 60 arcsec (see Figure 2.4). The majority of optometrists also believed that a 20-year-old should achieve the maximum stereoacuity of 40 arcsec (14/25 (56%)); but 'don't know' was the most frequent response to the level of stereoacuity for a 60 year old (10/25 (40%)) (see Figure 2.4).

The responses for Titmus stereoacuity expected for a 20-year-old were not dependent on profession (Fisher's test p = 0.12). The responses for stereoacuity expected for a 60-year-old were dependent on the profession (Fisher's test p < 0.01), probably a reflection of the higher number of optometrists compared to orthoptists replying 'don't know' to the expected stereoacuity value.

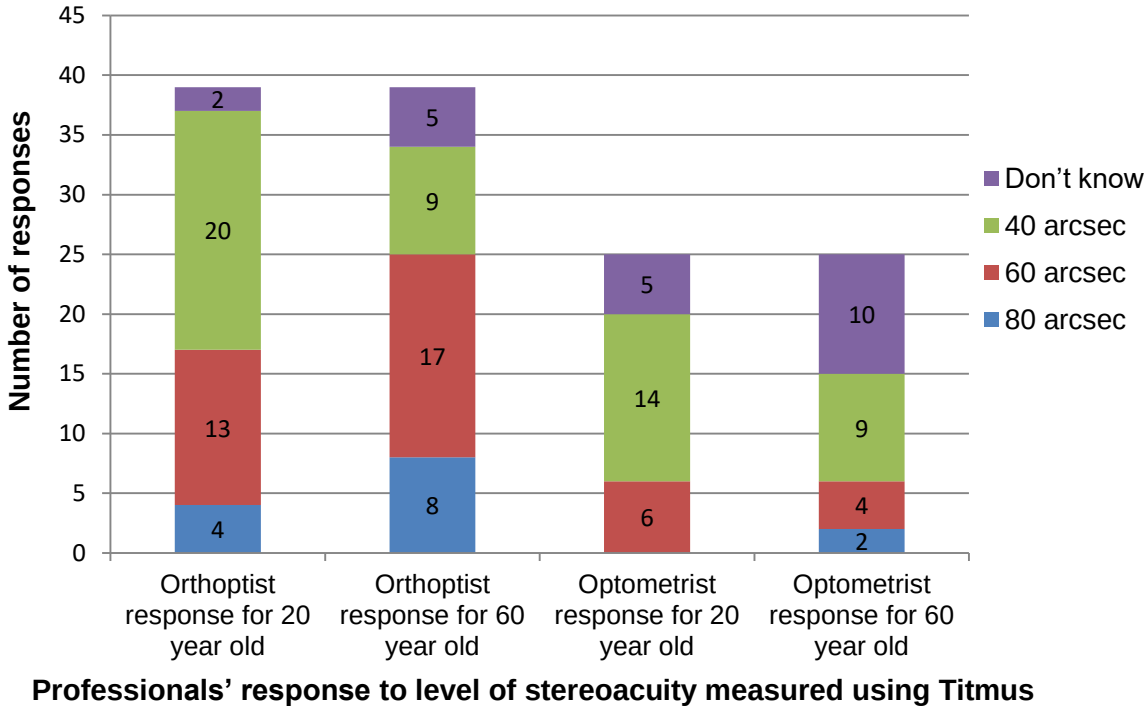


Figure 2.4 Responses to the survey questions on the association between age and near stereoacuity measured with Titmus stereotest. Questions set:

Q1 What do you think is the normal stereoacuity on Titmus for a 20-year-old?

Q1 What do you think is the normal stereoacuity on Titmus for a 60-year-old?

Frisby stereotest

The results showed that 10/39 (26%) orthoptists believed a 20-year-old should achieve the maximum stereoacuity on Frisby stereotest (20 arcsec), whereas, only 2/39 (5%) orthoptists believed a 60-year-old would achieve this level of stereoacuity. Instead, the majority of orthoptists believed that both a 20-year-old and a 60-year-old should achieve 55 arcsec (17/39 (44%) for both age questions) (see Figure 2.5). This was also the opinion of optometrists, 16/25 (64%) believed a 20-year-old would achieve 55 arcsec and 12/25 (48%) believed a 60-year-old would achieve 55 arcsec. Therefore,

the most frequent response from both professions for expected stereoacuity value for a 20-year-old was 55 arcsec (52% total population, 44% orthoptists, 64% optometrists).

There was a nearly equal response frequency of 'don't know' from both professions to Frisby questions (orthoptists 15/78 and optometrists 16/50), although, this is a greater percentage of the optometry responses as their cohort size is smaller (orthoptists 19% and optometrist 32%)

The responses from the professionals regarding the expected stereoacuity value for a 20-year-old using Frisby stereotest showed a statistically significant difference to each other (Fisher's test $p < 0.05$). Whereas, there are no statistically significant difference in the professionals' responses for the question of expected stereoacuity value for a 60-year-old (Fisher's test $p = 0.45$); again probably a reflection of the higher number of both professionals who answered "don't know".

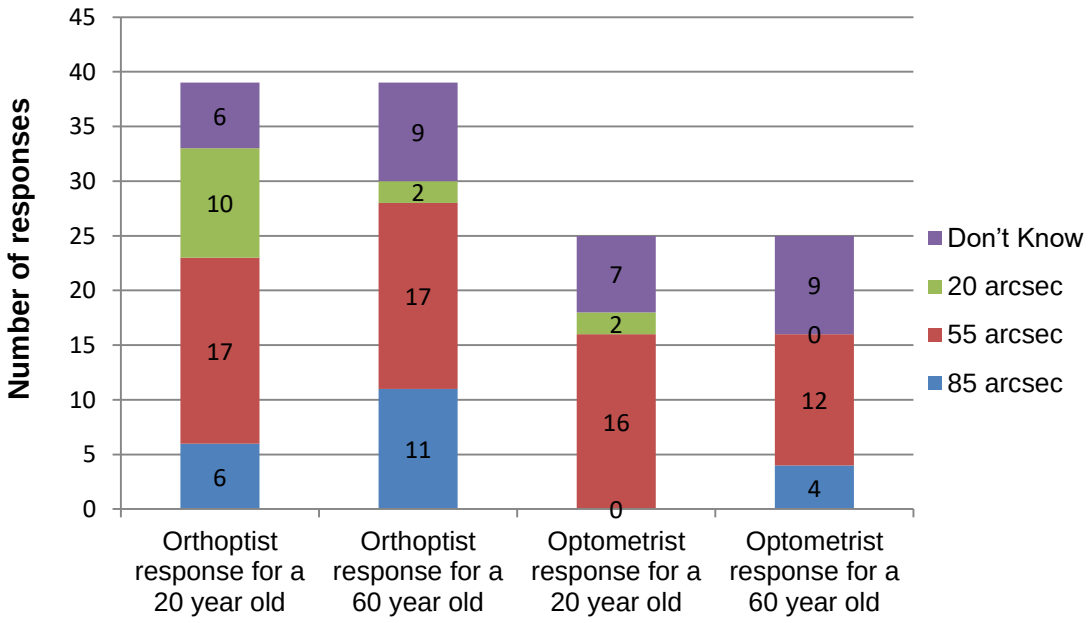


Figure 2.5 Responses to the survey questions on the association between age and near stereoacuity measured with Frisby stereotest. Questions set:

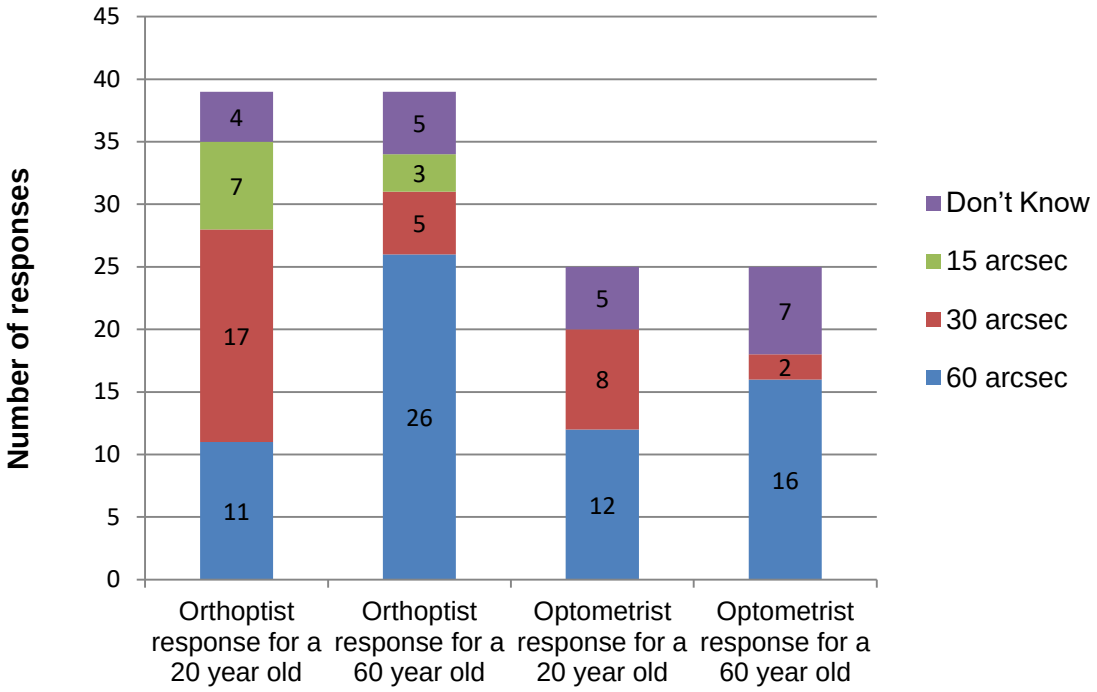
Q1 What do you think is the normal stereoacuity on Frisby for a 20-year-old?

Q1 What do you think is the normal stereoacuity on Frisby for a 60-year-old?

TNO stereotest

The results showed that 7/39 (18%) orthoptists believed a 20-year-old should achieve the maximum stereoacuity on TNO stereotest (15 arcsec). Whereas, only 3/39 (8%) orthoptists believed a 60-year-old would achieve this level of stereoacuity. Instead, the majority of orthoptists believed that a 20-year-old should achieve 30 arcsec (17/39 (44%)) and that a 60-year-old should achieve 60 arcsec (26/39 67%) (see Figure 2.6). In contrast, the opinion of optometrists showed majority believed that both a 20-year-old and a 60-year-old would achieve 60 arcsec (20-year-old 12/25 (48%), 60-year-old 16/25 (64%)). There was a greater response frequency of 'don't know' from optometrists for both age questions than from orthoptists (orthoptists 9/78 (12%) and optometrists 12/50 (24%)).

The responses from the professionals regarding the expected stereoacuity value for a 20-year-old using TNO stereotest showed a statistically significant difference between professions (Fisher's test $p < 0.05$). Whereas, there were no statistically significant difference in the professionals' responses for the question of expected stereoacuity value for a 60-year-old (Fisher's test $p = 0.32$), this probably reflects that the most frequent response from both professions of the expected stereoacuity value for a 60-year-old was 60 arcsec (66% total population, 67% orthoptists, 65% optometrists).



Professionals' response to level of stereoacuity measured using TNO stereotest

Figure 2.6 Responses to the survey questions on the association between age and near stereoacuity measured with TNO stereotest. Questions set:

Q1 What do you think is the normal stereoacuity on TNO for a 20-year-old?

Q1 What do you think is the normal stereoacuity on TNO for a 60-year-old?

2.5 Discussion

The aim of this preliminary research was to gain a better understanding of the current professional knowledge and views on the association between age and binocular functions.

From the small sample surveyed, the results confirmed that there was a gap in knowledge for both cohorts of professionals regarding any association between age and fusion and between age and stereoacuity. In addition, there was disagreement between eye care professionals regarding the impact of increasing age on fusion and on stereoacuity. To the author's knowledge there are no other studies of clinicians' opinions on the association between age and binocular functions, nor what clinicians' report as the normative value of stereoacuity with various stereotests, with which to

compare this survey. From a clinical perspective, this may mean that clinicians are unsure what are normative values, and what are abnormal values of fusion and stereoacuity in older patients. Conversely, the effect of age on NPC, which has been studied and published extensively by both professions, was confidently understood by all the surveyed clinicians, and had the lowest number of 'don't know' responses (4/64 (6%)). This finding supports the need for further research into the impact of age on fusion and age on stereoacuity, and to ensure that the research findings are disseminated to both professions.

In retrospect, personal details regarding age of participant, level of academic achievement (degree versus postgraduate level qualification), number of years of experience, current role description (e.g. hospital based versus high street based optometrist and traditional orthoptic role versus extended role orthoptist), and their National Health Service (NHS) banding level for those employed by the NHS should have been recorded, as any of these may have been confounding variables.

Another study limitation was selection bias. Orthoptists were selected to receive the survey via email based on a professional email database (including all orthoptists in the Republic of Ireland and a subset of those in the UK), and therefore all participants were professionally known to the researcher. Email surveys to optometrists where also based on the professional email database (mix of Irish and UK optometrists), however, this received zero responses. The researcher did not send reminders to complete the survey, or offer an incentive (i.e. a prize), and either may have encouraged more professionals to complete the survey. By using the researcher's professional email database, the researcher had hoped the 'personal touch' would encourage participation; however, on reflection the researcher should have used networks available via BIOS and the College of Optometrists to approach a larger pool of both optometrists and orthoptists. In order to have data from optometrists for comparison with orthoptist survey responses, the surveys were then carried out in physical format via the research supervisor's teaching activities, and therefore this targeted approach to recruitment may have created a volunteer bias. Consequently, the results cannot be generalized to the whole optometric population. On reflection, the selection and volunteer biases combined with the small sample size, may have potentially influenced the ratio of responses between professionals and thus the outcome of this preliminary research.

Whilst the survey was piloted, it was with work colleagues of the researcher, and this may have caused bias as they had prior knowledge of the aim of the survey and the

researcher's motivations. However, none of the researcher's work colleagues took part in the preliminary research, and therefore would not have directly influenced the results.

It is also possible that respondents may have used internet search engines to search for the answer to the survey questions. The researcher tried to overcome this by choosing two specific ages (i.e. a 20-year-old and a 60-year-old), which the researcher felt was less likely to give an easy response from an internet search. The researcher wanted to compare opinions of what is expected from a young patient versus an older patient; while, any two ages could have been chosen, the researcher chose a 20-year-old as this represents a young adult. Equally, the researcher could have chosen any age from 18 (legal adult age) to mid-40s (as ≥ 40 years is commonly associated with changes in vision due to presbyopia). Similarly, the researcher could have picked any age ≥ 60 years, but was conscious that normal age related vision changes from cataracts or age related macular degeneration are commonly found in patients older than 60 years. Again the researcher did not want to influence the answers from the participants, and therefore age 60 years was chosen.

As the researcher had undertaken a literature review on the effect of age on binocular functions before writing the preliminary research survey, it influenced the phrasing of the survey questions. As the researcher was aware that there was a lack of normative data published, the questions were phrased "what do you think is the normal stereoacuity…." rather than "what is the normal stereoacuity". The researcher was aware of published results on the effect of age on mean/median values, and of the potential stereoacuity values for each stereotest. This information informed the fixed response options used in the survey, i.e. the numerical stereoacuity values for Titmus, Frisby and TNO were all different and specific to that test; this potentially influenced the responses. An alternative would have been to have asked the participant to give a value or write 'don't know', rather than select from a list of improving stereoacuity values.

To the author's knowledge, there are no publications detailing the stereotests predominantly used by UK/Irish optometrists, or which stereotests are commonly found in non-hospital based optometry practices. However, orthoptists and optometrists do tend to work in different environments, for example orthoptists are predominantly based in hospital ophthalmology departments whereas optometrists are predominantly based in primary care settings (i.e. high street practices). This difference in working environment might influence what equipment the professional has experience with, and

therefore, their knowledge of the results expected with the stereoacuity tests named in this survey.

2.6 Conclusions

Reflecting on the survey nearly four years after it was conceived and distributed online, the researcher can appreciate several design flaws. As the thesis is critically studied, there is evidence of growth in the knowledge and skills of the researcher. For future work which involves measuring and evaluating health (i.e. patient reported outcomes), the researcher would bear in mind the reflections on this survey, and approach the undertaking of a survey differently.

However, despite the survey's flaws, the preliminary research helped formulate the research question for the main study and hypotheses. The preliminary research did demonstrate a knowledge gap, thus clarifying the need for further research and analysis, to guide best practice for ophthalmic practitioners. Orthoptists were shown to have less uncertainty than optometrists regarding the association between age and binocular functions. This was an expected finding and a reflection in the difference in the scope of practice between the two professions; orthoptists' primary role is the assessment of ocular motility and binocular functions (including stereopsis), and traditionally orthoptists work in amblyopia and strabismus clinics.

2.7 Summary/Key points

Two areas were identified with the highest absence of knowledge amongst optometrists and orthoptists:

- Association between age and fusion
- Association between age and distance stereoacuity

The information from this preliminary research influenced the design of the subsequent experimental chapters. There will be an experimental chapter on the association between age and stereoacuity (see Chapter 4), and an experimental chapter on the association between age and other binocular functions (including fusion) (see Chapter 5).

Chapter 3: Main Study Methods

Chapter 3: Main study methods

3.1 Introduction

From the small sample surveyed, the results of the preliminary research confirmed that there was a gap in knowledge for eye care professionals regarding any association between age and fusion, and between age and stereoacuity. This clarified the need for further research and analysis regarding normative values to guide best clinical practice. It could be argued that the first step to improve knowledge in this field would be to obtain normative values of fusion and stereopsis for various age groups, and in particular older age groups. Although there are studies which have provided normative ranges or proposed typical values for stereoacuity, these studies tend to be biased towards school-aged children and university enrolled students and staff. This cross-sectional study aimed to evaluate the association between age and binocular functions in a wider age population.

This chapter includes a description of the research ethics, the methods used to recruit participants and the inclusion/exclusion criteria applied. There is a description of the clinical procedures used to assess vision, ocular alignment, ocular refraction, ocular movements, NPC, fusion and stereoacuity. The literature regarding normative data and the association of clinical tests with increasing age were described in Chapter 1.

3.2 Aims of main study

- To evaluate any changes in stereoacuity, measured by four commercially available stereotests, associated with increasing age, for both near and distance.
- To evaluate any changes in positive and negative fusion associated with increasing age, for both near and distance.
- To evaluate any changes in vertical fusion associated with increasing age, for both near and distance.
- To evaluate any changes in NPC associated with increasing age.
- To evaluate any changes in ocular motility associated with increasing age.
- To evaluate any changes in ocular alignment associated with increasing age.

3.3 Research Ethics

The study received ethical approval from the Research Ethics Committees at Aston University and University Hospital Galway (UHG) (see Appendices 4 and 5). The methods and processes adhered to the tenets of the Declaration of Helsinki. Collection and storage of data followed the correct data protection protocols as outlined in the Data Protection Act 2018. Only the researcher had access to the research database which could identify the participants' names and ages; this was kept on an encrypted hospital computer. Participation in the research was voluntary; there was no payment for enrolment. The researcher did not have any financial or proprietary interest in any of the products used in this study.

3.4 Recruitment of Participants

Participants were initially recruited through advertisement posters located within UHG and an adjacent community health centre. The advertisement campaign began on 1st January 2016 and ceased 26th August 2019. The advertising campaign was shared with five local optometry practices (four independently owned practices and one large franchise outlet) to increase the participant recruitment pool. This campaign proved unsuccessful at recruiting participants (i.e. no participant was recruited via this method). The primary researcher presented the research project to two local active retirement clubs in August 2019. This approach was a successful method of recruiting participants (i.e. the majority of the participants over the age of 60 years were recruited by this method). Participants included members of the public, parents of children attending orthoptic clinics and staff members of UHG or the local health centre who were unfamiliar with an orthoptic examination.

All participants made initial contact with the primary researcher using contact methods outlined in the advertisement media (see Appendix 6). During the initial contact, the purpose of the research study was outlined and suitability for participation was determined through responses to questions relating to exclusion criteria (see section 3.7). A mutually suitable time was arranged to facilitate participation in the research study. Participants were electronically sent confirmation of their appointment date, time, and location along with a copy of the PIL (see Appendix 7). For participants younger than 16 years, a parent information leaflet and a child information leaflet (see Appendices 8 and 9) were provided via email. The child information leaflet was specifically written with images of the apparatus and tests used, so the child would have an understanding of what would take place on the day of the appointment. As per

UHG Ethics Committee instructions, the child information leaflet was approved by the UHG paediatric specialist speech and language therapist. The aim of sending the email was to ensure that there was an understanding of the research purpose and procedure before the scheduled appointment.

3.5 Informed Consent

Information relating to the purpose of the study, willingness to participate and their suitability for the study was again discussed with all participants at the start of their scheduled appointment. Time was given for questions, following which both the researcher and participant co-signed and dated the consent form (see Appendix 10). For participants aged under 16 years, written assent was additionally required. All information relating to the purpose of the study was discussed with the child using age appropriate language to confirm their willingness to participate, following which the primary researcher, the participating child and the parent/guardian co-signed and dated the consent form (see Appendices 11 and 12).

3.6 Sample size

The calculation of a sample size using a statistical software programme is dependent on the information provided for the calculation. While it does not calculate a definitive sample size, it gives an estimate of the number of participants required to make a study statistically 'powerful'. G*Power is a power analysis statistical program developed by the Institute for Experimental Psychology in Dusseldorf, German (182). Using the G*Power 3 ANOVA (fixed effects, omnibus and one-way), with 7 cohorts, a medium effect size (f = 0.25), 80% power and p-value of 0.05, the sample size calculated would be 231 participants. A sample size of 231 participants would be significantly different/ larger than the previous publications with similar designs; which had 120 participants (96), 80 participants (2), 79 participants (120), and 60 participants (113). If information is added on G*Power regarding the proportion of total variation in the data attributed to differences among age decades, for example, a medium sized eta square of 0.6, then the required sample size reduces to 21 participants.

The effect size is the strength of the relationship between two variables; there is a range to describe the effect size (for example, very small, small, medium, large, very large, huge) (183). A medium effect size is generally used by researchers and has a

range of 0.2 – 0.5 (183). By increasing the effect size to the larger end of the scale, for example, f = 0.45, the sample size calculated is 77 participants (see Appendix 13); this produced 65 degrees of freedom. It is recommended that there should be a minimum 15 degrees of freedom when designing an experiment (184); when the degrees of freedom are > 20 (as with this study), then the difference between the variables (for example, age and stereoacuity value), for a given level of significance and a given error mean square requires fewer participants than if the degree of freedom was < 10 (184).

For a sample size of 77, in order to have an equal number of participants in each age cohort, there would need to be 11 participants per cohort. The age cohorts were 10 - 19 years, 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, 60 - 69 years and 70 - 79 years. A post hoc analysis was performed using G*power to check for the power of the study. The power of a study represents its precision; power calculations stop errors arising from too large or too small a sample size. Generally, a power of 0.80 (80%) is the conventionally accepted (185). This means there is an 80% chance of detecting a difference as statistically significant, when a true difference exists. The post hoc analysis showed a power of 82% (see Appendix 13).

3.7 Inclusion criteria

- Aged 10 to 79 years.
- Any gender.
- From any ethnic group.
- Able to achieve a visual acuity of 0.10 LogMAR in each eye for near and distance, with spectacles/contact lenses if worn.
- Able to provide informed consent.

3.8 Exclusion Criteria

The following conditions caused exclusion from the study.

- Previous history of amblyopia treatment or a childhood or acquired strabismus.
- Latent deviation (horizontal or vertical) measuring more than 15^{Δ} (whilst wearing spectacles or contact lenses).
- Previous history of eye surgery (except phacoemulsification with monofocal intraocular lens, eyelid surgery, dry eye surgery).

- Unable to achieve 0.10 logMAR in each eye for near and distance, with spectacles/contact lenses if worn.
- Currently suffering from any acute physical or psychiatric illness.
- Participants (or parent/guardian) unable to give informed consent/assent.
- Any condition affecting ocular motility, whether
    - Neurological (for example, transient ischemic attack, stroke, multiple sclerosis).
    - Myogenic (for example, thyroid eye disease, myasthenia gravis, chronic progressive external ophthalmoplegia).
    - Mechanical condition (for example, blow out orbital fracture, Brown's syndrome, Duane's syndrome).
- Currently pregnant or less than one-year post-partum.
- Ophthalmic-trained professionals.

3.9 Equipment and Procedure

The study was conducted in the ophthalmology department at UHG. UHG is a Level 4 hospital in the west of Ireland with a catchment population of approximately 1 million people. The ophthalmology department is the main surgical eye unit for the Trust, with over 30,000 patient activities (out-patient and in-patient) per year. All data were collected by the author, a fully qualified and experienced senior orthoptist, using the same standardised examination parameters (for example, room, lighting levels, equipment and test set up) throughout the data collection periods (1st January 2017 - 1st December 2017 and 1st January 2019 - 30th August 2019). The illuminance measurement from the participant's chair at eye level was 214lux; illuminance was measured using a RaySafe X2 Light Senor, serial number 272446 (calibrated by UHG medical physics and clinical engineering department annually). The order of the tests was the same for each participant, and followed the order of tests on the data collection record (see Appendix 14). All data was recorded on the data collection record. All equipment was up to date with annual servicing with the hospital medical engineering department in advance of data collection.

Vision Assessment

Increasing age is associated with reducing visual acuity due to the impaired optical media clarity/quality of the eye, (for example, from cataracts, glaucoma, and

maculopathy) (186, 187). The vision or visual acuity (with the current refractive correction) assessment was performed to confirm the participants met the inclusion criteria and were eligible for the study. Any volunteer who did not have 0.1 logMAR vision or visual acuity with their current spectacles would not have been eligible to be a participant in the study.

Bailey-Lovie vision charts

Using the Bailey-Lovie (BL) logMAR chart (Precision Vision, Woodstock, IL, USA), the distance vision or visual acuity was measured monocularly. The BL chart (see Figure 3.1) uses a logarithmic progression of optotypes, with each line of letters decreasing/increasing in equal steps by a factor of 1.2589 (188). MAR is the minimum angle of resolution which expresses the angular size of the optotype (189). There are five optotypes per line, with the same number of optotypes on every line (188). There is an equal spacing between the optotypes, with the spacing proportional to the optotype size (190). On the logMAR scale, 0.0 corresponds to a 6/6 or 20/200 Snellen equivalent (190). Each optotype (letter) corresponds to 0.02 logMAR, this letter-by-letter scoring increases sensitivity allowing for a more precise vision recording (190). The chart follows the British Standards Institute recommendations that letters should be non-serif, on a framework that is 5-units high and 4-units wide, with the optotype limbs being 1-unit wide (190). The letters are reported to have similar legibility (190). The chart instructions state that three of the five optotypes must be read correctly to progress to subsequent smaller optotypes size (i.e. the next line) (188). The BL chart is designed for use at 6 m but can be converted for use at any testing distance (for example 1 m, 2 m, 4 m). The Snellen chart was not used to measure vision due to its inconsistencies including: optotype selection, font style, unequal number of letters per row, unequal spacing between letters and the unequal row progression (189); the LogMAR chart is the standard for scientific research.

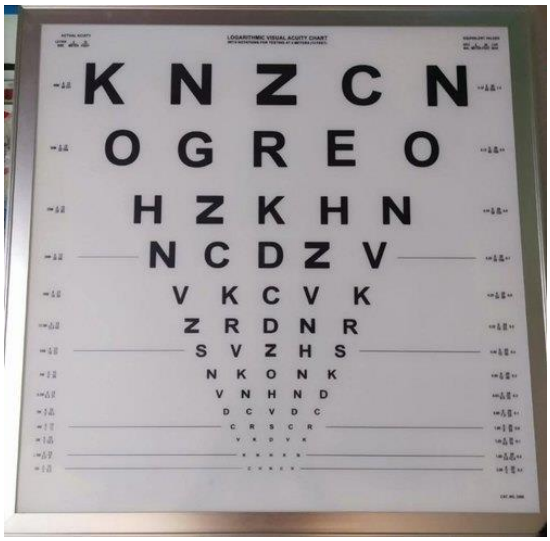


Figure 3.1 Bailey-Lovie LogMAR chart (Precision Vision, Woodstock, IL, USA)

Using the BL word reading chart (Precision Vision, Woodstock, IL, USA) (see Figure 3.2) the binocular and then monocular near vision or visual acuity was measured. The binocular assessment was to illustrate the natural reading capability of the participant. A word chart was chosen as reading words is regarded as a more complex visual function than reading individual letters (191). The BL word reading chart uses a logarithmic size progression (ratio = 1.26) to display unrelated four, seven and ten letter words twice per line, using Times New Roman serif (190, 191). The test is performed at 25 cm.

Figure 3.2 Image of the Bailey-Lovie Word Reading chart (Precision Vision, Woodstock, IL, USA)

Figure 3.3 Romanes Occluder (Haag-Streit, Harlow, UK)

Procedure for assessing distance vision and visual acuity

If a participant habitually wore spectacles for distance viewing, the monocular vision (right eye first) was tested before visual acuity. For participants who did not use distance spectacles the researcher pointed to the 0.10 logMAR line on the BL chart and asked the participant to commence reading from this line; there was no further pointing. A Romanes occluder (Haag-Streit, Harlow, UK) was used for the monocular vision/acuity assessments (see Figure 3.3). For participants who normally wore spectacles, their monocular vision (right eye first) was assessed before the visual acuity, with the participant asked to read the chart from the largest letters visible to them. The reason for commencing from the top of the chart was to prevent memorisation of optotypes. The participant was then tested with their spectacles with the researcher pointing to the 0.10 logMAR line for the participant to commence from that point, again commencing right eye first. The test was performed at 4 m. Each correct optotype on the line was noted for recording the acuity, the participant needed to correctly read three optotypes per line before progressing to the next line. When the participant had difficulty reading an optotype, he or she was encouraged to guess and to attempt all optotypes on the entire line. Using a manual Topcon focimeter (CL300, Topcon Corp. Tokyo, Japan), any spectacle prescriptions for distance were measured and recorded.

Procedure for assessing near vision and visual acuity

If a participant habitually wore a spectacle correction for near tasks, this was used for the near visual acuity assessment. The binocular near vision or visual acuity was tested before the monocular vision or visual acuity (right eye tested first for monocular

assessment); a Romanes occluder was used for the monocular assessments. The researcher pointed to the 0.10 logMAR line on the BL word reading chart and asked the participant to commence reading from this line; there was no further pointing. The test was performed at 25 cm. Each correct word on the line was noted for recording the acuity, the participant needed four words correct to be awarded that line of acuity and progress to the next line. When the participant had difficulty reading a word, they were encouraged to guess and to attempt all the words of that size (i.e. on the same line). Using a manual Topcon focimeter (CL300), any spectacle prescriptions used for near were measured and recorded.

Whilst typically an optometrist will calculate the reading addition based on a working distance of 40 cm, the Frisby stereotest testing distance commences at 30 cm and therefore, at the research design stage it was decided to select a reading test that would both ensure the participant had sufficiently clear vision at 30 cm and record vision/visual acuity in LogMAR unit.

Procedure for assessing ocular alignment

To elicit the presence of any latent deviation (phoria), an alternating cover test was performed with and without the participant's spectacles. This was performed by the participant fixating on a target at 1/3 m and at 6 m (Snellen stick and Snellen chart respectively), and one eye being covered using the Romanes occluder (Haag-Streit, Harlow, UK), which was then moved alternately between the eyes, ensuring complete dissociation. Movement of the uncovered eye was noted as the occluder was moved to the fellow eye. If no movement was seen, an orthophoria response was documented. If a temporal movement of the eyes was seen, then an esophoria was documented. If a nasal movement of the eyes was seen, then an exophoria was documented. If a vertical movement of the eyes was seen, then the eye which was hyperphoric (i.e. the eye which moved downward), was documented. If a vertical heterophoria was found, a Bielschowsky head tilt test was performed. The Bielschowsky head tilt test is part of a normal orthoptic clinical examination in all patients with a vertical heterophoria or heterotropia (132, 192). A Bielschowsky head tilt test is positive for a unilateral superior oblique palsy when the vertical heterophoria size increases on head tilting to one shoulder (i.e. the same side as the paretic muscle), and then decreases on head tilting to the other shoulder (99). For example, a left hyperphoria which increases in size on head tilt left, and decreases in size on head tilt right, indicates a left superior oblique palsy. Therefore, a positive Bielschowsky

head tilt test can confirm the presence of a superior oblique palsy. The speed at which binocularity is recovered after removal of the occluder was documented, for example, rapid or slow recovery.

For this test, the participant fixated on the 6/18 letter O on both the 6 m Snellen vision chart (Haag-Streit, Harlow, UK) and 1/3 m Snellen fixation stick (Haag-Streit, Harlow, UK) (see Figure 3.4); this optotype size is equivalent to 0.5 logMAR. The participant was asked to maintain a steady head position in primary position. If the participant was unable to view clearly the 6/18 size target without their spectacles, a larger target that could be seen clearly was used. If the participant was unable to see the 6/60 size letter on either the near or distance Snellen chart (Haag-Streit, Harlow, UK) then the test was not performed. Any latent deviation found on the alternating cover test was measured using the Clement Clarke prism bar (Haag-Streit, Harlow, UK) held in the frontal position (see Figure 1.6). This measurement was acquired by placing a prism of increasing strength, in the appropriate orientation (for example, base in for an exophoria, or base out for an esophoria), whilst performing an alternating cover test, until there was no longer a fixation movement in either eye. Standard orthoptic practice for UK trained orthoptists, is for the prism strength to be increased until a reversal movement is seen, and then prism strength reduced, with this prism power recorded as the magnitude of ocular deviation/heterophoria.

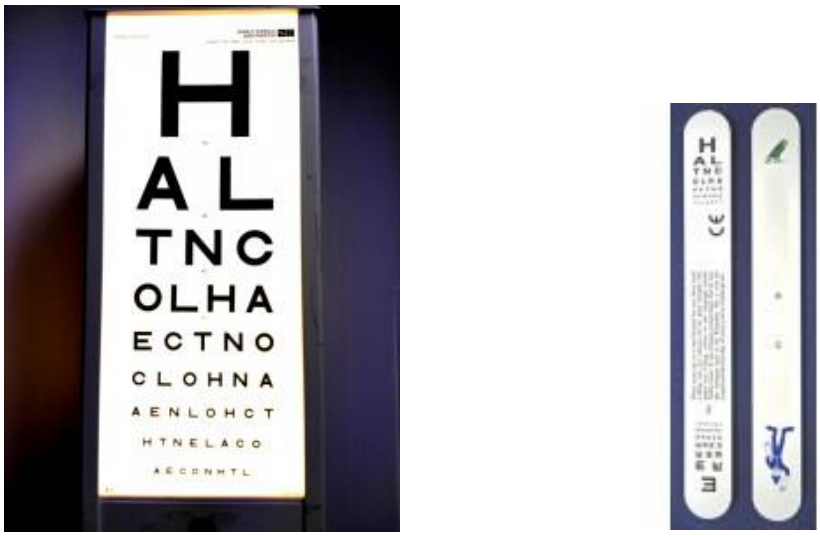


Figure 3.4 Left: Snellen vision chart (Haag-Streit, Harlow, UK) Right: Snellen fixation stick (Haag-Streit, Harlow, UK).

Procedure for assessing ocular movements

The actions of the EOMs were assessed via conjugate movements of the eyes together (versions), and by movements of the eyes considered individually (ductions) using the BIOS standardised clinical method (60). Ductions and versions were assessed in the eight positions of gaze (see Figure 3.5). The version movements of the eyes were tested binocularly using a spotlight. Without spectacle correction, the participant followed a spotlight held at 40 cm from primary position into each of the eight cardinal positions of gaze. The corneal light reflections were observed to ensure they remained central and symmetrical in both eyes. Abnormal head postures were documented at the outset and head position was kept immobile throughout testing. In each cardinal position, an alternating cover test was performed to assess for the presence of or change in amplitude of any phoria. The researcher observed the behaviour of the eyes, looking for movement underactions, overactions, or limitations/restrictions. Associated features were assessed, for example, if the movements were jerky or smooth, the presence of nystagmus, changes in lid or globe position, signs of fatigue, presence of any torsional movements, signs of discomfort on movement, and any abnormal head movements. All observations were recorded.

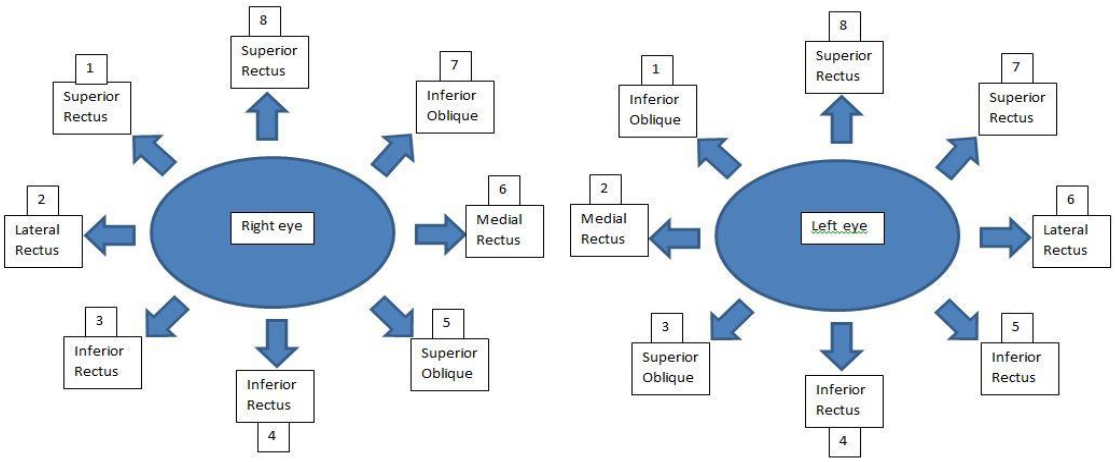


Figure 3.5 Schematic diagram of the eight cardinal eye movements. The diagram is labelled with the EOM which is innervated in each cardinal position. The cardinal positions are numbered in primary yoke pairs (i.e. synergistic muscles of the two eyes) that contract to achieve each version.

Procedure for assessing Near Point of Convergence (NPC)

The RAF binocular gauge was positioned on the participant's cheeks in a head position of slight depression. The target drum was moved slowly and steadily from 50 cm towards the participant until diplopia was reported. Using the centimetre scale on the RAF binocular gauge, the break point was recorded to the nearest 0.5 cm completed by the participant (see Figure 1.5). The target drum was moved slowly backwards until the participant reported a single image again. This process was repeated three times with the average of the readings taken as NPC. The test was performed with the participant's distance spectacles unless normally removed for near tasks. If the participant normally used a presbyopic correction, then those spectacles were used for the test. The researcher watched the participant's eye throughout the test to confirm that binocularity was being maintained.

Procedure for assessing prism fusion range

The positive fusional amplitudes were measured using base out prisms and the negative fusional amplitudes measured using base in prisms. Vertical fusion was measured using prisms held base up and subsequently base down. A direct measurement approach was used (using a prism bar) to create smooth step vergences. The prism bar was a Clement Clarke plastic prism bar (Haag-Streit, Harlow, UK). The prism bar was held with the long axis vertical and parallel to the coronal plane of the head.

The 6/18 letter O on both the 6 m Snellen vision chart (Haag-Streit, Harlow, UK) and 1/3 m Snellen fixation stick (Haag-Streit, Harlow, UK) (see Figure 3.4) was used as a distance and near fixation target, respectively. The participant's head was kept erect and held in primary position throughout the assessment. The test was performed with the participant's distance spectacles unless normally removed for near tasks. If the participant normally used a presbyopic correction then these spectacles were used for this test.

Each participant's fusion range was measured in the same order; base in (i.e. negative fusional amplitude) for distance, base out (i.e. positive fusional amplitude) for distance, base up (i.e. vertical fusional amplitude) for distance, and base down (i.e. vertical fusional amplitude) for distance, with a 30 second rest between each measurement. There was a break before performing the near measurements, during which all stereopsis tests were undertaken. The aim of the break between distance and near fusion measurements was to reduce the influence of fatigue on the fusion results. Fusion range was then measured for near, in the same order and manner as the distance measurements.

Before commencing the motor fusion test, the participant was warned that the image may become blurred or that they may see a rainbow effect from the prism, and advised that both of these could be ignored. The participant was counselled that they may feel a tugging or uncomfortable sensation from their eyes, but that this would be a momentary sensation that passed once the prism was removed and was not a sign of harm.

As the researcher increased the prism magnitude (strength) on the prism bar, the participant was instructed to inform the researcher when the letter O became double and would not re-join with effort after a few seconds; this '*break point'* was recorded in prism dioptres ($^{\Delta}$). The prism strength was decreased until the images re-joined, this '*recovery point'* was recorded in prism dioptres ($^{\Delta}$). The author observed the participant's eyes throughout the test to confirm that binocularity was being maintained.

While the patient maintained fixation on the distance or near target, the researcher placed the prism in front of the participant's right eye. The lowest prism magnitude was first introduced and this was increased at a rate two seconds per prism. The right eye was used as the primary researcher in this environment was seated to participant's right-hand side and the primary researcher is right handed. By using the participant's right eye there was no possibility of obstructing the participant's viewing of the fixation target. Only one prism bar was used (see early discussion), and therefore the maximum obtainable reading was 45^{Δ}.

Procedure for assessing Frisby stereoacuity

The 1.5 mm plate was inserted into the holding device (see Figure 3.6). The participant was shown both the forward projection of the circle (crossed) and the backward projection of the circle (uncrossed) before commencing. The participant was asked to locate the position of the circle in one of the four boxes. If a correct response was given, the plate holder was moved 10 cm further away from the participant, the circle position altered and participant asked to locate the circle again. This procedure was continued until the participant reached their maximum level of stereopsis. When the participant failed to identify the circle at a particular distance, the plate holder was brought forward by 10 cm and the participant was asked to identify the circle at that position again. If correctly identified for a second time, the plate holder was moved further away from the participant by 10 cm, the circle position altered and re-inserted into the plate holder. The participant was asked again to try to identify the position for

a second time. If they failed to identify the circle a second time, the previous distance at which the circle was correctly identified was documented. This process was then repeated with the circle projecting backwards. The test was performed with the participant's distance spectacles unless normally removed for near tasks. If the participant required a presbyopic correction for near tasks then these spectacles were used during the test. Using the measured distance the level of stereoacuity was determined (see Table 3.1). If the participant was unable to identify the circle in either the forward or backward projection with the 1.5 mm plate, then the 3 mm plate was used.

Test distance (cm)	3 mm plate	1.5 mm plate
30	300	150
40	170	85
50	110	55
60	75	40
70	55	30
80	40	20
90	10	5

Table 3.1 Frisby stereotest scores in arcsec at each testing distance. ©Haag Streit UK Ltd

Figure 3.6 The researcher's proprietary designed gantry system for holding the Frisby stereotest plates, the design aim was to ensure accurate measurement of the distance from participant to plate.

Gantry system for holding the Frisby stereotest

As discussed in Chapter 1.6.4, it is recognised that there can be a measurement bias from head movement allowing for a participant with absent or poor stereoacuity to achieve an over estimated stereoacuity. To overcome this challenge the researcher designed a gantry system with a head holding/stabilisation device to prevent head movement and with an extendable holding device for the Frisby plate which would facilitate the accurate measurement of stereoacuity to 1 m. The researcher along with a 2nd year mechanical engineering student at the National University of Ireland, Galway drew plans for the gantry system (see Figure 3.7), and then, using a decommissioned biometry machine table, built the gantry system together. The metal runner which glided out the Frisby plate away from the participant was marked at 10 cm intervals to ensure accurate measurement.

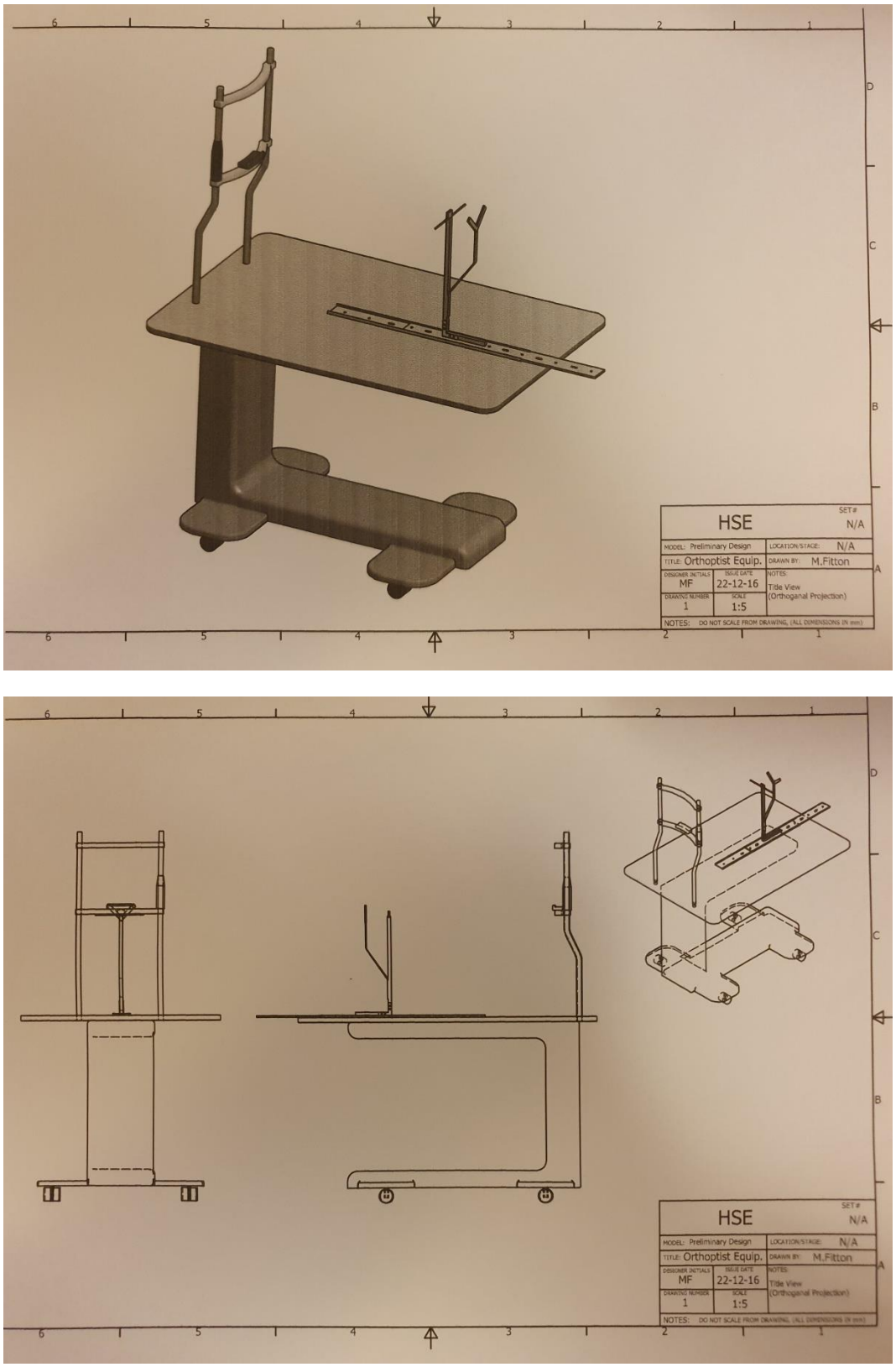


Figure 3.7 Computer aided designs of the gantry system for measurement of stereoacuity using Frisby stereotest (using a decommissioned biometry machine table). The metal runner which adjusted the distance of the Frisby plate from the participant was marked at 10 cm intervals to ensure accurate measurement.

Procedure for assessing TNO stereoacuity

TNO 13th Edition was used for all TNO measurements. TNO stereoacuity measurements were performed while the participant wore the TNO red/green glasses (Lameris Ootech BV, Nieuwegein, Netherlands) (see Figure 1.8), over any habitually worn distance or near spectacles, as per the manufacturer's guidelines. Using a measuring tape, a distance of 40 cm from the red/green glasses to the book was measured and the book and head were held in a slightly depressed position (i.e. chin down) at this distance. The screening plates were presented first to familiarise the participant with the images created by the test, before moving to the graded section of the test. For each level of TNO stereoacuity, there were two circles with a 60 degree triangular wedge/segment missing. The participant was asked to identify where in each circle the segment was missing (i.e. in which quadrant). The participant was required to identify both missing segments correctly to attain/score that level of stereoacuity. The stereoacuity was recorded as the last plates in which the missing triangular wedge/segment from both circles were correctly identified (see Figure 1.9). After completion of test, the viewing distance was re-measured to ensure it had remained constant throughout. In the event the viewing distance had changed the test would have been repeated after completion of the near fusion measurements, to prevent memorization of answers.

Procedure for assessing Titmus stereoacuity

For the Titmus stereoacuity test (Stereo Optical Company, Inc. Chicago, IL USA) (see Figure 1.10), the participants wore polarised filter glasses, worn over any habitually worn distance/presbyopic spectacle correction. Using a measuring tape, a distance of 40 cm from the polarised glasses to the book was measured and the book and head held in a slightly depressed position (i.e. chin down) at this distance. Using only the nine Wirt boxes, the participant was asked to identify which of the four circles appeared to protrude forwards. With each correct response the participant moved to the next box. If an incorrect response was given the previous box was rechecked. As the position of the protruding circle cannot be altered, the participant was not given a second opportunity to correctly identify the protruding circle. The stereoacuity was documented by the number of correctly identified circles (see Table 1.7). After completion of test, the viewing distance was re-measured to ensure it had remained constant throughout. In the event the viewing distance had changed the test would

have been repeated after completion of the near fusion measurements, to prevent memorization of answers.

The procedure for assessing FD2 stereoacuity

Distance stereoacuity was measured using the FD2 stereotest at 6 m (see Figure 1.11). The primary researcher followed the manufacturer's FD2 protocol (Stereotest Ltd, Sheffield, UK) (see Figure 3.8). The participant wore any distance spectacles normally used for distance viewing. The stereoacuity disparity for the FD2 is found on the rods inside the FD2 box. Before commencing, the researcher showed the participant one of the four shapes sitting at the 50 arcsec position and asked if they could see the shape's position as closer to them (i.e. relatively displaced forward) than the other three shapes. If the participant reported that all four shapes were in the same position, the test was recorded as a negative result.

If the participant was able to correctly identify that one shape was closer to them, the FD2's front door was closed so that the participant could no longer see the four shapes. Using the FD2's side door the primary researcher changed the position of the rods so that a different shape was positioned forward, representing 50 arcsec. If the participant reported that all four shapes were now in the same position, the test was recorded as a negative result. The manufacturer's testing instructions do facilitate reducing the testing distance to 4 m or 3 m when there is a stereo negative response at 6 m. However, the researcher had decided in the design stage that only a 6 m testing distance would be performed, as 6 m is in line with the standard testing distance for distance ocular alignment and distance fusion measurements. If the participant was able to identify the shape that was positioned closer to them correctly, the test proceeded. Between each correct response, the front door to the FD2 box was closed so that the participant could not view the primary researcher moving the rods via the FD2's side door.

Any rod was randomly selected by the primary researcher to move each time. If a correct response was received for the 50 arcsec position, the next rod was placed at the 40 arcsec position, then the 30 arcsec position, then the 20 arcsec position, then the 10 arcsec position and finally the 5 arcsec position. If at any stage an incorrect response was made, the rod was moved back by 5 arcsec, rather than returning by a 10 arcsec interval, (for example, incorrect response at 20 arcsec, next rod position 25

arcsec). The participant was required to give two correct responses out of three to be awarded that level of stereoacuity.

After identifying the participant's level of stereoacuity, the monocular threshold test was performed. The participant was asked to wear an occlusion patch over one eye and the test repeated. If the participant reported that all four shapes were in the same position for the 50 arcsec position, then the awarded level of stereoacuity was deemed valid. If a correct response was received for the 50 arcsec position, the next rod was placed at the 40 arcsec position, then the 30 arcsec position, then the 20 arcsec position, then the 10 arcsec position and finally the 5 arcsec position, until the stage at which the participant reported that all shapes were in the same position. If the monocular stereoacuity level was equal to or better than to the binocular stereoacuity level the test was deemed invalid and recorded as inconclusive. If the monocular stereoacuity level, was worse than the binocular stereoacuity level the test was deemed valid and level of achieved stereoacuity recorded. This monocular threshold procedure was repeated for the fellow eye. The results were recorded as either, the minimum stereoacuity achieved, an invalid result or a negative result.

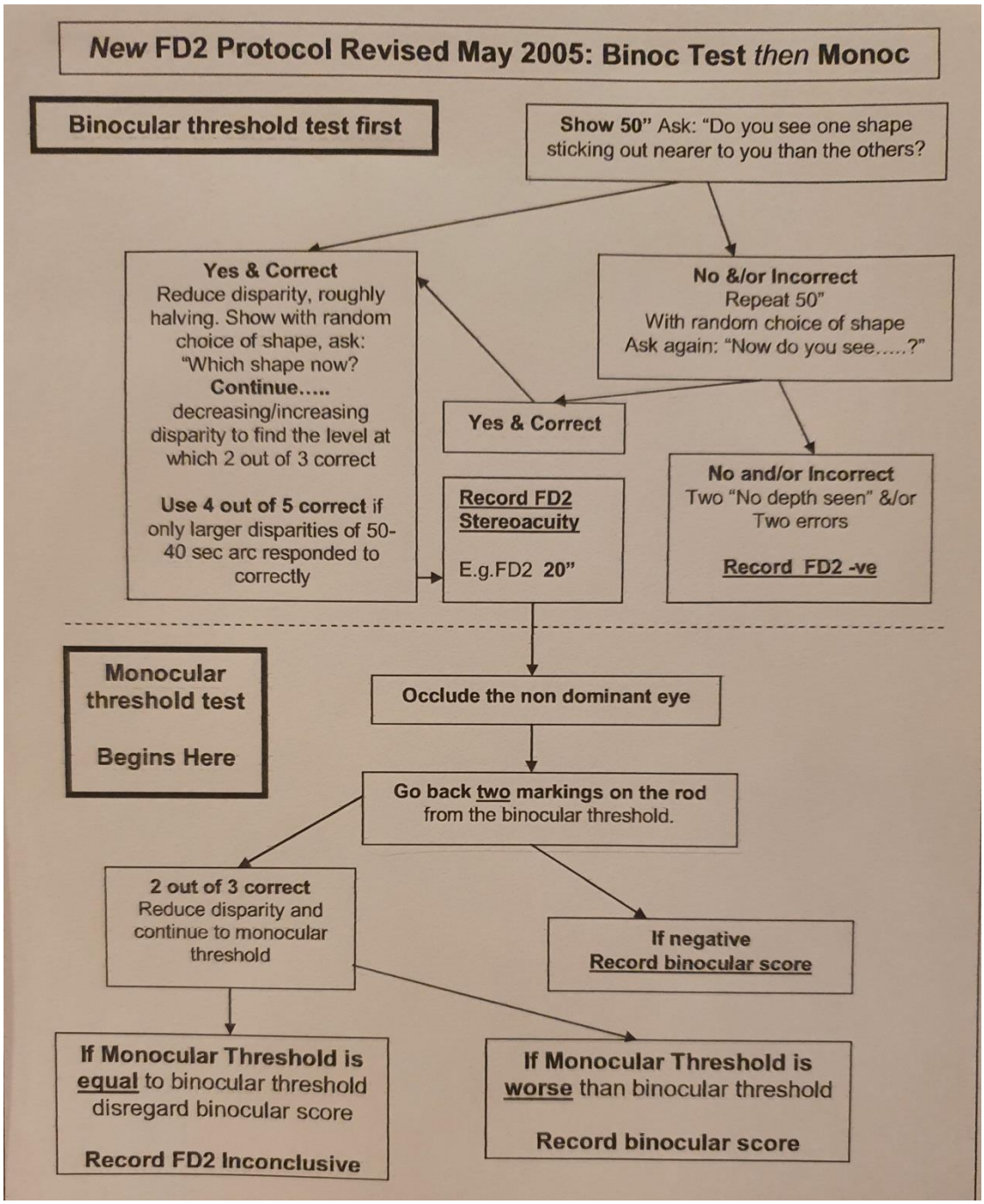


Figure 3.8 The FD2 manufacture's protocol summary sheet for performing the FD2, supplied when the test is purchased. Permission granted from Professor Frisby via personal email to researcher to include protocol in thesis. Full 17 page test design and test instructions booklet can be found at: http://frisbystereotest.co.uk/wp3/wp-content/uploads/2014/01/NFD2-Instruction-Booklet-4sep12.pdf

Procedure for assessing ocular refraction

A noncycloplegic automated refraction of the eyes was measured and recorded using the Topcon KR800 auto kerato-refractometer (Topcon Medical Systems Incorporated, Fukuoka, Japan) (see Figure 3.9). The autorefractor was annually serviced and calibrated by engineers from Topcon. The KR800 uses rotary prism technology (a patented system for measuring ocular refraction) (193). With rotary prism technology, the target is projected into the participant's eye and then rotated within their pupil (193). The KR800 is an open-field auto-refractor which allows binocular viewing through a measuring window of an actual fixation target located at far distance (194). The KR800 measures spherical refractive power from -25 dioptres (D) to +22D (0.12/0.25 dioptres sphere (DS) steps; measures cylindrical refractive power 0D to ±10D (0.12/0.25 dioptres cylinder (DC) steps); and measures astigmatic axial angle in either 1^{O} or 5^{O} steps (193). The KR800 uses an automatic fogging mechanism to control the effects of accommodation on the measurement of refraction (194). There have been two published studies assessing the accuracy of the KR800 in measuring refraction in a paediatric population (194, 195). To the author's knowledge there are no studies published on the accuracy of the KR800 in an adult population. The first study was performed on 308 children aged 6 - 17 years from Taiwan and found the KR800 produced a reliable accurate measurement of refraction (both noncycloplegic and cycloplegic refractive measurements), which was in agreement with the ophthalmologist's cycloplegic retinoscopy measurement (194). The authors did find that, without cycloplegic dilation, children aged 6 - 11 years measured a more negative result, for example, it under calculated any hyperopia and over calculated any myopia (194). A post-hoc comparison of the measurement discrepancies found the difference between noncycloplegic auto refraction and cycloplegic retinoscopy to be -0.205 ± 0.517 D; and between cycloplegic auto-refraction and cycloplegic retinoscopy to be 0.207 ± 0.430 D, for both comparisons this was a statistically significant finding (194); but, may not be a clinically significant difference. For the total population of 6 - 17 year olds (n = 308), they found the noncycloplegic (as was in this thesis) sensitivity of 98% and specificity of 84% for myopia, and a sensitivity of 40% and specificity of 99% for hypermetropia (194). The authors commented that a limitation of their study was comparisons on intra- and inter-observer measurements were not performed due to time constraints, and therefore, the accuracy and the repeatability of the measurements could not be provided (194). The second study (n = 881), aged 6 - 17 years from China, compared the KR800 noncycloplegic and cycloplegic measurements to another auto-refractor (Grand Seiko WAM-5500), but not to a retinoscopy

measurement; the study found that for myopia the sensitivity was 90% and specificity was 92%, while with hypermetropia the sensitivity was 84% and specificity was 87% and finally with astigmatism the sensitivity was 90% and specificity was 93% (195). This second publication does not add further information relevant/applicable to this thesis; however these are the only studies on the KR-800 published to date. The author requested details on the KR-800 accuracy and repeatability from unpublished studies from the Topcon representative in Ireland, but these studies were not available.

The participant was asked to place their chin on the chin rest and head against the headrest, with the researcher adjusting the chin rest height so that the height marker of the measuring window was aligned with the participant's visual axis. The KR800 was set to automatic mode, where three measurements are taken automatically once the eye is correctly aligned. The KR800 automatically prints the sphere, cylinder, cylinder axis and a reliability reading. The reliability reading is a number between 1 and 9 denoting the percentage of light incident on the eye which was reflected back into the machine. A reading of 9 is the best reading, indicating 100% reflection while 1 is the worst indicating a minimal percentage of reflected light. The researcher used the joy stick to move the measuring window in front of the participant's fellow eye. The KR800 would automatically take three measurements once the second eye was corrected aligned, and print the sphere, cylinder, cylinder axis and a reliability reading as per the first eye.

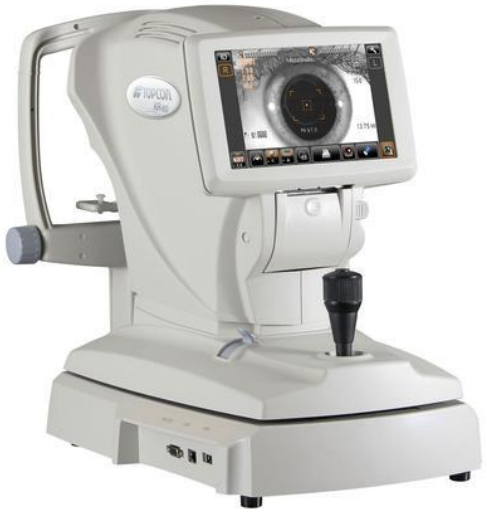


Figure 3.9 Topcon KR800 auto kerato-refractometer (Topcon Medical systems Incorporated, Fukuoka, Japan) (193), used to measure the ocular refraction.

3.10 Statistical Analysis

Analysis of variance (ANOVA) was used in the calculation of sample size based on the use of age cohorts in the research. ANOVA is a parametric test that depends on the data in each cohort being normally distributed around a mean and that the variances are equal from each population sampled (196). To confirm that the data were normally distributed, a Shapiro-Wilk and Kolmogorov test were conducted prior to deriving the results to ensure normal distribution criteria for ANOVA had been satisfied (197). If the normality assumption was not met, data were transformed using logarithm. If, after transformation, the data failed to attain normality, then the non-parametric Kruskal Wallis test was performed, to establish if there were a statistically significant difference in the medians values between at least three cohorts (198, 199). The Kruskal Wallis test established whether the variable medians (for example, stereoacuity), of the seven cohorts were significantly different.

The stereoacuity results of experiments/investigations in chapter 4 followed an ordinal scale. Usually ANOVA can also be applied to ordinal data, when each cohort distribution can be approximately normal or when the response has many categories (200). However, when normality cannot be achieved for ordinal responses, an ordinal regression analysis is a more appropriate statistical analysis method. Ordinal regression is one of the regression analysis methods; estimating the relationship between a predictor and a response (201), (i.e. age as the predictor/ordinal variable and stereoacuity as the response/dependent variable). The uses of ordinal regression are to understand the strength of the association between a predictor (age) and an outcome (level of stereoacuity), to forecast effects, and to predict trends (201). For an ordinal regression analysis, there are assumptions that the data is normally distributed and that the response is linearly related to the ordinal variable (201); also ordinal regression analysis assumes a uniform scale of measurements, for example with the TNO stereoacuity test the change from 60 to 120 arcsec, is the same amount of change as from 120 to 180 arcsec; implying that the reduction in stereoacuity from 60 to 240 arcsec is twice the amount of change from 120 to 240 arcsec.

A one-way ANOVA was performed using IBM SPSS Statistics for Windows Version 23.0 (IBM Corp., NY, USA). Where the normality assumption was not met due to limited data options in a cohort, an ordinal regression model was fitted with age category as a predictor. The ordinal regression analysis displays parameters (for example, standard errors), and these were also reported as they show the direction of effects. Standard errors indicate the amount of uncertainty associated with the

coefficient and intercept estimates, when those estimates are used to describe a relationship in the population (201). Standard errors are used in the calculation of p values and confidence intervals (201). The null hypothesis test that for a given age cohort, the odds of having lower scores than a given threshold are the same as the odds of having scores above that threshold (parameter = 0 versus parameter ≠ 0); for example, the odds of having a TNO stereoacuity ≤ 120 arcsec against the odds of TNO stereoacuity > 120 arcsec. A $p < 0.05$ indicates a statistically significant difference in the odds of a TNO stereoacuity ≤ 120 arcsec against the odds of TNO stereoacuity > 120 arcsec. The parameter estimate gives the log odds of having scores up to a threshold against having higher scores (200). If the parameter is negative, it means that the age cohort is more likely to have a better stereoacuity value.

The mean, mode, standard deviation, and range for each stereotest, are reported in the results for chapter 4. These descriptive statistics show different aspects of the results and have different applications. The mean is a measure of the central position of the data (i.e. the average value), and is appropriate for continuous data with a linear scale (202). However, the mean is affected by extreme observations or when the data was skewed, for example, when population data for Titmus stereotest was skewed towards the best stereoacuity value recordable (i.e. 40 arcsec). When data is linear and symmetrically distributed, the mean and median are very similar (202). The stereoacuity mean for the population and for the cohorts may be a value not clinically recordable by the stereotest (i.e. Titmus stereotest mean: 46 arcsec), but it is useful for comparisons to other published studies. Whereas, the median is an actual stereoacuity value found with the stereotest, and therefore has better clinical application; for example, the mean for Titmus stereotest may be 46 arcsec and the median 40 arcsec (the actual stereoacuity values recordable on the Titmus stereotest are 40 arcsec, 50 arcsec, 60 arcsec etc.). The median is the middle value of stereoacuity when all the values are based in increasing order, it was provided for the total population and for the cohorts. Non-normally distributed data should be presented by the median and interquartile range (IQR), IQR is the range of values in the middle 50% of the data set (203). From a clinical perspective, it is also interesting to know the mode, the mode is the most frequency occurring value/response, and is the response that the clinician will most often be given by patients, it is also an actual value recordable by the stereotest. Variation is an expected aspect of the data (202); standard deviation is a measure of this variation, it is presented along with the mean, as a measure to describe the variation from the mean, and like mean, it is appropriate when the data is parametric and continuous along a linear scale (198, 202). The range

of stereoacuity values for each age cohort gave an indication of the dispersion, and the difference between the lowest and highest values of stereoacuity, for each stereotest. The range allowed for some evaluation of the whole dataset, both by showing the spread of stereoacuity values within an age cohort for a stereotest, and the spread of the entire dataset for the stereotest. Where the stereoacuity response had fewer values, bar and pie charts demonstrate how stereoacuity values were distributed for the population and within each age cohort.

For the null hypothesis in chapter 5 that there is no statistically significant decrease in fusion with increasing age, a one-way ANOVA was used to identify any variability within the data, both between the age cohorts and within the same age cohort. ANOVA measures the total variation and divides up the variation into portions.

As explained earlier with regard to the chapter 4 results, the mean, mode, range, and standard deviation were provided for chapter 5 results. Additionally, correlations were obtained and presented for ungrouped age. The values for each type of horizontal and vertical fusion were represented in the analysis (for example, positive for near, positive for distance, negative for near, negative for distance, vertical for near, and vertical for distance). The range of fusion values for each age cohort gave an indication of the dispersion and difference between the lowest and highest values for each measurement. The range allowed for some evaluation of the whole dataset, by showing both the spread of values within an age cohort for a fusion measurement, and the spread of the entire dataset for fusion. The standard deviation values were used to give an indication of how the dataset for each age cohort varied from the mean value of fusion for that age cohort; standard deviation is a powerful measure of variation as takes into account every value within data set. Where some datasets had small or large standard deviations, possible explanations are provided in chapter 5. The IQR (middle 50% of values in the dataset) was given, as this related to the variation from the median.

Chapter 5 had two further null hypotheses: firstly, that there was no statistically significant decrease in NPC with increasing age, and secondly, that there was no statistically significant change in ocular alignment with increasing age. NPC was analysed using Pearson's correlation and the non-parametric Kruskal-Wallis test. Pearson's correlation established whether there is a 'linear' relationship between two variables (for example, variable 1 = ungrouped age and variable 2 = NPC) (198). Pearson's correlation value 'r', measured the strength of the relationship between the two variables, but not the agreement between them (198). The Kruskal-Wallis test

was used to compare the cohorts; the Kruskal-Wallis test is the non-parametric equivalent of ANOVA, used to test whether the medians of the seven cohorts are significantly different. Ocular alignment was analysed using the Fisher's exact test for an association between ungrouped age and alignment (see Chapter 2.5 for further details on Fisher's exact test), and the Kruskal-Wallis test for a comparison between the cohorts, near and distance ocular alignment measurements were analysed separately. Changes in eye movements were described qualitatively; however, the presence of end point nystagmus will undergo logistic regression analysis.

3.11 Summary

This chapter described the main study research method along with details of the clinical assessments (equipment and procedure) that were conducted. There was a description of the research ethics, the recruitment of participants, the consent process and how the sample size was calculated. The inclusion and exclusion criteria were specified. There was a discussion on the statistical analysis methods employed to analysis the main study investigation.

Chapter 4: The association of increasing age on stereoacuity as measured by four types of stereotests.

Chapter 4: The association of increasing age on stereoacuity as measured by four types of stereotests.

4.1 Introduction

This chapter will describe the findings of the research, which assessed the association between age and stereoacuity using four commercially available stereotests. A detailed description of each stereotest and the method of testing can be found in chapter 3.

The following is a summary of the literature review found in chapter 1 outlining the grades of binocular vision and the reported effect of age on stereoacuity. Originally described by Claud Worth in 1903, there are three grades of binocular functions: simultaneous perception, fusion, and stereopsis (83, 84). Simultaneous perception is the ability to perceive simultaneously two images, one from each eye (62). Sensory fusion is the cortical process of blending the retinal images from each eye to perceive a single image (62, 74). Motor fusion is the ability to maintain sensory fusion through a range of vergences: horizontal, vertical and cyclovergence (62, 74). The third grade of binocular functions is the ability to achieve stereopsis. Stereoacuity, the measurement of stereopsis, is the smallest threshold disparity that can be discriminated between two adjacent surfaces (i.e. depth perception) (1).

Association between age and Frisby tested stereoacuity

Three studies have looked at the effect of age on stereoacuity measured using Frisby stereotest over a wide age range. One study found a decline in stereoacuity after the age of 35 years (3). Using crossed disparity, they found a decrease in stereoacuity from mean 6.7 arcsec for cohort 25 - 34 years to 19.5 arcsec for cohort 35 - 60 years; however, in this study, there were an uneven number of participants and an uneven number of years in each cohort (3). The results were similar with uncrossed disparities demonstrating a decline in mean stereoacuity from 5.2 - 13.6 arcsec for the two age cohorts, respectively, which were statistically significant findings (3). The second study, with similar limitations, compared 196 participants aged 11 - 49 years to 16 participants aged 50 - 82 years, found the median stereoacuity dropped from 20 to 80 arcsec between the younger and older cohorts (1). Finally, the Moorfields study which was based on 60 participants in uneven age cohorts, reported no difference between cohorts 17 - 29 and 30 - 49 years, but reported a decrease in median stereoacuity with

cohort 50 - 69 years, and a further decrease for cohort 70 - 83 years when using the Frisby stereotest. Unfortunately, the authors failed to provide the stereoacuity values in the results section, but reported the p values from the statistical analysis, which showed a statistically significant deterioration in stereoacuity with age (113). The authors discussed how this decrease in stereoacuity could be related to a decline in cortical disparity detector function with age (113). To the author's knowledge, there is no published study comparing the effect of increasing age on stereoacuity measured with the Frisby stereotest, which has used an equal number of participants in each age cohort and/ or used a more regular age division.

Association between age and TNO tested stereoacuity

Two studies have looked at the effect of age on stereoacuity measured using the TNO stereotest with a wide age range of participants. The Moorfields study again reported no difference in stereoacuity between cohorts 17 - 29 years and 30 - 49 years, but then a decrease in stereoacuity for cohort 50 - 69 years, and a further decrease in the stereoacuity for cohort 70 - 83 years when using the TNO stereotest, producing a statistically significant deterioration in stereoacuity with age (113). A second study comparing stereoacuity with age using the TNO stereotest, found that mean stereoacuity remains stable until cohort 51 - 60 years, and then mean stereoacuity decreases with cohorts 61 - 70 years and 71 - 80 years; it was reported as a statistically significant change (2). The Keimyung study took a regimented approach to sampling; there were regular age progression groupings and a consistent number of participants in each cohort (2).

Association between age and stereoacuity as measured by the Titmus stereotest

The same two studies mentioned above with the TNO stereotest, also looked at the effect of age on stereoacuity measured using the Titmus stereotest. The Moorfield study again reported no difference in stereoacuity between cohorts 17 – 29 years and 30 - 49 years, but then a decrease in stereoacuity for cohort 50 - 69 years, and a further decrease in stereoacuity for cohort 70 - 83 years when using the Titmus stereotest, producing a statistically significant deterioration in stereoacuity with age (113). The Keimyung study supported the Moorfields study, but with the statistically significant reduction in stereoacuity only found in cohort 71 - 80 years (2).

Association between age and distance stereoacuity as measured by the FD2 stereotest

There have been two studies which compared the FD2 stereoacuity across a wide age range. The first study (referred to in the Frisby, TNO and Titmus sections as the Moorfields study), found a deterioration in median distance stereoacuity for cohorts 30 - 49 years and 50 - 69 years, with no further deterioration noted until cohort 70 - 83 years; they reported this as statistically significant (113). The second study, with similar limitations (i.e. unequal cohort sizes and unequal number of years in each age cohort), compared 211 participants in two cohorts, they compared 195 participants aged 11 - 49 years to 16 participants aged 50 - 82 years, and found a minimal change in median stereoacuity from 10 to 12.5 arcsec between the younger and older cohorts, which was statistically significant (1).

4.2 Aim

The aim of this chapter is to present the investigation into whether there is a decrease in stereoacuity with increasing age using four commercially available stereoacuity tests (i.e. Titmus, Frisby, TNO and FD2), on healthy volunteer participants, when visual acuity is controlled. It is hoped the investigation into the association between stereoacuity and age, and the presentation of age appropriate normative values, will benefit clinicians when developing patient management strategies.

In this study, there was standardization of cohort sizes, regulation of the number of years in each cohort, and a comparison of the most commonly used near stereotests, recommended by the RCOphth clinical guidelines (106). Although, Lang stereotest was additionally mentioned in the RCOphth clinical guidelines, it was not included in this research. Lang stereotest is predominantly used on pre-verbal children, or children and adults with significant intellectual disability, and this study was performed on participants aged at least 10 years without intellectual disability.

4.3 Hypothesis and statistical analysis

This chapter had four null hypotheses:

1. There is no statistically significant decrease in stereoacuity with increasing age using Titmus stereotest.

2. There is no statistically significant decrease in stereoacuity with increasing age using TNO stereotest.
3. There is no statistically significant decrease in stereoacuity with increasing age using Frisby stereotest.
4. There is no statistically significant decrease in stereoacuity with increasing age using FD2 stereotest.

Descriptive statistics were obtained and models fitted in accordance to the type of data (See Table 4.1). Data without the minimum number of values were assumed to be ordinal, as there were too few values to achieve normality in each cohort, with or without transformation, i.e. all members of some cohorts achieved the same value of stereoacuity with a particular test, (for example, cohort 30 - 39 years, all participants scored 40 arcsec on the Titmus stereotest, the maximum achievable score with this stereotest). An ordinal regression model was fitted for Titmus and TNO stereotests. The ordinal regression model compares the log odds of having 'worse' stereoacuity value in one cohort to the odds of having 'better' stereoacuity value in a different cohort (for example, log odds of observing ≥ 40 arcsec against odds of obtaining < 40 arcsec). The relationship with log odds can be assumed to be the same regardless of the given threshold, (i.e. for different threshold we assume the same effect of age); this is called the proportional odds model (204). A proportional odds model was fitted for Titmus stereotest and TNO stereotest analysis. As the observed values for the variable increased (in this study greater than 6), normality was assumed and normality tests were performed. If normality was satisfied, then an ANOVA model was fitted to the data (for example, FD2 stereotest); otherwise, the non-parametric Kruskal Wallis test was performed to determine if there are any differences between the age cohorts (for example, Frisby crossed and uncrossed) (see Chapter 3.9 for further information on ANOVA and Kruskal Wallis test).

Parameter (stereotest)	Ordinal Regression	ANOVA	Kruskal- Wallis
Titmus	X		
TNO	X		
Frisby (uncrossed)			X
Frisby (crossed)			X
FD2		X	

Table 4.1 The method of statistical analysis utilized for each stereotest. Parameters were analysed with either the parametric test ANOVA or the non-parametric test Kruskal-Wallis. Data with too few values to achieve normality were analysed using ordinal regression.

4.4 Results

Participant demographics

There were 77 participants aged 10 - 77 years, mean 44.6 ± 19.7 years. (see Table 4.2). There were 60 (78%) female and 17 (22%) male participants. There were 2 (3%) Black African participants and 75 (97%) White Irish participants. There were two participants using lubricant eye drops. Details regarding the participants' general health and ophthalmic family history did not form part of the study analysis; they are presented in Appendix 15.

Table 4.2 shows that the mean distance vision/VA in LogMAR for the total population right eye was -0.09 ± 0.08, and for the left eye was -0.10 ± 0.09, reflecting that all participants had a minimum of 0.10 logMAR distance acuity in each eye to be included in the study.

Table 4.2 shows the expected finding that the mean reading addition power increases from a minimum value of +0.36 ± 0.63 D in cohort 40 - 49 years to +1.75 ± 0.81 D in cohort 50 - 59 years, to +2.02 ± 0.80 D in cohort 60 - 69 years, and finally to the highest power +2.18 ± 0.37 D in cohort 70 - 79 years; with the participants in the three youngest cohorts (10 - 19, 20 - 29 and 30 - 39 years) not requiring a reading addition, as they are pre-presbyopic.

Cohort (years)	Age Mean (± SD) (years)	Gender Female: Male % Female	Ethnicity	Distance Spherical Equivalent (dioptres) Right Eye	Distance Spherical Equivalent (dioptres) Left Eye	Distance Vision/Visual Acuity mean (± SD) (LogMAR) Right Eye	Distance Vision/Visual Acuity mean (± SD) (LogMAR) Left Eye	Near Add mean (± SD) (dioptres)	Near Vision/ Visual Acuity mean (± SD) (LogMAR) Right Eye	Near Vision/ Visual Acuity mean (± SD) (LogMAR) Left Eye	Near Vision/ Visual Acuity mean (± SD) (LogMAR) Both Eyes	Ocular Lubricants
10 – 19	15.0 ± 3.6	8:3 73%	100% WI	-1.28 ± 2.07	-1.33 ± 2.16	-0.10 ± 0.08	-0.09 ± 0.07	0 ± 0	0.01 ± 0.04	0.01 ± 0.01	0 ± 0	Nil
20 – 29	26.55 ± 2.66	9:2 82%	100% WI	-0.61 ± 1.37	-0.58 ± 1.19	-0.14 ± 0.08	-0.13 ± 0.08	0 ± 0	0.01 ± 0.03	0.01 ± 0.03	0 ± 0	Nil
30 – 39	34.18 ± 2.93	6:5 55%	18% BA 82% WI	-0.31 ± 0.43	-0.37 ± 0.40	-0.12 ± 0.10	-0.14 ± 0.09	0 ± 0	-0.04 ± 0.08	-0.04 ± 0.08	0 ± 0	Nil
40 – 49	43.82 ± 3.16	10:1 91%	100% WI	-1.62 ± 2.91	-1.48 ± 2.60	-0.09 ± 0.06	-0.11 ± 0.08	0.36 ± 0.63	0.04 ± 0.07	0.04 ± 0.07	0.03 ± 0.06	Nil
50 – 59	54.91 ± 2.02	7:4 64%	100% WI	-0.41 ± 1.08	-0.40 ± 0.94	-0.06 ± 0.06	-0.08 ± 0.08	1.75 ± 0.81	0.03 ± 0.06	0.03 ± 0.05	0.01 ± 0.06	Nil
60 – 69	64.36 ± 2.50	10:1 91%	100% WI	0.76 ± 1.84	0.67 ± 1.82	-0.09 ± 0.05	-0.09 ± 0.07	2.02 ± 0.80	0.05 ± 0.05	0.04 ± 0.05	0.03 ± 0.06	1/11 (9%)
70 – 79	73.18 ± 2.09	9:2 82%	100% WI	1.02 ± 1.59	0.94 ± 1.53	-0.03 ± 0.11	-0.04 ± 0.10	2.18 ± 0.37	0.05 ± 0.05	0.04 ± 0.05	0.04 ± 0.05	1/11 (9%)
10 - 79	**44.57 ± 19.67**	**60:17 78%**	**97% WI**	**-0.35 ± 1.93**	**-0.36 ± 1.82**	**-0.09 ± 0.08**	**-0.10 ± 0.09**	**0.69 ± 0.37**	**0.02 ± 0.06**	**0.02 ± 0.05**	**0.02 ± 0.06**	**2/77 (2.6%)**

Table 4.2 The demographic data for each cohort and the total population. NB: When the participant wore habitual glasses the visual acuity was used, when the participant did not wear glasses the vision was used in the calculation of cohort mean acuity; this reflects the participants' visual function during the remainder of the binocular vision tests. WI = White Irish and BA = Black African

The automated non-cycloplegic ocular refraction for the population

The spherical equivalent (SE) was used to determine the mean refractive status of each participant, 97 of 154 participants' eyes were emmetropic, with 25 being hypermetropic and 26 eyes being myopic (see Table 4.3). Table 4.2 shows that mean distance SE for the total population right eye was -0.35 ± 1.93 D, and left eye was -0.36 ± 1.82 D. With powers > 5.00 D SE considered high ametropia, there were three participants (six eyes) who had high myopia, and no participant with high hypermetropia. There were two participants (2.6%) with anisometropia, one participant was myopic, and one participant was hypermetropic. Astigmatism ≥ 2.00 DC was only recorded in five eyes (3.2%). There were 33 participants (42.9%), who required the use of a presbyopic spectacle addition, with a further 8 (10.4%), participants removing their myopic correction for near viewing tasks (therefore, 41 participants (53.2%) who were presbyopic). The refractive status of the study population is presented in Table 4.3.

Refraction	**Values**	**Number of eyes (n = 154)**
High Myopia	SE ≥ -5.00 DS	6 (3.9%)
Myopia	SE ≥ -1.00 DS	26 (16.9%)
Emmetropia	SE -0.99 to +0.99 DS	97 (63.0%)
Hypermetropia	SE ≥ +1.00 DS	25 (16.2%)
High Hypermetropia	SE ≥ +5.00 DS	0 (0%)
Moderate astigmatism	≥ 2.00 DC	4 (2.6%)
Significant astigmatism	≥ 4.00 DC	1 (0.6%)
		Number of participants (n = 77)
Presbyopia Add required		33 (42.9%)
Anisometropia	≥ 1 D between eyes	2 (2.6%)

Table 4.3 Study population measurements from auto refractor KR-800.

Stereoacuity

The full descriptive results of mean, median, standard deviation and minimum and maximum stereoacuity values for each cohort, and for the total population, are presented in Appendix 16. The outputs for the statistical analysis can be found in Appendix 17. After completion of Titmus and TNO stereotests, the viewing distance

was re-measured, there was no instances where the viewing distance had changed from 40 cm for either the Titmus stereotest or the TNO stereotest

Titmus Stereotest

The mean stereoacuity for the total population as measured with the Titmus stereotest was 49.5 ± 20.3 arcsec, mode 40 arcsec, and the range 40 - 140 arcsec. Cohort 30 - 39 years achieved the best mean stereoacuity of 40 arcsec, with all 11 participants achieving the maximum stereoacuity value. Cohort 70 - 79 years had the worst mean stereoacuity value (69.1 arcsec), and the largest standard deviation (38.1 arcsec), reflecting the wide range of values achieved by this cohort (40 - 140 arcsec).

The median stereoacuity for the total population was 40 (IQR 40 - 50) arcsec. Cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years and 60 - 69 years recorded same median value (40 arcsec), but with different distributions. Cohort 70 - 79 years was the only cohort to have a higher (i.e. weaker) median stereoacuity of 50 (IQR 40 - 80) arcsec; for all the other cohorts the median stereoacuity was 40 arcsec (see Figure 4.1). There is no IQR range for cohort 30 - 39 years, as this cohort had a high level of concordance, with all participants achieving 40 arcsec (as mentioned above). There is no IQR for 40 - 49 years as this cohort had a high level of agreement, with 9/11 participants achieving 40 arcsec (see Figure 4.1).

From Figure 4.1, it can be seen that no cohort showed normally distributed data, cohorts 10 - 19 years, 20 - 29 years, 50 - 59 years, 60 - 69 years and 70 - 79 years showed positively skewed data. Therefore, it was more appropriate to present and discuss the median stereoacuity rather than the mean stereoacuity. Cohort 70 - 79 years had the largest boxplot reflecting low level of agreement between participants. Cohort 70 - 79 years had the longest upper whiskers, indicating most variability in the positive quartile (see Figure 4.1). There are no lower whiskers for any of the cohorts because the lower quartile was equal to the maximum stereoacuity value achievable (40 arcsec).

Titmus stereotest had a potential for nine values of stereoacuity (800, 400, 200, 140, 100, 80, 60, 50, and 40 arcsec). All participants were able to identify a minimum of 3 out of 9 boxes correctly (200 arcsec), and therefore, only six stereoacuity values were recorded, ranging from 40 - 140 arcsec (as shown in Figure 4.2B). Only three participants achieved the lower stereoacuity range of 100 - 140 arcsec (aged 29, 72 and 76 years); with the ‘worst’ stereoacuity value of 140 arcsec recorded by two

participants, both in cohort 70 - 79 years. In summary, older aged participants (≥ 70 years) are more likely to achieve a weaker stereoacuity value, and show a greater variability in results.

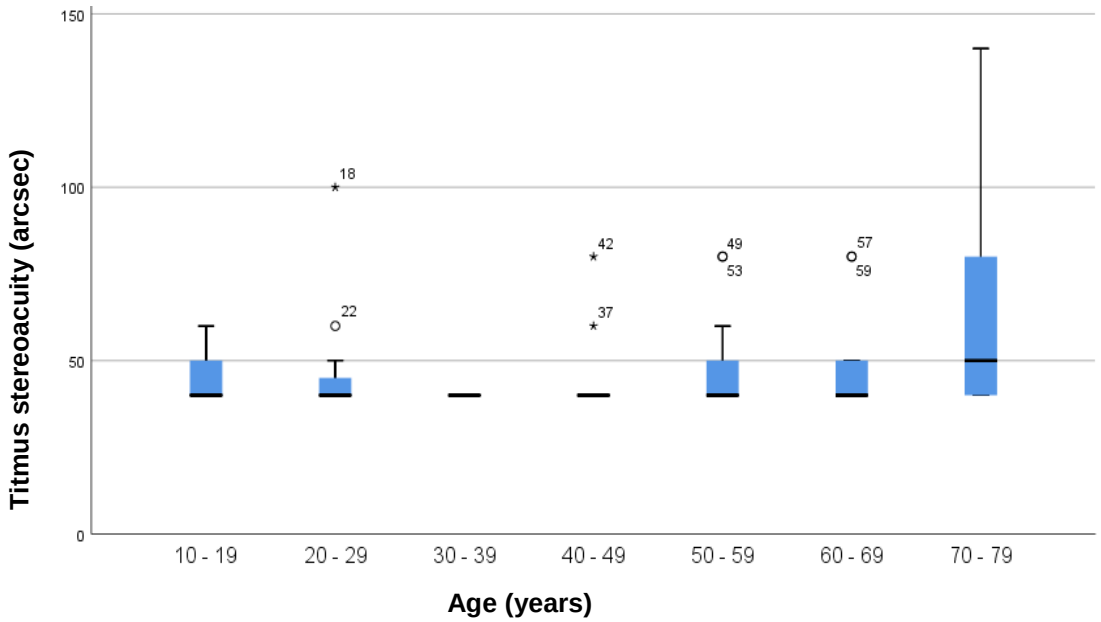


Figure 4.1 Box plot displaying the median, IQR range, and the minimum and maximum stereoacuity of Titmus stereotest. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers (NB participant ID not age is depicted in graph) were individually plotted.

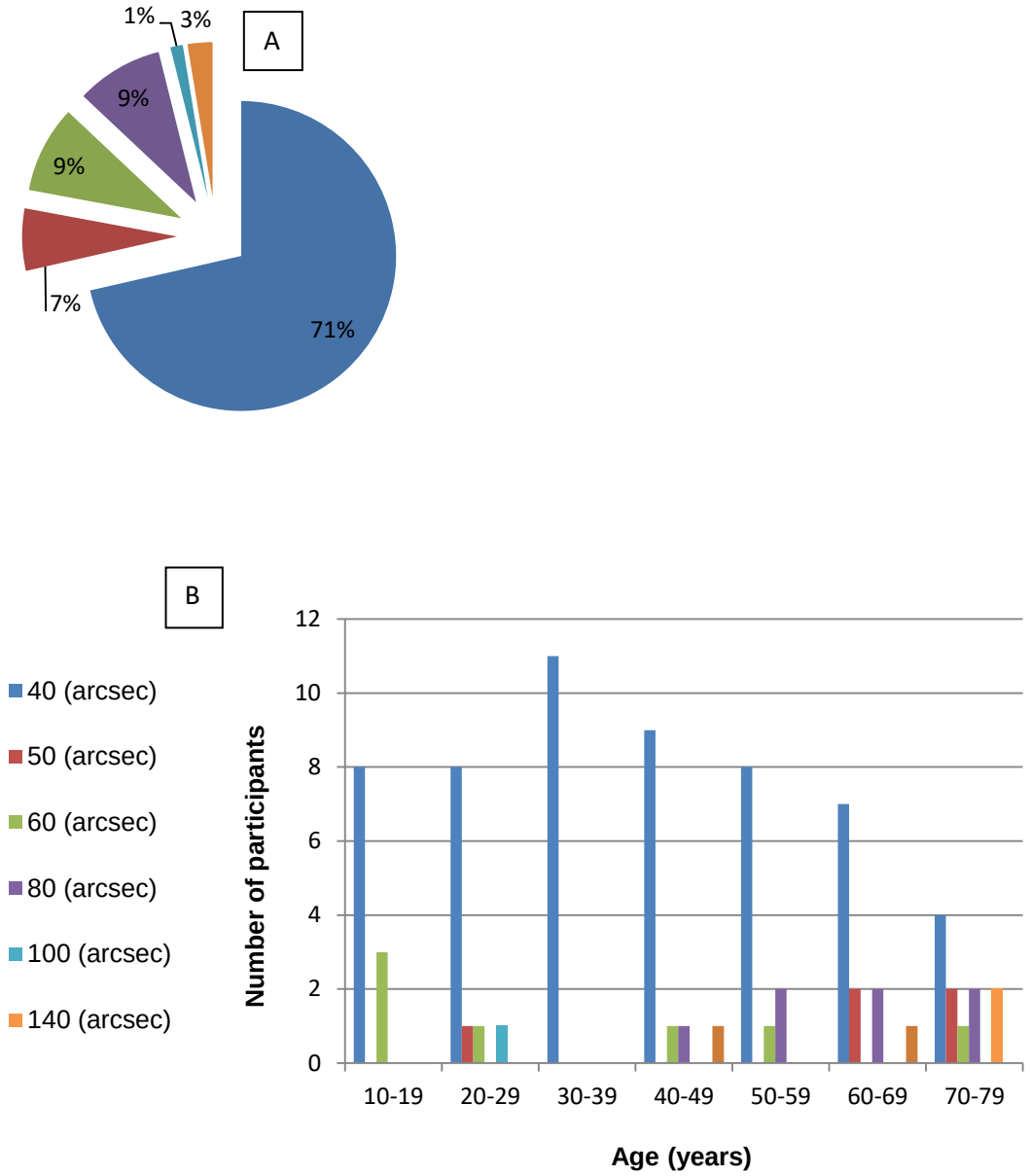


Figure 4.2 A: Pie chart showing the distribution of Titmus stereoacuity values (40, 50, 60, 80, 100, 140 arcsec) for the total study population (n = 77). The pie chart shows the majority of participants (71%), achieved 40 arcsec. B: Bar graph showing the frequency of stereoacuity values obtained across the total population using Titmus stereotest. It can be seen that all participants in cohort 30 - 39 years were able to achieve the maximum 40 arcsec, in comparison to cohort 70 - 79 years which recorded five different stereoacuity values.

Association between age and stereoacuity with Titmus

Initially, an analysis between stereoacuity with ungrouped age was performed using ordinal regression model. This showed that there was a statistical association between stereoacuity and age ($p < 0.05$) (see Table 4.4); as age increases, the value of stereoacuity increases numerically (i.e. stereoacuity worsens). From the ordinal regression model analysis, for a year increase in age, the log odds of having stereoacuity increases (worsens) by 0.031 arcsec (see Table 4.4).

Parameter	Raw regression coefficient parameter	Significance
Age	.031	.024

Table 4.4 Ordinal regression model was fitted with Titmus stereoacuity as the variable and ungrouped age as the threshold. There was a significant association between ungrouped age and stereoacuity ($p < 0.05$). Value in purple indicates a statistical significance.

The results from the ordinal regression model for Titmus stereotest per cohort are shown in Table 4.5. Using cohort 70 - 79 years as the reference, a positive raw regression coefficient parameter indicates that the cohort was more likely to observe a stereoacuity value greater than cohort 70 - 79 years (i.e. weaker stereoacuity), and a negative parameter indicates the cohort was more likely to observe a lower stereoacuity value compared to cohort 70 - 79 years (i.e. better stereoacuity). When compared to cohort 70 - 79 years all other cohorts demonstrated better stereoacuity values (see Table 4.5 column B). In Table 4.5 column B, it can be seen that cohort 30 - 39 years had the highest negative value of raw regression coefficient (-21.981) (i.e. this cohort was most different from cohort 70 - 79 years), reflecting the previously mentioned result, that cohort 30 - 39 years had the best mean stereoacuity of the population. However, when cohorts were compared to cohort 70 - 79 years, only cohort 40 - 49 years was statistically different ($p < 0.05$).

Age (years)	Raw regression coefficient parameter	Significance
10 – 19	-1.597	.066
20 – 29	-1.553	.076
30 – 39	-21.981	.999
40 – 49	-2.020	.036
50 – 59	-1.442	.100
60 – 69	-1.210	.143

Table 4.5 Ordinal regression model was fitted with Titmus stereoacuity as the dependent variable and cohort 70 - 79 years as the threshold. Only cohort 40 - 49 years had a statistically significantly better stereoacuity using Titmus stereotest when compared to cohort 70 - 79 years ($p \leq 0.05$). Value in purple indicate statistical significance.

Summary

The total ungrouped population showed a statistically significant relationship between increasing age and a decline in stereoacuity measured using the Titmus stereotest. However, only cohort 40 - 49 years had a statistically significantly better stereoacuity using Titmus stereotest when compared to the eldest cohort 70 - 79 years, making it difficult to make clinical based applications from this grouped analysis.

TNO stereotest

The mean stereoacuity for the total population was 94.3 ± 82.1 arcsec, mode 60 arcsec, and stereoacuity range 15 - 480 arcsec. Despite some fluctuation, the overall mean stereoacuity shows a decline with increasing age, with the weakest stereoacuity value recorded in cohort 70 - 79 years (130.9 ± 58.9 arcsec). The mean stereoacuity for cohorts 30 - 39 years and 50 - 59 years were unusually better than the mean stereoacuity recorded by the preceding age cohorts 20 - 29 years and 40 - 49 years respectively (refer to TNO descriptive statistics in Appendix 16). Similar to the Titmus stereotest, cohort 30 - 39 years achieved the best mean stereoacuity (43.6 ± 15.7 arcsec). Cohort 60 - 69 years had the largest standard deviation (130 arcsec), reflecting greatest variability in the results obtained in this cohort, with a range of values obtained from 60 - 480 arcsec.

The median stereoacuity for the total population was 60 (IQR 60 - 120) arcsec. Cohort 70 - 79 years has the worst median stereoacuity (120 arcsec, no IQR). Cohort 30 - 39 years with best median stereoacuity (30 arcsec, IQR: 30 - 60 arcsec). Whilst cohorts 10 - 19 years, 20 - 29 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years cohorts recorded the same median value (60 arcsec), the box plot for cohort 10 - 19 years displayed a different IQR (45 - 60 arcsec) from the other four cohorts (20 - 29 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years), for whom the IQR was 60 - 120 arcsec. Cohort 10 - 19 years had the smallest of the six boxplots (i.e. smallest IQR), reflecting a high level of agreement between participants.

From Figure 4.3 it can be seen that no cohort showed normally distributed data, and therefore median rather than mean would be the correct measure for describing the variable. Cohorts 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years showed positively skewed data, whilst cohort 10 - 19 years showing negatively skewed data. There is no IQR range for cohort 70 - 79 years, as this cohort had a high level of agreement, with 7 of the 11 participants achieving 120 arcsec.

TNO had a potential for six values of stereoacuity (15, 30, 60, 120, 240, 480 arcsec); the majority of participants (49 of the 77 participants, 63.3%) achieved 60 arcsec or better. Only two participants (both aged 19 years) achieved the maximum value of stereoacuity of 15 arcsec (see Figure 4.4). Cohort 30 - 39 years achieved the best level of stereoacuity overall, with 100% of the cohort achieving 60 arcsec or better. Cohort 70 - 79 years scored the ‘worst’ stereoacuity, with 9/11 (81.8%) participants achieving ≥ 120 arcsec. Cohort 10 - 19 years may not have had the largest standard deviation but it had the widest range of values obtainable (15 - 240 arcsec) (see Figure 4.4). Figure 4.4 shows that TNO values > 120 arcsec are more likely to be seen in older ages (cohorts 50 - 59 years, 60 - 69 years and 70 - 79 years), whilst, the best stereoacuity value (15 arcsec), was only found in the cohort 10 - 19 years. However, cohort 10 - 19 years recorded the widest range of values obtainable (15 - 240 arcsec). Participants in cohorts 40 - 49 years and 60 - 69 years recorded the ‘worst’ potential stereoacuity value 480 arcsec. In summary, older aged participants (≥ 70 years) are more likely to achieve a weaker stereoacuity value with the TNO stereotest.

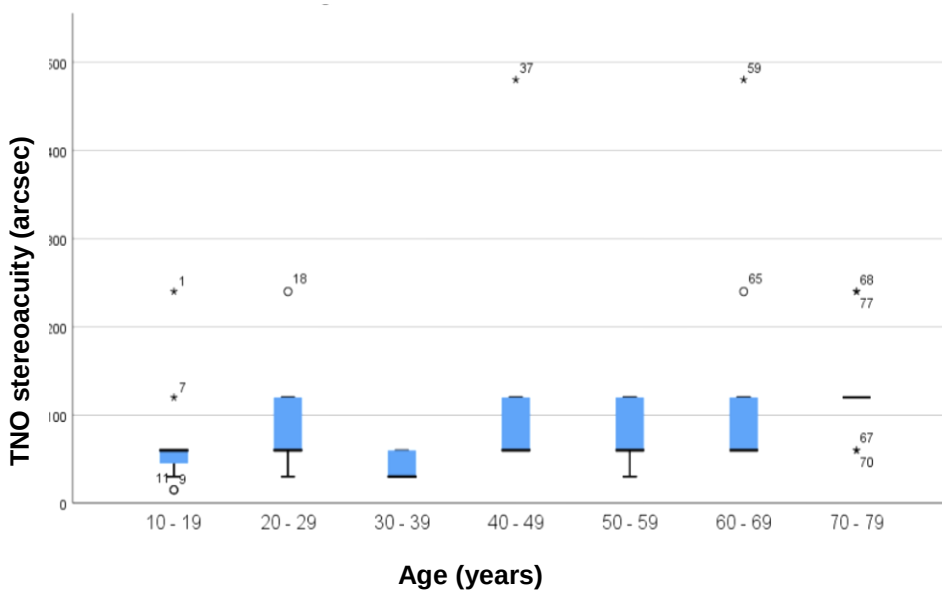


Figure 4.3 Box plot displaying the median, IQR range, and the minimum and maximum stereoacuity of TNO stereotest. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers (NB participant ID not age is depicted in graph) were individually plotted.

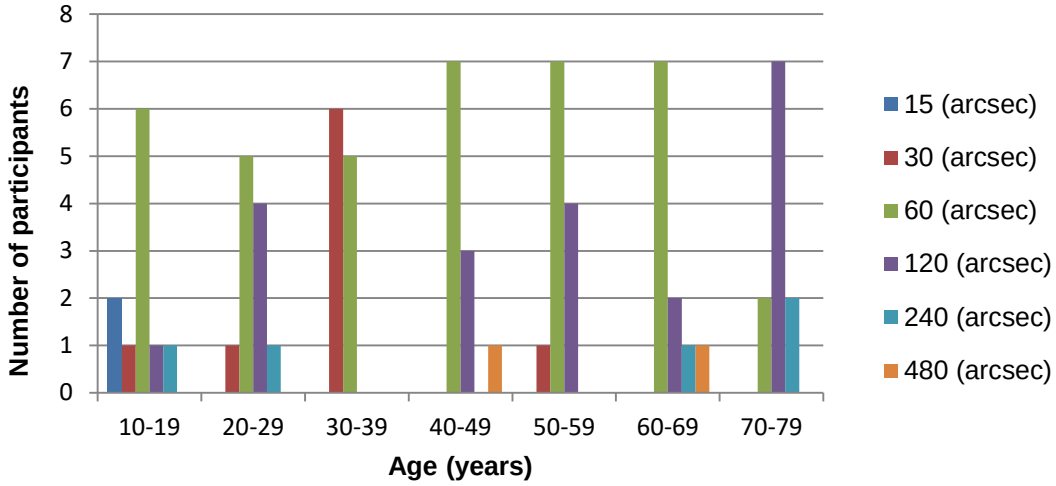


Figure 4.4 Distribution of TNO stereoacuity values across the population. It can be seen the TNO values > 120 arcsec are more likely to be seen in older ages (cohorts 50 - 59 years, 60 - 69 years and 70 - 79 years). Stereoacuity value 15 arcsec was only found in the cohort 10 - 19 years. Cohort 10 - 19 years showed the widest range of values obtainable (15 - 240 arcsec). One participant in cohorts 40 - 49 years and 60 - 69 years recorded the 'worst' stereoacuity value (480 arcsec).

Association between age and stereoacuity with the TNO stereotest

Initially an analysis between stereoacuity with ungrouped age was performed using an ordinal regression model. This showed that there was a statistically significant association between stereoacuity and age ($p < 0.005$) (see Table 4.6); as age increased, the value of stereoacuity increased numerically (i.e. stereoacuity worsened). Using log odds, for each year of increase in age, TNO stereoacuity increased (worsens) by 0.037 arcsec.

Parameter	Raw regression coefficient parameter	Significance
AGE	.037	.002

Table 4.6 An ordinal regression model was fitted with TNO stereoacuity as the dependent variable and ungrouped age as the threshold. There was a significant association between ungrouped age and TNO stereoacuity ($p < 0.005$). Values in purple indicate a statistical significance.

The results from the ordinal regression model for the TNO stereotest are shown in Table 4.7, using cohort 70 - 79 years as the reference; a negative raw regression coefficient parameter indicates the cohort was more likely to observe a numerically lower stereoacuity value compared to the 70 - 79 years cohort (i.e. better stereoacuity). The results from the ordinal regression model for TNO stereotest showed that all other cohorts are likely to observe lower stereoacuity values when compared to cohort 70 - 79 years (i.e. better stereoacuity).

Age (years)	Raw regression coefficient parameter	Significance
10 – 19	-3.093	.001
20 – 29	-1.277	.110
30 – 39	-4.259	.000
40 – 49	-1.345	.092
50 – 59	-1.697	.036
60 – 69	-1.208	.135

Table 4.7 An ordinal regression model was fitted with TNO stereoacuity as the dependent variable and cohort 70 - 79 years as the threshold. Cohorts 10 - 19 years, 30 - 39 years, and 50 - 59 years had a statistically significantly better stereoacuity using the TNO stereotest when compared to cohort 70 - 79 years ($p \leq 0.05$). Values in purple indicate statistical significance.

Despite cohort 70 - 79 years demonstrating a higher TNO stereoacuity value (i.e. worse stereoacuity) than all other cohorts, there was no statistically significant difference found between cohort 70 - 79 years and cohorts 20 - 29 years ($p = 0.11$), 40 - 49 years ($p = 0.09$) and 60 - 69 years ($p = 0.14$) (see Table 4.7).

Summary

Whilst, the total ungrouped population showed a statistically significant relationship between increasing age and a decline in stereoacuity measured using the TNO stereotest, only cohorts 10 - 19 years, 30 - 39 years and 40 - 49 years had a statistically significantly better stereoacuity using the TNO stereotest when compared to the eldest cohort 70 - 79 years ($p \leq 0.05$), making it difficult to make clinical applications based on the grouped analysis.

Frisby stereotest

The results for the Frisby stereotest were separated into crossed and uncrossed (reminder: circle protruding towards the participant is crossed disparity, and circle recessed away from the participant is uncrossed disparity).

Uncrossed Frisby stereotest

As measured by the Frisby stereotest (uncrossed disparity), the mean stereoacuity for the total population was 44.6 ± 42.8 arcsec, mode 20 arcsec, and range 20 - 150 arcsec. As with the TNO and Titmus stereotests, cohort 30 - 39 years achieved the best mean stereoacuity for the population (20 arcsec), with all participants in the cohort achieving 20 arcsec. Once more, cohort 70 - 79 years had the worst mean stereoacuity value (83.2 ± 35.9 arcsec). The mean stereoacuity for the youngest cohort 10 - 19 years (48.2 ± 40.0 arcsec), was weaker than for the subsequent four cohorts (20 - 59 years). Whilst, there is a steady decline in mean stereoacuity with increasing age from all cohorts after 30 - 39 years, there was a slight improvement in mean stereoacuity from cohort 20 - 29 years (25.9 ± 19.6 arcsec) to cohort 30 - 39 years (20 ± 0 arcsec). Cohort 60 - 69 years had the largest standard deviation (77.5 arcsec), reflecting greatest variability in the results obtained in this cohort, with a range of stereoacuity values of 20 - 300 arcsec.

The median stereoacuity for the total population was 30 arcsec (IQR 20 - 55 arcsec). Cohort 70 - 79 years has the worst median stereoacuity of 85 arcsec (IQR 55 - 110 arcsec). Cohorts 20 - 29 years, 30 - 39 years, and 40 - 49 years demonstrated the best median stereoacuity of 20 arcsec. Cohorts 10 - 19 years and 50 - 59 years recorded median stereoacuity 30 arcsec (IQR 20 - 55 arcsec, for both cohorts), and 60 - 69 years recorded median stereoacuity 55 arcsec (IQR 40 - 55 arcsec). As Figure 4.5 shows, there is no IQR for three cohorts (20 - 29 years, 30 - 39 years and 40 - 49 years), as these cohorts had a high level of agreement, with 30/33 participants achieving 20 arcsec.

While, cohort 70 - 79 years showed normally distributed data, the remaining cohorts were not normally distributed; therefore, the median stereoacuity is a more appropriate measure than mean stereoacuity for describing the results of the variable for this cohort. Cohorts 10 - 19 years and 50 - 59 years showed positively skewed data and cohort 60 - 69 years showing negatively skewed data. As mentioned above, cohorts 20 - 29 years, 30 - 39 years and 40 - 49 years had no IQR, and therefore, the data does not have any distribution. Cohort 70 - 79 years had the largest boxplot reflecting a low level of agreement between participants.

The Frisby stereotest had a potential for 12 values of stereoacuity (5, 10, 20, 30, 40, 55, 75, 85, 110, 150, 170 and 300 arcsec); however, within this population there were 8 observation stereoacuity values recorded. The majority of participants, 64 of 77 participants (83.1%), achieved 55 arcsec or better. No participant in this study achieved 5 or 10 arcsec stereoacuity. A stereoacuity of 20 arcsec was measured in 40/77 (51.9%) participants (the mode stereoacuity value for the population); with all participants in cohort 30 - 39 years, 10/11 participants in cohort 20 - 29 years and 9/11 participants in cohort 40 - 49 years achieved 20 arcsec. In contrast, no participants achieved 20 arcsec in cohort 70 - 79 years, and in cohort 60 - 69 years only one participant achieved 20 arcsec. In summary, older aged participants (≥ 60 years) are more likely to achieve a weaker stereoacuity value with the Frisby (uncrossed) stereotest.

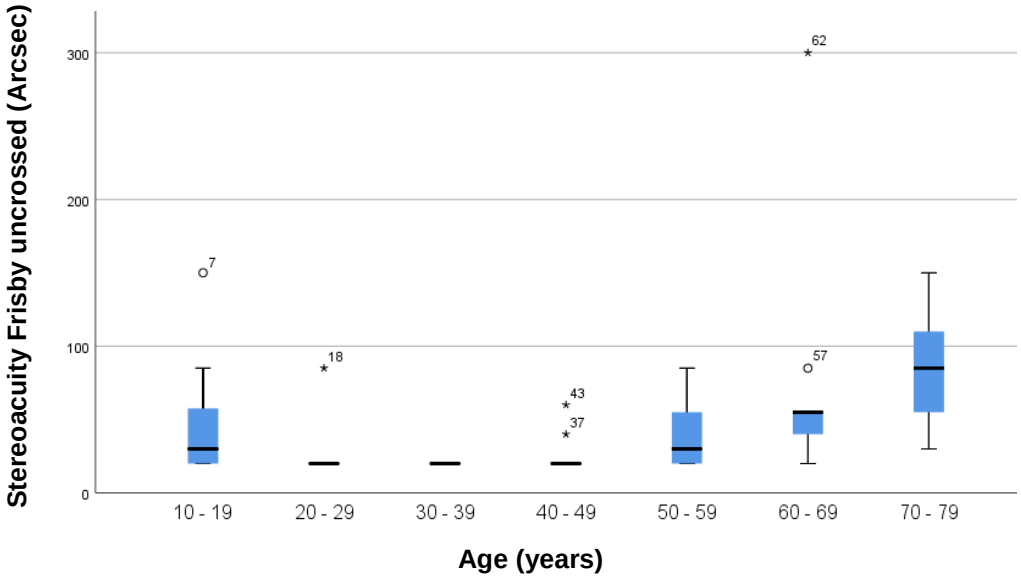


Figure 4.5 Box plot displaying the median, IQR, and the minimum and maximum stereoacuity of the Frisby stereotest (uncrossed disparity). Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers (NB the participant ID not age is depicted in graph) were individually plotted.

Crossed Frisby stereotest

For the Frisby stereotest (crossed disparity), the mean stereoacuity for the total population was 43.7 ± 37.7 arcsec, mode 20 arcsec, and range 20 - 150 arcsec. For a fourth time, cohort 30 - 39 years achieved the best mean stereoacuity for the population (20 ± 0 arcsec) and cohort 70 - 79 years had the worst mean stereoacuity value (89.1 ± 39.4 arcsec). Again, cohort 60 - 69 years had the largest standard deviation (42.8 arcsec); reflecting greatest variability in the results obtained in this cohort, with a range of stereoacuity values 20 - 150 arcsec.

The median stereoacuity for the total population was 20 arcsec (IQR 20 - 55 arcsec), this was a slightly better median stereoacuity compared to uncrossed measurements (median 30 arcsec IQR 20 - 55 arcsec). Cohort 70 - 79 years has the worst median stereoacuity (85 arcsec IQR 55 - 120 arcsec), compared to cohorts 20 - 29 years, 30 - 39 years, 40 - 49 years, and 50 - 59 years with the best median stereoacuity 20 arcsec. Cohort 10 - 19 years recorded median stereoacuity 30 arcsec (IQR 20 - 55 arcsec), which is the same median and IQR as uncrossed Frisby. Cohort 60 - 69 years recorded median stereoacuity 40 arcsec (IQR 20 - 70 arcsec), which is an

improvement from the uncrossed Frisby median (55 arcsec IQR 40 - 55 arcsec). There is no IQR for cohort 30 - 39 years as this cohort had a high level of agreement, with all participants achieving 20 arcsec. There is no IQR for cohort 20 - 29 years; this cohort had a high level of agreement with 10 of 11 participants achieving 20 arcsec.

From Figure 4.6, it can be seen that no cohort showed normally distributed data, therefore, the median stereoacuity is a more appropriate measure than mean stereoacuity for describing the results of this variable. Cohorts 10 - 19 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years showed positively skewed data and cohort 70 - 79 years showed negatively skewed data. Additionally, Figure 4.6 shows that whilst cohorts 20 - 29 years, 30 - 39 years, 40 - 49 years, and 50 - 59 years recorded same median value (20 arcsec), there were different distributions. Cohort 70 - 79 years had the largest boxplot, with long upper and lower whiskers reflecting a low level of agreement between participants.

The Frisby stereotest (crossed disparity) had potentially 12 values of stereoacuity (5, 10, 20, 30, 40, 55, 75, 85, 110, 150, 170 and 300 arcsec), and, like the uncrossed presentation, within this population there were eight observed stereoacuity values recorded. The majority of participants (64 of 77 participants, 83.1%) achieved 55 arcsec or better on the Frisby stereotest (crossed disparity), the same number of participants as the Frisby stereotest (uncrossed disparity). No participant in this study achieved 5 or 10 arcsec stereoacuity using the Frisby stereotest (crossed or uncrossed disparities).

A stereoacuity of 20 arcsec was measured in 44 of 77 participants (57.1%), the mode was 20 arcsec; this is four more participants than the Frisby stereotest (uncrossed disparity); all participants in cohort 30 - 39 years, 10/11 participants in cohort 20 - 29 years and 8/11 participants in cohort 40 - 49 years. In contrast, no participants achieved 20 arcsec in cohort 70 - 79 years, and only three participants in cohort 60 - 69 years achieved 20 arcsec. In summary, like with the Frisby stereotest (uncrossed disparity), older aged participants (≥ 60 years) were more likely to achieve a weaker stereoacuity value with the Frisby stereotest (crossed disparity).

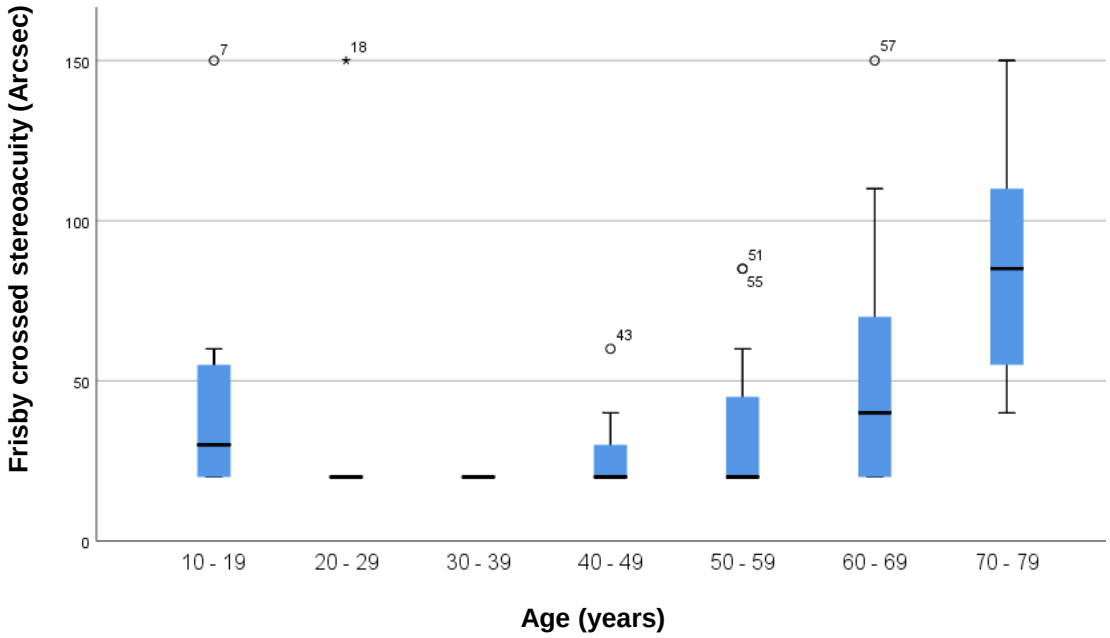


Figure 4.6 Box plot displaying the median, IQR, and the minimum and maximum stereoacuity of the Frisby stereotest (crossed disparity). Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers were individually plotted.

Association between age and stereoacuity with the Frisby stereotest

Initially, tests for normality were performed for the Frisby stereoacuity as there were eight observed values. For the Frisby stereotest (uncrossed and crossed disparity), normality was not achieved for each cohort. As presented earlier cohort 30 - 39 years had one observed stereoacuity value (20 arcsec), for both variables (uncrossed and crossed). It was not possible to transform one value to create normality, so no transformation was performed on the Frisby stereotest variables.

To determine if there was an association between ungrouped age and the Frisby stereoacuity (crossed and uncrossed disparity), a simple linear regression model was fitted to the data. Assumptions for linear regression were checked using histogram of residuals and dot plot of residuals, against predicted values (see Appendix 18). The linearity of the scatterplot for the Frisby uncrossed stereoacuity and ungrouped age showed a significant linear correlation ($r = 0.364$, $p < 0.001$) (see Appendix 17). The linearity of the scatterplot for the Frisby crossed stereoacuity and ungrouped age

showed a significant linear correlation (r = 0.377, p <0.001) (see Appendix 17); and therefore a linear regression model could be applied.

Using the linear regression model, there was a significant increase in the Frisby stereoacuity (uncrossed and crossed) with increasing age (p < 0.005). Consequently, for a one year increase in age, the Frisby stereoacuity (uncrossed disparity) value increased by 0.791 arcsec (i.e. stereoacuity worsens by 0.791 arcsec); and the Frisby stereoacuity (crossed disparity) value increased by 0.722 arcsec (i.e. stereoacuity worsens by 0.722 arcsec) (see Table 4.8).

Dependent Variable: FRISBY STEREOTEST (UNCROSSED DISPARITY)		
Parameter	**Raw regression coefficient parameter**	**Significance**
Ungrouped Age (years)	.791	.001
Dependent Variable: FRISBY STEREOTEST (CROSSED DISPARITY)		
Parameter	**Raw regression coefficient parameter**	**Significance**
Ungrouped Age (years)	.722	.001

Table 4.8 Simple linear regression model analysis displaying p value for the regression parameters. This shows a statistically significant positive relationship between ungrouped age and the Frisby stereoacuity (p < 0.005). Values in purple indicate a statistically significant result. Values in green indicate how a one-year in age will yield a change in stereoacuity.

The Kruskal-Wallis test compared the median stereoacuity between the cohorts for Frisby stereoacuity (uncrossed and crossed disparities). The ranked scores obtained highlighted any cohorts with higher stereoacuity values. The hypothesis tested was the equality of medians in all cohorts against the alternative hypothesis of a difference in cohort medians. The results from Kruskal-Wallis analysis test for the Frisby stereoacuity (uncrossed and crossed disparities), showed a highly statistically significant correlation between cohorts and stereoacuity (p < 0.0005). As cohort age increased, the stereoacuity measured with the Frisby stereotest declined.

Unfortunately, SPSS does not have the option to do pairwise comparisons for medians to identify which cohorts were different; it can only do this for means (dependent on

assumption of normality). However, in the descriptive results, it was presented that cohort 30 - 39 years achieved the best median stereoacuity, for the Frisby stereotest (crossed and uncrossed disparities), 20 arcsec with no IQR. A linear regression model analysis was performed to establish if this was a statistically significant different finding from the other cohorts. Cohorts 60 - 69 years and 70 - 79 years had a statistically significantly weaker value for stereoacuity when compared to cohort 30 - 39 years ($p < 0.05$), for both uncrossed and crossed Frisby stereotest (see Table 4.9). Cohort 10 - 19 years had a statistically weaker value for stereoacuity when compared to cohort 30 - 39 years using the uncrossed Frisby projection only ($p < 0.05$). There was no statistically significant difference in the values obtained for cohorts 20 - 29 years, 40 - 49 years, and 50 - 59 years, when compared to cohort 30 - 39 years (see Table 4.9).

Age (years)	P-value (Frisby uncrossed)	P-value (Frisby crossed)
10 - 19	.009	.079
20 - 29	.577	.393
40 - 49	.606	.598
50 - 59	.097	.213
60 - 69	.009	.011
70 - 79	.000	.000

Table 4.9 Results from the linear regression analysis for the Frisby stereotest (uncrossed and crossed disparities) when cohort 30 - 39 years is used as a reference category. Values in purple indicate a statistical significant finding.

Summary

In summary, cohorts 60 - 69 years and 70 - 79 years recorded higher Frisby uncrossed and crossed median stereoacuity values (i.e. weaker stereoacuity) than the other cohorts. Cohort 70 - 79 years had the weakest median stereoacuity of the total population. Cohort 30 - 39 years had the strongest median stereoacuity value (both uncrossed and crossed), but was not statistically different to cohorts 20 - 29 years, 40 - 49 years, and 50 - 59 years. There does appear to be a continuing improvement in stereoacuity in children during their 2nd decade of life, when measured by Frisby stereotest, but this was only statistically significant with uncrossed Frisby. Overall, there was a highly statistically significant correlation between ungrouped age and

stereoacuity, as age increases, stereoacuity measured with the Frisby stereotest declines.

FD2 stereotest

Using the FD2 stereotest, the mean distance stereoacuity for the total population was 23.0 ± 11.0 arcsec, mode 20 arcsec, and range 0 - 50 arcsec. Cohort 40 - 49 years achieved the best mean stereoacuity for the population (17.7 ± 9.3 arcsec). As with the four near stereoacuity tests, cohort 70 - 79 years had the worst mean stereoacuity value (35.8 ± 17.4 arcsec), with 5 of 11 participants reporting no stereoacuity response. The mean stereoacuity remained fairly static for the younger cohorts (10 - 19 years, 20 - 29 years, 30 - 39 years, and 40 - 49 years), and then declined for the older three cohorts (50 - 59 years, 60 - 69 years, and 70 - 79 years), therefore, the mean stereoacuity worsened with increasing age.

Cohorts 70 - 79 years and 60 - 69 years were the only cohorts to have a stereo-negative response, 5 of 11 in cohort 70 - 79 years, and 1 of 11 in cohort 60 - 69 years. Cohort 70 - 79 years had the largest standard deviation (17.4 arcsec) and was based on six participants who reported stereoacuity, reflecting the greatest variability in the results obtained in this cohort. The range of stereoacuity values for cohort 70 - 79 years, based on raw data, was no stereoacuity detected to 50 arcsec.

The median FD2 distance stereoacuity for the total population was 42.50 arcsec (IQR 15 - 30 arcsec). Cohort 70 - 79 years had the worst median stereoacuity (42.5 arcsec IQR 20 – 50 arcsec). Cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years, and 40 - 49 years all had a median stereoacuity 20 arcsec but with differing IQR (see Figure 4.7). Cohort 50 - 59 years recorded median stereoacuity 25 arcsec (IQR 18 - 30 arcsec), and cohort 60 - 69 years recorded median stereoacuity 27.5 arcsec (IQR 21 - 34 arcsec).

FD2 had a potential for 10 values of stereoacuity (5, 10, 15, 20, 25, 30, 35, 40, 45 and 50 arcsec). The mode stereoacuity response was 20 arcsec and was achieved in 20 of 77 (26.0%) participants. The majority of the participants achieved ≤ 20 arcsec, i.e. better than or equal to 20 arcsec (36 of 71 participants, 50.1%). There were four participants (5.2%), (aged 29 years, 29 years, 40 years, and 48 years) who achieved the best stereoacuity value of 5 arcsec.

From Figure 4.7 it can be seen that cohort 30 - 39 years showed normally distributed data, whereas, cohorts 10 - 19 years and 60 - 69 years showed positively skewed data, and cohorts 20 - 29 years, 40 - 49 years, 50 - 59 years, and 70 - 79 years showed negatively skewed data. Therefore, the median stereoacuity is a more appropriate measure than mean stereoacuity for describing the results of the variable. Figure 4.7 displays the increase in the median stereoacuity in the cohorts subsequent to cohort 40 - 49 years. Cohort 70 - 79 years had the largest boxplot reflecting low level of agreement between participants. Cohort 60 - 69 years had the longest upper and lower whiskers indicating a wider distribution of stereoacuity values.

In summary, older age participants (> 50 years) are more likely to record a weaker distance stereoacuity value with the FD2 stereotest, with participants older than 70 years frequently reporting a stereo-negative response.

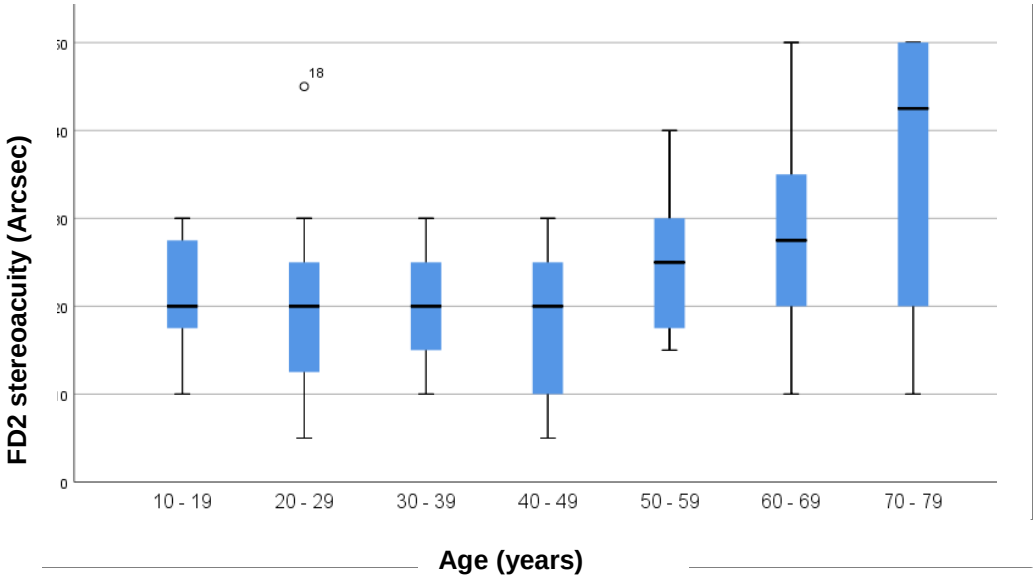


Figure 4.7 Box plot displaying the median, IQR, and the minimum and maximum stereoacuity of FD2 stereotest. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. Participant 18 was a box outlier for cohort 20 - 29 years, and was individually plotted. This was the first box plot that displays an IQR for every cohort.

Association between age and distance stereoacuity with FD2

Initially, a Pearson correlation coefficient analysis was used to determine if there was a linear relationship between the two continuous variables of ungrouped age and FD2 stereoacuity. There was a statistically significant correlation between ungrouped age

and FD2 stereoacuity ($r = 0.357$, $p < 0.005$) (see Appendix 17). As ungrouped age increases, the value for mean FD2 increases (i.e. stereoacuity declines). As ungrouped age increases by one year, FD2 stereoacuity value increases by 0.211 arcsec (i.e. stereoacuity worsens by 0.211 arcsec).

To determine the relationship between grouped age and FD2, the simple linear regression model was fitted to the data. Before assessing for an association between cohorts and stereoacuity, tests for normality were performed for FD2 stereotest, as there were > 8 observed values. For the FD2 stereotest the null hypothesis regarding normality was accepted (i.e. the data were normally distributed), and both Shapiro-Wilk and Kolmogorov Smirnov tests had p values > 0.05. Assumptions for simple linear regression were checked by histogram of residuals and dot plot of residuals, against predicted values. The histogram of residuals and residual plots indicated that normality assumption was met, and the residual plot showed a random scatter, indicating that constant variance was not violated (see Appendix 18).

As normality was achieved, an ANOVA was performed to determine if there were significant differences in FD2 stereoacuity across the cohorts. ANOVA tested the hypothesis that the mean stereoacuity in all cohorts were the same, by comparing the variation between cohorts and the variation within cohorts. If the p value in the ANOVA table is < 0.05, then there exists at least two cohorts that are different, otherwise there is no difference between cohorts mean stereoacuity. For FD2 $p < 0.05$ indicated that there are some cohorts who are different, and the results from ANOVA show that at least two age cohorts have statistically significantly different FD2 stereoacuity values ($p < 0.05$). To determine which cohorts are significantly different, pairwise comparisons of mean stereoacuity were performed.

From the pairwise comparisons of mean stereoacuity, cohort 10 - 19 years had a statistically significant difference from cohort 70 - 79 years. Cohort 20 - 29 years had a statistically significantly difference from cohorts 60 - 69 years and 70 - 79 years. Cohort 30 - 39 years had a statistically significant difference from cohort 70 - 79 years. Cohort 40 - 49 years had a statistically significant difference from cohorts 60 - 69 years and 70 - 79 years. Cohort 50 - 59 years had a statistically significant difference form cohort 70 - 79 years. Cohort 60- 69 years had a statistically significantly difference from cohorts 20 - 29 years and 40 - 49 years. Cohort 70 - 79 years had a statistically significant difference from all cohorts except cohort 60 - 69 years ($p < 0.05$) (see Table 4.10).

From the descriptive results it was presented that cohorts 10 - 19 years, 20 - 29 years, 33 - 39 years, and 40 - 49 years had the same median stereoacuity (20 arcsec). Cohort 40 - 49 years achieved the best mean stereoacuity for FD2 stereotest (17.73 arcsec). An ordinal regression model analysis was performed to establish what cohorts were statistically different from cohort 40 - 49 years. Cohorts 60 - 69 years and 70 - 79 years had a statistically significant weaker value for stereoacuity when compared to cohort 40 - 49 years using the FD2 stereotest ($p < 0.05$). There was no statistically significant difference in the stereoacuity values obtained for cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years and 50 - 59 years, when compared to cohort 40 - 49 years.

Age (years)	Age (years)	P value
10 – 19	70 – 79	.007
20 – 29	60 – 69	.048
	70 – 79	.002
30 – 39	70 – 79	.003
40 – 49	60 – 69	.018
	70 – 79	.001
50 – 59	70 – 79	.032
60 – 69	20 – 29	.048
	40 – 49	.018
70 – 79	10 – 19	.007
	20 – 29	.002
	30 – 39	.003
	40 – 49	.001
	50 – 59	.032

Table 4.10 Results showing the pairwise comparisons that identified cohorts which were different for the FD2 stereotest (see Appendix 17 for full table). Column 1 is the dependent variable, column 2 is the threshold variable, and column 3 shows the p values (in purple) which were significant ($p < 0.05$).

Summary

In summary, using FD2 stereotest, cohorts 60 - 69 years and 70 - 79 years recorded a higher median stereoacuity values (i.e. weaker stereoacuity) when compared to the five younger cohorts; and cohort 70 - 79 years had the weakest median stereoacuity of the total population. Although, cohort 40 - 49 years had the best mean stereoacuity, it had the same median stereoacuity value to cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years, and was not statistically different to cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years and 50 - 59 years. Overall, there was a highly statistically significant association between ungrouped age and stereoacuity, as age increases distance stereoacuity measured with FD2 stereotest declines.

Outline of stereoacuity results

All five tests of stereoacuity showed that increasing age (ungrouped) was associated with a decline in stereoacuity, and that this was a statistically significant finding for all stereotests.

When participants were grouped by age into cohorts, cohort 30 - 39 years recorded the best near stereoacuity result when based on median and IQR (also the best mean stereoacuity value on every test), but was not statistically different to cohorts 20 - 29 years, 40 - 49 years, and 50 - 59 years with either crossed or uncrossed disparity. Cohort 30 - 39 years was statistically different (i.e. stronger stereoacuity) to cohort 10 - 19 years with uncrossed disparity but not statistically different with crossed disparity. Cohort 40 - 49 years recorded the best distance stereoacuity result when based on mean stereoacuity value (and SPSS ranking). Only cohorts 60 - 69 years and 70 - 79 years had a statistically significant weaker stereoacuity value compared to cohort 40 - 49 years.

A direct comparison between stereotests and their mean stereoacuity values for age cohorts and total population will not be reliable due to the difference in the stereotest designs, difference in values measurable, difference in the angular size of the test (see Chapter 1). However, it is interesting to see the amount of change between the best median stereoacuity value and worst median stereoacuity value for each stereotest. The most marked decline in near stereoacuity was found using the Frisby stereotest, and the least decline in near stereoacuity was found using the Titmus stereotest (see Table 4.11). This finding supports the importance of stereotest selection when performing clinical examination of stereoacuity when diagnosing or monitoring changes

in stereoacuity, i.e. the Frisby stereotest will be more sensitive to changes earlier than the Titmus stereotest in progressive conditions.

Stereotest	**Best stereoacuity (arcsec)**	**Worst stereoacuity (arcsec)**	**Factor change**	**Reduction in stereoacuity per year (arcsec/year)**
Titmus	40	50	1.25x	0.031
TNO	30	120	4x	0.037
Frisby (uncrossed)	20	85	4.25x	0.791
Frisby (crossed)	20	85	4.25x	0.722
FD2	20	42.5	2.125x	0.211

Table 4.11 Table showing the best and worse median stereoacuity values achieved by participants in this study as measured for all stereotests, the factor change and the reduction in stereoacuity per year. The best median for the Titmus stereotest was taken from cohorts 10 - 19 years, 20 - 29 years, 30 - 39 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years, and the worst median stereoacuity value was taken from cohort 70 - 79 years. Best median stereoacuity for the TNO stereotest was taken from cohort 30 - 39 years, and the worst median stereoacuity was taken from cohort 70 - 79 years. Best median for the Frisby stereotest (uncrossed disparity) was taken from cohorts 20 - 29 years, 30 - 39 years, and 40 - 49 years, and the worst median stereoacuity was taken from cohort 70 - 79 years. The best median stereoacuity for the Frisby stereotest (crossed disparity) was taken from cohorts 20 - 29 years, 30 - 39 years, 40 - 49 years, and 50 - 59 years, and the worst median stereoacuity was taken from cohort 70 - 79 years. The best median stereoacuity for the FD2 stereotest was taken from cohorts 20 - 29 years, 30 - 39 years, and 40 - 49 years, and the worst median stereoacuity was taken from cohort 70 - 79 years.

Finally, a comparison of the p values gives an indication of the likelihood an observed difference is caused by chance (203). The ‘real’ depth near stereotest (Frisby) had a smaller statistical significance by a factor of 0.15 in comparison to TNO stereotest, and a factor of 0.0125 in comparison to Titmus stereotest. Hence, the possibility of eliciting an age related reduction in stereoacuity ‘by chance’ on Frisby is least likely compared to other near stereotests (see Table 4.12).

Stereotest	Method of statistical analysis	P value (4dp)
Titmus	Ordinal regression	0.0236
TNO	Ordinal regression	0.0019
Frisby crossed	Kruskal- Wallis	0.0003
Frisby uncrossed	Kruskal- Wallis	0.0003
FD2	ANOVA	0.0020

Table 4.12 Table showing the statistical outcome (p value) and the method of statistical analysis for stereoacuity versus age, for each stereotest.

4.5 Discussion

In this chapter, a single, experienced orthoptist measured stereoacuity with four commercially available stereotests in a wide age range of children and adults (equally distributed between seven 10-year age brackets), with normal vision, and without ocular or general health issues. The study found that, regardless of the clinical stereotest used, there was a statistically significant relationship between age and stereoacuity. The reduction in stereoacuity was found in participants older than 60 years, and most evident in participants older than 70 years. The decline in Titmus stereoacuity was 0.031 arcsec/year; the decline in TNO stereoacuity was 0.037 arcsec/year; the decline in Frisby (crossed disparity) stereoacuity was 0.722 arcsec/year; the decline in Frisby (uncrossed disparity) stereoacuity was 0.791 arcsec/year; and the decline in FD2 stereoacuity 0.211 arcsec/year (see Table 4.11).

An unexpected finding was the improvement in median stereoacuity between cohorts 10 - 19 years and 30 - 39 years with the TNO stereotest and the Frisby stereotest (uncrossed and crossed disparity), as it is reported that stereoacuity matures by age 10 years. The studies that have used commercially available stereotests show variability as to when stereoacuity reaches adult level, but it is reported to occur before 9 years of age (1, 92-95); one study of 115 children aged 3 - 6.5 years suggested that stereoacuity values with TNO improve between ages 4 - 5.5 years and reach adult like levels at age 5.5 years (93). As this finding was only statistically significant with Frisby uncrossed, it is unlikely to have clinical significance with the numbers of participants enrolled in this present study.

Comparisons between stereotests are difficult, as the minimum levels of stereoacuity measured by each test differ and the tests do not measure continuous linear data (i.e.

large steps/jumps in the stereoacuity values within a test itself). However, in this study the biggest change in stereoacuity between the best cohort median and worst cohort median was found using the 'real depth' stereoacuity test (i.e. the Frisby stereotest), followed by the TNO stereotest. This conflicts with a previous study (Moorfields study), which used the same commercially available stereotests and reported the most marked decline in stereoacuity with the TNO stereotest (113). However, this study had uneven number of years in its cohorts and an unequal number of participants in each cohort (cohort 17 - 29 years, n = 12; cohort 30 - 49 years, n = 29; cohort 50 - 69 years, n = 19; and cohort 70 - 83 years, n = 13)

The Newcastle study had three age cohorts of unequal number of years (i.e. 5 - 10 years, 11 - 49 years, and 50 - 82 years) and an unequal number of participants in each age cohort (n = 22, 195 and 16 respectively) (1). Excluding the children aged under 10 years, the results from the Newcastle study are presented in Table 4.19, the current study results were adapted into two age cohorts for comparison purposes. Table 4.18 shows that the median stereo acuities with the Frisby stereotest for those aged ≤ 49 years were the same for both studies (20 arcsec) (1). However, the older cohort ≥ 50 years performed better in this present study than in the Newcastle study (1). Table 4.18 shows that the median FD2 stereoacuity for both studies declined with age, but the present study found median stereoacuity to be double (i.e. weaker) than that measured by the Newcastle study (1) for both cohorts. The Newcastle study, concluded that stereoacuity matures before the age of 10 years, remains unchanged between the ages of 10 and 50 years and then declines (1). In this present study, the median stereoacuity also remained unchanged between age 10 and 49 years and then declined, but was only statistically reduced for cohorts 60 - 69 and 70 - 79 years.

Stereotest	Age (years) (1)	N (1)	Stereoacuity Median & IQR (arcsec) (1)	Age (years)	N	Stereoacuity Median & IQR (arcsec)
Frisby	11 – 49	195	20 (20 - 30)	10 - 49	44	20 (no IQR)
Frisby	50 – 82	16	80 (20 - 130)	50 - 79	33	55 (30 - 85)
FD2	11 – 49	195	10 (5 - 15)	10 - 49	44	20 (15 - 25)
FD2	50 – 82	16	12.5 (10 - 27.5)	50 - 79	33	25 (20 - 35)

Table 4.13 Table comparing the median stereoacuity results from the Newcastle study (1) (in black), to the current study (in blue). N = number of participants.

The Keimyung study (2), shown in Table 4.14 had eight age cohorts from 7 - 76 years; for the purposes of comparisons, the youngest and eldest cohort were selected to compare (the authors presented their results as mean stereoacuity, therefore, the mean stereoacuity from the current study will be used for the comparison). Table 4.14 shows that when using the Titmus stereotest, participants in the younger cohorts had similar mean stereoacuity; however, the older cohort ≥ 70 years performed better in the current study than in the Keimyung study (2), both in terms of the mean stereoacuity and a smaller standard deviation. Whilst both studies showed a decline in stereoacuity with increasing age using the TNO stereotest; the values of mean stereoacuity using the TNO stereotest were dissimilar between the two studies. This present study found mean stereoacuity to be weaker than that measured in the Keimyung study (2) for the younger cohort, and considerably stronger in the older cohort (both smaller mean stereoacuity and narrower standard deviation). The Keimyung study concluded that as age increases, stereoacuity decreases, that it was evident from age ≥ 50 years and was most evident in participants aged ≥ 70 years (2); in this present study, using Titmus and TNO stereotests, there was only a statistically significant decline in stereoacuity for cohort 70 - 79 years. The Keimyung study, also showed that the stereoacuity standard deviation for each cohort widens with increasing age (2), an observation not found in this present study. Whilst, there appears to be no gross variances in the methods of the two studies to explain the differences (i.e. same test, same manufacturer's instructions followed, and same minimal level of visual acuity), the dissimilarities which potentially resulted in the different results are different examiner background (ophthalmologist versus orthoptist), different cohort gender mix (50% female versus 78% female), or different genetics and environments (Korean versus Irish).

Stereotest	Age (years) (2)	Stereoacuity Mean & SD (arcsec) (2)	Age (years)	Stereoacuity Mean & SD (arcsec)
TNO	11 - 20	49 ± 26.3	10 - 19	70.9 ± 63.0
TNO	71 - 80	300 ± 180	70 - 79	130.9 ± 58.9
Titmus	11 - 20	41 ± 3	10 - 19	45.5 ± 9.3
Titmus	71 - 80	118.5 ± 145.9	70 - 79	69.1 ± 58.9

Table 4.14 Table comparing the mean stereoacuity for TNO and Titmus in this present study to the Keimyung study (n = 79) (2). The current study results are in blue (n = 77).

The Sao Paulo study (3), had three age cohorts and for comparison purposes the current study's results were adapted into similar age cohorts. Additionally, the Sao Paulo study (3), presented their results as mean stereoacuity, therefore the mean stereoacuity from the current study will be presented in Table 4.15. Table 4.15 shows that the mean stereoacuity for both studies improved between cohort 1 and cohort 2 for uncrossed Frisby stereoacuity. The Sao Paulo study (3), had a minor change in mean stereoacuity between cohort 1 and cohort 2 for crossed Frisby, whereas this current study found a considerable improvement in mean stereoacuity between cohort 1 and cohort 2. Whilst, the Sao Paulo study (3), showed a deterioration in stereoacuity in the 3rd cohort (age 35 - 60 years), this current study's results do not support this finding when using participants aged 30 - 59 years. Within this current study, cohort 30 - 39 years measured the best stereoacuity value across all the near stereotests; therefore, improved the overall mean stereoacuity in this present study 35 - 60 years. Additionally, within the present study the deterioration in mean stereoacuity was only found in cohorts 60 - 69 years and 70 - 79 years. The Sao Paulo study (3), was performed in an optometry university department in Brazil on students and staff, it is unclear whether they were naïve or experienced with stereoacuity testing, and certainly the very high levels of stereoacuity achieved by their population suggests significant differences in methodology. The participants in the Sao Paulo study (3), also had a minimum 0.0 LogMAR vision and < 0.50 D refractive error indicating a more restrictive inclusion criteria than in the present study (reminder present study inclusion criteria: 0.1 LogMAR vision/ visual acuity and any spectacle corrected refractive error).

Frisby Stereotest	Age (years) (3)	N (3)	Stereoacuity Mean (arcsec) (3)	Age (years)	N	Stereoacuity Mean (arcsec)
Crossed	15 - 24	24	6.3 ± 4	10 - 19	11	44.6 ± 38.5
Crossed	25 - 34	11	6.6 ± 3.4	20 - 29	11	31.8 ± 39.2
Crossed	35 - 60	11	13.8 ± 11.2	30 - 59	33	27.9 ± 17.4
Uncrossed	15 - 24	24	5.3 ± 2.6	10 - 19	11	48.2 ± 39.8
Uncrossed	25 - 34	11	4.9 ± 2.5	20 - 29	11	25.9 ± 19.6
Uncrossed	35 - 60	11	10.7 ± 9.9	30 - 59	33	27.4 ± 15.7

Table 4.15 Table comparing the mean stereoacuity results from Costa *et al.* (3) (in black) to the current study (in blue). N = number of participants.

The Moorfields study of 60 adults aged 17 - 83 years (divided into four age cohorts), used the same stereotests as this present study, also finding that all near stereotests reported a reduction in stereoacuity with increasing age (113). The Moorfields study reported that the decline was statistically significant between their 3rd and 4th cohorts (i.e. cohorts 50 - 69 years and 70 - 83 years) (113). The Moorfields study reported the decline in stereoacuity was most marked with the TNO stereotest (113), whist in this present study the decline in stereoacuity was most noticeable with the Frisby stereotest. With the FD2 stereotest, the Moorfields study reported that there was a decline in stereoacuity between cohorts 30 - 49 years and 50 - 69 years, but no further deterioration for older age cohorts (113). In contrast, in this present study, there was a continual deterioration in median stereoacuity for the oldest three cohorts. Unfortunately, the Moorfields study's authors did not provide the mean or median stereoacuity values to facilitate a direct comparison with the present study.

The Mount Sinai study of 120 participants aged 20 - 79 years in six decade based age cohorts with 10 women and 10 men in each cohort, found a linear relationship between increasing age and decreasing stereoacuity, with a marked deterioration from age > 60 years and the regression line crossing the demarcating 'abnormal stereoacuity' line at age 65 years (96). As vision and optical factors were controlled, the authors concluded the deterioration in stereoacuity with increasing age could be attributed to neural factors (96). Unfortunately, comparisons cannot be made directly between the Mount Sinai study and this current study as threshold retinal disparity rectangular test stimuli were used rather than a commercially available stereoacuity test (96). Although, a number of previous studies have reported the deterioration in stereoacuity with increasing age, they did not provide information on all the commercially available tests included in this current study. Additionally, the previous publications did not all use the same number of participants in each cohort, use age decades as the cohorts, or exclude older participants with reduced vision. Therefore, the previous publications could not identify what decade or age at which stereoacuity decline occurs, like the Mount Sinai stimuli-based study detailed.

It is estimated that 1 in 3 adults aged over 65 years have some form of vision reducing eye disease, including age-related macular degeneration, glaucoma, cataract and diabetic retinopathy (205). Age-related changes can be seen in the cornea (e.g. changes in the shape and optical properties of the cornea and corneal degeneration), the trabecular meshwork (i.e. open angle glaucoma), the crystalline lens (i.e. cataract), the vitreous (i.e. posterior vitreous detachment and/or retinal tears and detachment),

the retina (e.g. age-related macular degeneration and diabetic retinopathy), and in the number of optic nerve axons (i.e. glaucoma, optic neuropathy) (206, 207). These anatomical changes to the eye and optic nerve result in decreased visual acuity, decreased sensitivity of the visual field, decreased contrast sensitivity, and increased dark adaption (206). In the absence of reduced vision or ocular disease, previous studies postulated reasons for the association between increasing age and a decline in stereoacuity; these include a decline in the function of cortical disparity detectors or a reduction in cerebral processing, either of which may be due to age-related changes to the microvasculature of the brain (2, 96, 113, 208, 209). One description was “As time passes, the functional abilities of the eye wane, as do the receptive, storage, and the analytical capacities of the central visual system” (206). The dissociative effect from red/green glasses with the TNO test may affect the participant’s fusion and ultimately their measured stereoacuity (113). Another postulated reason was the reduction of light incident on the retina in older adults (i.e. due to miosed pupils and cataract), caused poorer performance on visual tasks, such as stereoacuity (96, 208).

It was reported that there is no standard clinical definition of what stereo-blindness means, it was assumed to be when the participant or patient fails to correctly respond to stereoacuity tests at the largest available disparity (210). It has been suggested that 2% of asymptomatic adults have stereo-blindness (85); although, the authors provided no evidence or references to support this statement. By this definition, in this current study there were six participants (aged 62 years, 72 years, 73 years, 75 years, and two participants aged 76 years), who were stereo-negative, when stereoacuity was measured at 6 m. However, all the stereo-negative participants achieved stereoacuity on the four measurements of near stereoacuity, therefore, perhaps, distance stereoacuity could exist in a gross form, and under different circumstances or with a commercially available stereotest which measured levels of distance stereoacuity > 50 arcsec at 6m, the participants could have had a recordable stereoacuity value.

It has been proposed that the reduction/loss of stereoacuity in the elderly, combined with other musculoskeletal comorbidities limiting mobility, is linked with an increased risk of falls (211). A study of 156 residential living participants aged 63 - 90 years (mean age 76.5 ± 5.1 years) found a strong association between reduced stereoacuity measured on the Frisby stereotest and a previous history of ‘falling’ (211). In fact, there was a stronger correlation between reduced stereoacuity and the occurrence of multiple falls, than for the correlations with other factors (for example, contrast sensitivity, visual acuity or size of visual field) (211).

There are conflicting reports as to whether a child without stereoacuity has subnormal academic and sports performances than children with stereoacuity (212-214). A study of 117 children (mean age 7 years) were assessed using a stereotest commercially available in North America, the Randot 2 stereotest (a vector based stereotest similar to Titmus that can measure up to 12.5 arcsec), and had their stereoacuity value compared to the assessment performed by the classroom teacher. There was a statistically significant association between better stereoacuity and educational ability (reading $p < 0.001$, mathematics $p < 0.001$, writing $p < 0.001$). The authors concluded that better stereoacuity was significantly correlated with better academic performance (213). Whereas a parental questionnaire study of academic and non-academic performance of 117 children aged 6 - 16 years with a strabismus, to their siblings aged 6 - 12 years without a strabismus (control cohort), reported that there was no statistical difference between the cohorts on the number of children with reading difficulties (214). However, the study found that there was a statistically significant finding of parental reports of difficulty in physical education in the children with a strabismus ($p < 0.05$) (214). There was also a statistically significant finding of difficulty in non-academic areas, such as catching a ball ($p < 0.05$); having headaches ($p < 0.05$); and complaining of eye strain ($p < 0.05$) (214). When two cohorts of nine participants aged 18 - 23 years were compared for their ability to successfully catch a ball, the binocular cohort performed statistically better than the binocular cohort who were occluded (i.e. functionally monocular for the purposes of the test) (212). A study of 26 participants (age unknown), asked to walk a 7 m path both binocularly and monocularly (twice each), showed 10% slower trials and higher foot raises when stepping over obstacles when acting monocularly (215). This indicated that stereoacuity is important for aspects of daily living, such as navigating in a standard environment. However, losing stereoacuity with increasing age may have a greater impact on everyday life skills, than for lifelong monocular viewers, who have adapted their activities and visuo-motor coordination to monocular conditions. Absent or reduced stereoacuity is typically associated with amblyopia, manifest strabismus or anisometropia (216). It has been shown that one can adapt long term to the absence of stereoacuity, for example a study comparing long-term monocular participants (i.e. nil stereoacuity demonstrated from childhood, $n = 15$), to short-term monocular participants (binocular participants occluded for purpose of the test, $n = 102$), found the long-term monocular participants were significantly quicker at performing bead threading tasks (217).

In conclusion, the results of this present study using commercially available stereotests, has supported previous studies that found a decline in stereoacuity with

increasing age (1-3, 96, 113). However, this present study adds to the existing literature, because it is the only study which has studied all four stereotests using decade based cohorts of equal participant numbers.

4.6 Strengths and limitations of the study

The use of Titmus stereotest in this study may have led to a research measurement error as the maximum obtainable stereoacuity was limited by the test design. In this study, the majority of participants (55 of 77 participants, 71%) achieved the maximum stereoacuity of 40 arcsec using the Titmus stereotest, supporting a publication of 67 participants aged 18 - 24 years where 95% (n = 65) achieved 40 arcsec (150). Therefore, the accuracy of the mean stereoacuity for the population and the age cohorts were affected and limited due to the maximum stereoacuity measurable by the stereotest. It has also been suggested that the Titmus stereotest may not be useful for detecting early or small changes in stereoacuity (150).

There are two measurement biases that the researcher was conscious of from the study design stage and attempted to limit. Firstly, participant fatigue, by changing from distance fusion measurements to stereoacuity measurements, and completing the data collection with the near fusion measurements, the researcher was attempting to reduce the impact of participant fatigue. However, participant fatigue is impossible to completely eliminate, and the effect on this present study's results cannot be quantified. A second measurement error is the potential for a learned response to stereoacuity. The researcher was unable to identify any published studies which have investigated the effect on stereoacuity performance on naïve participants after exposure to commercially available stereoacuity tests. However, it is potentially possible that cerebral processes became more attune to the measurement of stereoacuity after each stereotest. This has been proposed by a single-study of 16 participants aged 16 - 45 year using a computer generated Randot stereotest, in their study the participants were faster at identifying the stereoscopic image after three training days (i.e. repeated exposure to the computer generated images), this was a statistically significant finding ($p < 0.0005$) (218). The participants also showed better stereoacuity values after three days of training, and this was a statistically significant finding ($p < 0.05$) (218). Whilst the stereotests have different designs (Titmus is a vectograph stereotest in which two targets are polarised at 90 degrees to each other, with the targets are then viewed through polarised filters; TNO is an anaglyph test based on chromatic random dot stereograms which are displaced horizontally, using

red and green filter glasses; and Frisby and FD2 are free space actual depth stereotests), the researcher cannot quantify if participants' cortical awareness became heightened with each stereotest, and thus affected the results, as repeat assessments on subsequent days were not performed with the stereotest completion times recorded (potentially a further study).

Additional confounders to the measurement of accurate stereoacuity include motion parallax (i.e. participant moves head whilst viewing a stationary object), image size, linear perspective, lateral displacement, vergence, luminance, chromostereopsis (i.e. visual illusion created by red and green or red and blue), shadows and texture (85, 216, 219-221). The confounders are like clues in that they provide indirect information on depth (85). Motion parallax cues are present for Titmus, Frisby and FD2 stereotests, although it is reported that motion perception also decreases with increasing age (219). However, by having a single experienced orthoptist as the researcher, and a head holding device used when measuring Frisby stereoacuity, it is hoped that head movement was minimal/absent and the stereoacuity measured was accurate. A second strength is that this research has confirmed findings in other studies whilst having more age cohorts, cohorts based on decades of life and an equal number of participants in each cohort. The study has added to the researcher's clinical knowledge and will add to the evidence base when published.

Finally, optical defocus may have influenced the stereoacuity results measured by the Frisby stereotest in the older cohorts. Whilst the pre- presbyopic participants would have been able to focus clearly for all testing distances possible (30 - 80 cm), it is conceivable that older participants may have experienced some optical blur when the testing distance was 60 cm and beyond; as their habitual reading addition would have typically been calculated at a testing distance of 40 cm. A study of 11 participants aged 35 - 60 years using the Frisby stereotest, found that optical blur of 3 - 5 D did result in a statistically significant effect on stereoacuity (i.e. reducing stereoacuity), but that up to 2 D of optical blur did not have a statistically significant effect on stereoacuity values (3). As discussed in Chapter 3, the researcher chose a near visual acuity test which was performed at 25 cm to ensure participants had sufficient acuity for commencing the Frisby stereotest at 30 cm, but had not considered the need to reduce the reading addition powers for longer distances. For example, if the near add was +2.00 D tested at 40 cm, then the range of clear vision would be 35 - 55 cm, and an intermediate add power of +1.25 D would then give the participant a range of clear vision of 50 - 75 cm (222). Therefore, on reflection, if the research study was being

repeated, the researcher would reduce the reading spectacles power by 0.75 D to exclude any possible effect from optical blur.

4.7 Key findings applicable to clinical practice

Clinical stereotests typically found in orthoptic examination rooms in the UK and Ireland were chosen for this study to maximize takeaway outcomes applicable to standard clinical practice, rather than using research based psychophysical tests. This methodology allowed for rapid testing of stereoacuity by several tests, minimising participant fatigue and frustration. The aim of using commercially available stereotests was to enable the clinical application of the findings. The key clinical findings were:

1. Stereoacuity was reduced in older adults (70+ years) irrespective of stereotest used (see Table 4.13).
2. There was a further improvement in stereoacuity in the 2nd decade of life.
3. The Titmus stereotest may not be as sensitive at detecting changes or reduction in stereoacuity as the other stereotest types.
4. Patients aged 70+ years may report distance stereo-negative results on FD2.
5. Stereoacuity was unaffected by whether Frisby plates were presented with crossed disparity or uncrossed disparity. Therefore, clinically it is not necessary to record the direction of the disparity.
6. Stereoacuity values were different for each stereotest, and, as discussed earlier, this relates to the design of each test. As Table 4.16 shows, the best median stereoacuity value of 20 arcsec was recorded by tests able to measure more discrete levels of stereoacuity (Frisby and FD2 stereotests); whereas 40 arcsec (a stereoacuity value twice as big, and weaker), was the maximum achievable using Titmus stereotest. Therefore, tests are not interchangeable when monitoring changes in stereoacuity over time or during a treatment intervention.

Stereotest	Age (years)	Median and IQR stereoacuity (arcsec)
Titmus	10 - 19	40 (IQR 40 - 50)
	30 - 39	40 (IQR 0)
	70 - 79	50 (IQR 40 - 80)
TNO	10 - 19	60 (IQR 45 - 60)
	30 - 39	30 (IQR 30 - 60)
	70 - 79	120 (IQR 0)
Frisby (uncrossed & crossed)	10 - 19	30 (IQR 20 - 55)
	30 - 39	20 (IQR 0)
	70 - 79	85 (IQR 55 - 110)
FD2	10 - 19	20 (IQR 17.5 - 25.5)
	40 - 49	20 (IQR 10 - 25)
	70 - 79	42.5 (IQR 20 - 55)

Table 4.16 The median and IQR stereoacuity for the youngest, eldest and best cohorts using the four stereotests.

4.8 Conclusions

There appears to be a further improvement in stereoacuity in the 2nd decade of life, and therefore stereopsis may not be fully developed by age 10 years, as previously suggested by the literature as discussed in Chapter 1. There is a decline in stereoacuity with increasing age; this can be found in participants older than 60 years, and is most evident in participants older than 70 years. This decline in stereoacuity should be taken into account when undertaking a binocular assessment in older patients. The high numbers of “best” stereoacuity findings with the Titmus stereotest suggest that it is not the most useful measure of stereoacuity clinically and rather proves that test subjects meet a ‘minimal standard’ of normal stereoacuity, without accurately quantifying the degree of stereopsis. Therefore, based on the results of this present study, it is recommended that the Frisby and FD2 stereotests are used as the gold standard for the assessment and monitoring of stereoacuity where available.

Chapter 5:
The associations of increasing age on motor fusion, NPC, ocular alignment, and ocular motility.

Chapter 5: The associations of increasing age on motor fusion, NPC, ocular alignment, and ocular motility.

5.1 Introduction

This chapter will describe the main findings of the research which assessed the associations between age and horizontal and vertical motor fusion, age and near point of convergence (NPC), age and ocular motility, and finally age and ocular alignment. A detailed description of the methods used to assess motor fusion, NPC, ocular alignment and ocular motility can be found in Chapter 3.

The literature relating to the normative values of horizontal fusion and the effects of age on fusion were presented and discussed in Chapter 1.6.3. As noted previously, the presence of an intermittent strabismus or a large latent strabismus may influence the fusion range. Additionally, testing factors may cause inconsistencies in fusional ranges, these include target size, testing distance, prisms being placed in front of one eye versus prisms being placed in front of both eyes, placing prism bar in front of the dominant or non-dominant eye, the order of testing (for example, testing positive fusion before or after testing negative fusion), the testing time (i.e. the time duration each prism strength is held in front of the eye) and using a non-prism bar method (for example, loose prisms or phoropter prisms). Participant factors which may cause inconsistencies include abnormalities of ocular alignment (for example, an intermittent manifest strabismus), visual activity prior to measurement, the use of naive versus non-naive participants (for example, orthoptic or optometry students and or clinicians), and the participant's state of alertness. Having reviewed the literature on the association between age and horizontal fusion (see Chapter 1.6.3), there is a lack of conclusive evidence to establish whether older adults have the same horizontal motor fusion as pre-presbyopic adults and children.

The vertical fusion range is the smallest fusional range, increasing in the presence of vertical heterophoria (99), or vertical anisometropia (223). An increased vertical fusion range and a vertical heterophoria occur in cases of a long standing or congenital superior oblique palsy (35, 99, 224). The reported normal vertical fusion range is 3 to 9^{Δ} (to nearest whole prism) for near and distance (130, 132-136); however, the effect of age on vertical fusion remains unanswered.

The normal NPC ranges from 6 - 10 cm depending on the method of measurement, for example, 6 cm (RAF rule) (35), 6 - 7 cm (method of measurement not stated) (225), 9 cm (with a Gulden fixation stick and a ruler) (114), and 8 to 10 cm (with a fixation

target and a ruler) (99). A survey of American optometrists reported that they would commonly diagnose convergence insufficiency when the NPC is worse than 10 cm (226). There are conflicting publications as to whether NPC changes with increasing age, with some publications reporting a decline in NPC as a function of age (112, 114, 225). One of these publications used an RAF rule (112), one assessed NPC with a Gulden fixation stick and a ruler (114), whilst one did not explain how NPC was measured (225), therefore, the outcomes of these studies may not be generalizable to this current study. Conversely, the Moorfield's study of 60 participants aged 17 - 83 years found no statistically significant relationship between age and NPC (mean NPC 6 cm across all age cohorts), however, their method of testing was not described, so comparability to the current study is difficult (113). Whilst there are no specific guidelines on how to assess NPC published by the Irish College of Ophthalmologists, BIOS, the College of Optometrists or the American Academy of Ophthalmology, the RCOphth "Guidelines for the Management of Strabismus in Childhood" have recommended the measurement of NPC with a RAF rule (106).

Whilst there are no specific guidelines on how to assess and document ocular movements published by many eye care professional bodies (the Irish College of Ophthalmologists, the College of Optometrists, or the AAO), there are clinical guidelines available to members of the BIOS; the guidelines recommend a diagrammatic representation of ocular movements (60). As described in Chapter 1, the examiner moves a fixation target (for example, a pen torch) from the primary position to the eight cardinal positions of gaze whilst observing the position of the corneal light reflection (61), with the eye professional typically performing a cover/uncover test in each cardinal position. The direct elevation and depression positions are assessed to confirm the presence or absence of an alphabet pattern (i.e. variable magnitude of horizontal strabismus between upgaze, primary position, and downgaze) (61). Movements can be quantified/graded -4 to +4, with -4 indicating maximum limitation or underaction (no movement of the eye past the midline) and +4 indicating maximum overaction (62, 63); -3 = 75% underaction, -2 = 50% underaction, and -1 = 25% underaction limitation, and zero representing a normal movement, +1 = 25% overaction, +2 = 50% overaction, and +3 = 75% overaction (60, 62). This method can lead to some inter-observer variability (63), and inexperienced professionals may struggle with both describing and quantifying what they are observing. The present study used the BIOS standard clinical method of assessing EOMs in eight cardinal positions of gaze with a pen torch.

Studies have shown that there is a progressive limitation in elevation with advancing age (67, 112, 227); it was proposed that this was as a result of infrequent use of upgaze as adults (67). These studies used a hand held perimeter (227), fusion slides on a synoptophore (112), and the lateral version light reflex test of Urist (67) to assess a range of eye movements. The main limitation of using a perimeter is that the researcher is unable to view the eyes as they move; with the synoptophore method there is a maximum measurement of 30^{o} in the vertical direction, which is not a true reflection of the full EOM version, considered to be 45^{o}. With the lateral version light reflex test of Urist, the examiner is making a subjective judgement, to the nearest 15^{o}, on the cornea as to where the light reflex is. The value is then converted to degrees by adding the ocular rotation of the light reflex to the corneoscleral limbus to the ocular rotation of the light reflex on the sclera, and then converted into a percentage (67); which seems all very complicated, subject to bias, and potential calculation error.

As discussed in Chapter 1, a study found a statistically significant relationship between age and decreasing horizontal eye movements, and a statistically significant relationship between age and decreasing upgaze eye movements, but no statistically significant relationship between age and downgaze eye movements (68). This study was performed in Korea on 261 subjects aged 5 - 91 years, and for the purposes of analysis participants were divided into two cohorts based on median age (cohort sizes were not provided) (68). Again, the authors did not use a standardised clinical method, but used photographs taken in primary position and in each extreme gaze position; with the aid of imaging software, they overlapped the photographs to establish the amount the eyes had moved (68). For their software based calculation, a number of assumptions were made to facilitate the software functions, one example, the shape of the eye was a perfect sphere; this assumption was made without any calculation or comment of auto-refraction, the authors did not comment on whether any participant had astigmatism, but merely stated that the axial length was between 21 and 26.5 mm for inclusion in the study (68). To the author's knowledge there are no publications confirming limitation of eye movements using the BIOS standard clinical method.

Most infants are orthophoric or exophoric (98). A study measuring ocular alignment using Maddox rod in a cohort of 1016 children aged 6 - 12 years reported a mean near exophoria of 0.4^{Δ} and a mean distance esophoria of 0.6^{Δ}, with no statistically significant associated with age (127). A retrospective audit of medical charts involving 100 Israeli Airforce men who performed a routine eye examination yearly, found a small esophoria for distance fixation (0.9^{Δ} base out) when the men were aged 18 - 22 years that increased significantly to 1.8^{Δ} base out when the same men were retested aged 34 - 48

years (225). Similarly, the mean near deviation was a small exophoria (2.7$^{\Delta}$ base in) when the men were aged 18 - 22 years, the esophoria increased significantly to 3.3$^{\Delta}$ base in, when the same men were retested aged 34 - 48 years (225). It has been postulated that there might be an association between ocular alignment with age, that, due to weakening of the medial recti, an exophoria would develop for near, due to weakening of the lateral recti, an esophoria would develop for distance (225). A study of 271 participants aged 21 - 80 years supported this theory, finding the mean distance heterophoria was minimal exophoria for all age cohorts, except cohort 71 - 80 years, which had minimal esophoria (0.2$^{\Delta}$ base out) (144). A further large cross-sectional study of 663 participants aged 5 - 85 years measuring distance heterophoria using with Maddox rod reported no clinical or statistically significant change with age (169). However, the same cross-sectional study did find that the near heterophoria changed towards exophoria with increasing age (approximately 5$^{\Delta}$), the change was noted from 25 years, and most evident from 60 years; this change in ocular alignment for near was statistically significant (169). The authors concluded that their results were not as a consequence of presbyopia (169).

5.2 Aim

The aim of this chapter is to present the investigation into whether there is a decrease in stereoacuity with increasing age as measured by fusion, NPC, ocular motility, and ocular alignment.

5.3 Hypothesis and statistical analysis

This chapter had four null hypotheses:

1. There was no statistically significant decrease in fusion with increasing age.
2. There was no statistically significant decrease in NPC with increasing age.
3. There was no statistically significant change in ocular motility with increasing age.
4. There was no statistically significant change in ocular alignment with increasing age.

Fusion

For this null hypothesis, several measurements were taken from each participant. For example, horizontal fusion was measured for near and for distance for both the positive and negative fusion ranges, documenting all break and recovery points, and additionally the total vertical fusion for near and distance. ANOVA was the planned method of statistical analysis in the study design phase, performed on each variable to assess for the presence of association with age. A p value ≤ 0.05 was the predetermined level of statistical significance.

Tests for normality were performed for all fusion parameters using the Shapiro Wilk's test (198). Results that were not normally distributed were log transformed and normality tests performed again (see Table 5.1). Dependent variables that did not satisfy normality after transformation were analysed used the Kruskal-Wallis test (see Table 5.1). The Kruskal-Wallis test is a non-parametric test for comparing medians between independent cohorts. Six variables were analysed using ANOVA (see Table 5.1). When a difference between cohorts existed, further pairwise comparisons were performed to determine which cohorts were different and the direction of the difference. Four fusion variables were analysed using the Kruskal-Wallis test (see Table 5.1). If there was a significant difference among cohorts, ranks were used to determine cohort with higher/lower ranks (NB for this type of test there are not pairwise comparisons to determine significant difference between the two cohorts).

NPC

For NPC, a Pearson correlation analysis was performed for the total population. The Kolmogorov-Smirnov and Shapiro-Wilk normality tests were performed for age cohort versus NPC on raw and log transformed data. Normality was not achieved, so ANOVA could not be applied; a non-parametric Kruskal-Wallis test was used to determine differences between cohorts, by comparing their median NPC.

Ocular alignment

The Fisher's exact test was used to determine if there were associations between age and ocular alignment for near and distance. The non-parametric Kruskal-Wallis test was then performed as ANOVA assumptions were not met.

Ocular movements

For changes in eye movements with age, only one aspect was could be statistically analysed; the presence of end point nystagmus underwent logistic regression analysis.

Parameter	Converted to Log	ANOVA	Kruskal-Wallis	Logistic regression
Near positive Break			X	
Near positive Recovery			X	
Near negative Break		X		
Near negative Recovery		X		
Distance positive Break	X	X		
Distance positive Recovery	X	X		
Distance negative Break		X		
Distance negative Recovery		X		
Vertical near total			X	
Vertical distance total			X	
NPC			X	
Near ocular alignment			X	
Distance ocular alignment			X	
Presence of end-point nystagmus				X

Table 5.1 Parameters evaluated and their method of statistical analysis. To satisfy normality some parameters were converted to Log. Parameters were analysed with either the parametric test ANOVA or the non-parametric test Kruskal-Wallis.

5.4 Results

The full descriptive statistics (mean, standard deviation, confidence intervals, minimum value and maximum value) for motor fusion are presented in Appendix 19. The SPSS outputs for Chapter 5 are presented in Appendix 20.

Horizontal Motor Fusion- near positive break point

The mean near positive fusion for the total population was $36.6^{\Delta} \pm 10.1^{\Delta}$ base out, the mode break point was 45^{Δ} base out (35 of 77 participants, 45.5%) and the range 14 - 45^{Δ} base out. The mean near positive fusion was weakest for the 30 - 39 years cohort ($32.2^{\Delta} \pm 10.3^{\Delta}$ base out) and strongest for the 60 - 69 years cohort ($42.4^{\Delta} \pm 8.7^{\Delta}$ base out). The weakest mean near positive fusion (14^{Δ} base out) was recorded in two participants, aged 30 and 73 years. The maximum positive fusion value was attained by 35 of 77 participants (43%), of which 22 of 35 participants (63%) were able to maintain binocularity at this point; 45^{Δ} base out was the maximum fusion measurable in

this experiment as only a single Clement Clarke prism bar was selected in the study design (see Chapter 3 for rationale). Cohort 50 - 59 years showed the least variability with a standard deviation of 6.8$^{\Delta}$ in comparison to cohort 70 - 79 years, which showed the most variability with a standard deviation of 12.5$^{\Delta}$.

Figure 5.1 shows that no cohort had normally distributed data, with cohort 30 - 39 years showing positively skewed data, and the remaining cohorts showing negatively skewed data (10 - 19 years, 20 - 29 years, 40 - 49 years and 70 - 79 years). Cohorts 10 - 19 years, 40 - 49 years, and 60 - 69 years recorded the same median value (45$^{\Delta}$ base out), but with different distributions. There was no IQR for 60 - 69 years as this cohort had a high level of agreement, with 10 of 11 participants achieving 45$^{\Delta}$ base out positive fusion. Cohorts 50 - 59 years and 70 - 79 years recorded same median value (40$^{\Delta}$ base out), but with different distributions. Cohort 20 - 29 years recorded a median of 35$^{\Delta}$ base out, and cohort 30 - 39 years recorded the lowest median near positive fusion (30$^{\Delta}$ base out). Cohort 70 - 79 years had the largest boxplot reflecting a low level of agreement between participants. Cohort 10 - 19 years had the longest lower whiskers indicating most variability in the negative quartile. There are no upper whiskers for cohorts 10 - 19 years, 40 - 49 years, 50 - 59 years, and 70 - 79 years because the upper quartile is equal to the maximum fusion value (45$^{\Delta}$ base out).

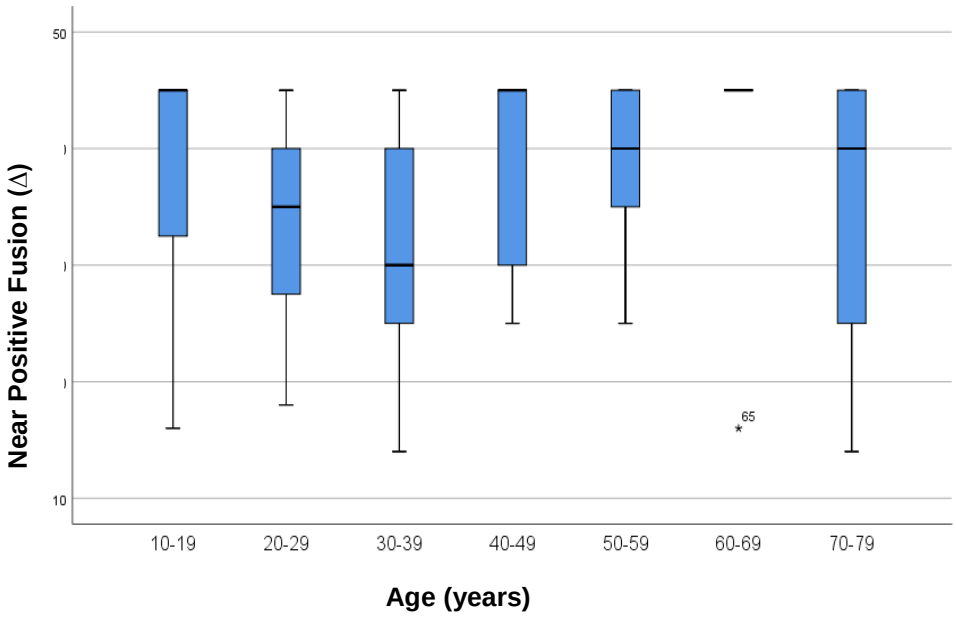


Figure 5.1 Box plot displaying the median, IQR, and the minimum and maximum measurements of near positive fusion. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. Note the participant who was a box outlier for cohort 60 - 69 years was individually plotted (participant ID 65: age 63 years).

Horizontal Motor Fusion- near positive recovery point

The mean near positive fusion recovery point for the total population was $31.6^{\Delta} \pm 11.4^{\Delta}$ base out and the range was 29 - 34^{Δ} base out. The difference from the mean break point to the mean near positive fusion recovery point for the total population was $5.0^{\Delta} \pm 1.2^{\Delta}$ base out, and the range was 2 - 7^{Δ} base out. The cohorts requiring the biggest reduction in prism to regain fusion were cohorts 10 - 19 years and 50 - 59 years (7^{Δ}), and the cohort requiring the smallest reduction in prism to regain fusion was cohort 60 - 69 years (2^{Δ}). Again, cohort 50 - 59 years showed the least variability with a standard deviation of 7.7^{Δ} in comparison to cohort 70 - 79 years, which showed the most variability with a standard deviation of 14.6^{Δ}.

Figure 5.2 shows that no cohort had normally distributed data, cohorts 20 - 29 years, 30 - 39 years, and 70 - 79 years showed positively skewed data and cohorts 10 - 19 years and 40 - 49 years showed negatively skewed data. Cohorts 20 - 29 years and 30 - 39 years recorded same median value (25^{Δ} base out), but with different distributions. Cohorts 50 - 59 years and 70 - 79 years recorded same median value (30^{Δ} base out), but with different distributions. Cohort 10 - 19 years recorded a median value (35^{Δ} base out), with cohort 40 - 49 years recording the highest median value (40^{Δ} base out). There was no IQR for cohort 60 - 69 years, as this cohort had a high level of concordance (9 of 11 participants recorded 45^{Δ} base out). Cohort 70 - 79 years had the largest boxplot reflecting low level of agreement between participants. There are no upper whiskers for cohort 70 - 79 years because the upper quartile is equal to the maximum fusion value (45^{Δ} base out).

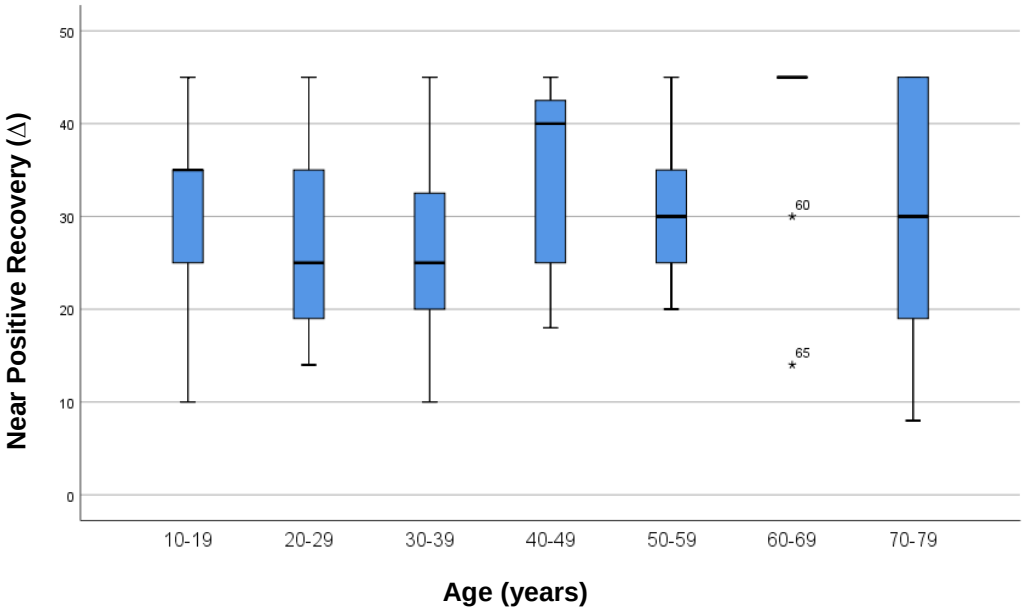


Figure 5.2 Box plot displaying the median, IQR, and the minimum and maximum measurements of the near positive recovery point. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for cohort 60 - 69 years were individually plotted (participant IDs 60 and 65: both aged 63 years).

Horizontal Motor Fusion- near negative break point

The mean near negative fusion for the total population was 15.1$^{\Delta}$ ± 5.8$^{\Delta}$ base in, the mode break point was 14$^{\Delta}$ base in (13 of 77 participants) and the range 4 - 30$^{\Delta}$ base in. The mean near negative fusion was weakest for cohort 70 - 79 years (12$^{\Delta}$ ± 3.7$^{\Delta}$ base in) and strongest for cohort 50 - 59 years (18.4$^{\Delta}$ ± 8.6$^{\Delta}$ base in). The weakest mean near negative fusion (4$^{\Delta}$ base in) was recorded in two participants, aged 32 and 58 years. No participant achieved the maximum negative fusion value of 45$^{\Delta}$ base in. The cohort 70 - 79 years showed the least variability with a standard deviation of 3.7$^{\Delta}$, in comparison to cohort 50 - 59 years which showed the most variability with a standard deviation of 8.6$^{\Delta}$.

Figure 5.3 shows that no cohort had normally distributed data, with all cohorts showing positively skewed data. Cohorts 10 - 19 years, 30 - 39 years and 40 - 49 years all recorded same median value (14$^{\Delta}$ base in), but with different distributions. Cohorts 50 - 59 years and 60 - 69 years recorded same median value (16$^{\Delta}$ base in), but with different distributions. Cohorts 20 - 29 years and 70 - 79 years recorded the lowest median value (12$^{\Delta}$ base in), but with different distributions. Cohort 50 - 59 years had

the largest boxplot reflecting a low level of agreement between participants; it also showed the longest lower whiskers indicating most variability in the negative quartile values.

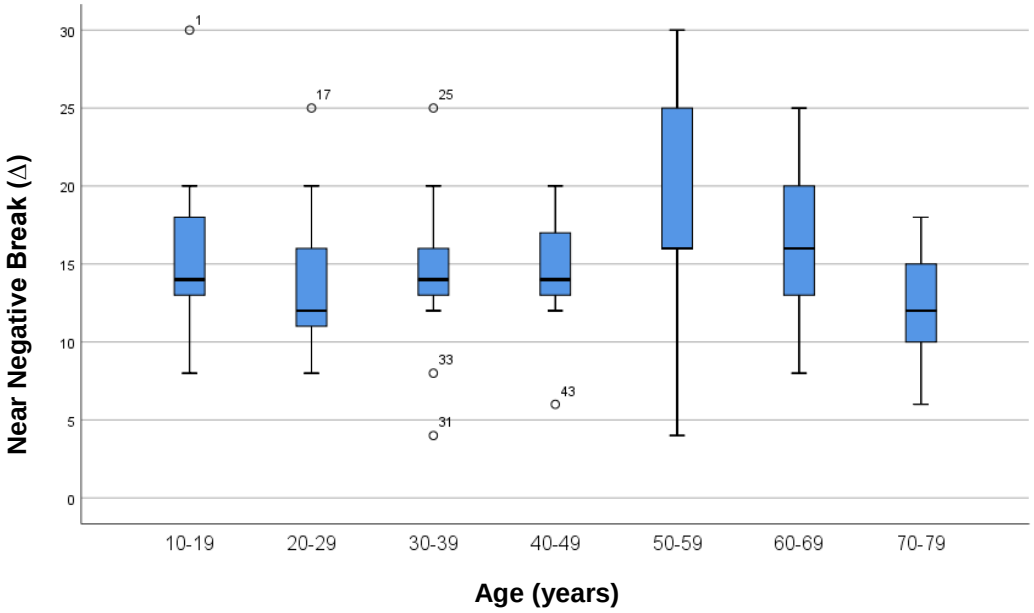


Figure 5.3 Box plot displaying the median, IQR, and the minimum and maximum measurements of the near negative fusion. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohort were individually plotted (participants' ages: 19, 25, 30, 32, 37, and 44 years).

Horizontal Motor Fusion- near negative recovery point

The mean near negative recovery for the total population was 11.4$^{\Delta}$ ± 4.9$^{\Delta}$ base in and the range was 2 - 25$^{\Delta}$ base in. The difference from the mean break point to mean recovery point for the total population was 3.7$^{\Delta}$ ± 0.8$^{\Delta}$ base in and the range was 3 - 5$^{\Delta}$ base in. The cohort requiring the biggest reduction in prism to regain fusion was 50 - 59 years (4.9$^{\Delta}$). The cohort requiring the smallest reduction in prism to regain fusion was 70 - 79 years (3.1$^{\Delta}$). Cohort 70 - 79 years had the weakest near negative fusion and showed least variability in standard deviation for near negative fusion. Cohort 40 - 49 years showed the least variability with a standard deviation of 3.1$^{\Delta}$, in comparison, cohort 60 - 69 years showed the most variability with a standard deviation (6.4$^{\Delta}$).

Figure 5.4 shows that only cohort 60 - 69 years had normally distributed data, with all other cohorts showing positively skewed data. Cohorts 10 - 19 years, 20 - 29 years, 30

- 39 years, and 40 - 49 years all recorded the same median value (10$^{\Delta}$ base in), but with different distributions. Cohorts 50 - 59 years and 60 - 69 years recorded the same median value (14$^{\Delta}$ base in), but with different distributions. Cohorts 70 - 79 years recorded the lowest median value (8$^{\Delta}$ base in). Cohort 50 - 59 years showed the longest lower whiskers, indicating most variability in the negative quartile values. Cohort 10 - 19 years showed the longest upper whiskers, indicating most variability in the positive quartile values.

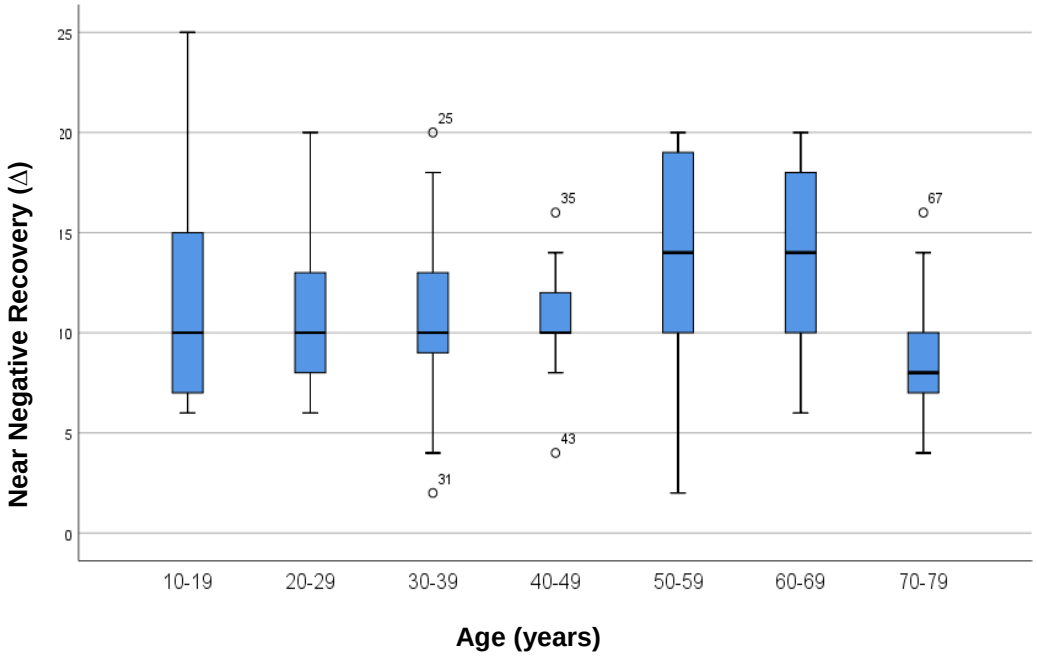


Figure 5.4 Box plot displaying the median, IQR, and the minimum and maximum measurements of the near negative recovery point. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. Participants who were box outliers for the cohort were individually plotted (participant ages: 30, 32, 40, 44, 73 years).

Horizontal Motor Fusion- distance positive break point

The mean distance positive fusion for the total population was 22.1$^{\Delta}$ ± 8.9$^{\Delta}$ base out, mode break point was 25$^{\Delta}$ base out (18 of 77 participants, 23.4%), and the range was 8 - 45$^{\Delta}$ base out. The mean distance positive fusion was weakest for the 70 - 79 years cohort (16.4$^{\Delta}$ ± 7.9$^{\Delta}$ base out) and strongest for the 40 - 49 years cohort (26.6$^{\Delta}$ ± 10.5$^{\Delta}$ base out). The weakest mean distance positive fusion (8$^{\Delta}$ base out) was recorded in two participants, aged 30 and 76 years. The maximum positive fusion value (45$^{\Delta}$ base out), was attained by 2 of 77 participants (3%), aged 40 and 62 years, of which one

participant (aged 62 years) was able to maintain binocularity at this point. The 50 - 59 years cohort showed the least variability with a standard deviation of 5.7$^{\Delta}$, in comparison to 60 - 69 years cohort, which showed the most variability with a standard deviation of 11.2$^{\Delta}$.

Figure 5.5 shows that no cohort demonstrated normally distributed data, with cohorts 10 - 19 years, 20 - 29 years, 40 - 49 years, 50 - 59 years, and 60 - 69 years showing positively skewed data and cohorts 30 - 39 years and 70 - 79 years showing negatively skewed data. Cohorts 10 - 19 years, 40 - 49 years, and 50 - 59 years all recorded same median value (25$^{\Delta}$ base out), but with different distributions. Cohorts 20 - 29 years and 30 - 39 years had same median value (18$^{\Delta}$ base out), but with different distributions. Cohorts 60 - 69 years and 70 - 79 years had the same median value (16$^{\Delta}$ base out), but different distributions. The 50 - 59 years had the smallest boxplot reflecting high level of agreement between participants, the box plot also showed no lower whiskers indicating no variability in the negative quartile values.

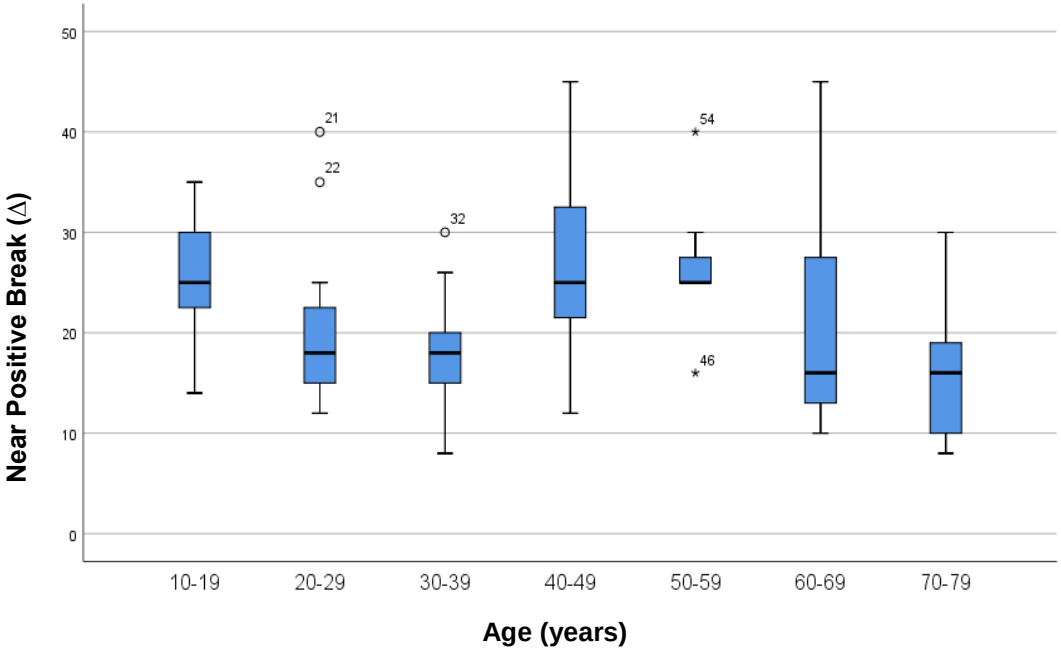


Figure 5.5 Box plot displaying the median, IQR, and the minimum and maximum measurements of the distance positive fusion. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohort were individually plotted (participants' ages: 24, 29, 38, 52 and 54 years).

Horizontal Motor Fusion- distance positive recovery point

The mean distance positive recovery for the total population was $16.4^{\Delta} \pm 8.3^{\Delta}$ base out and range was 1 - 25^{Δ} base out. The difference from the mean break point to mean distance positive recovery for the total population was $5.7^{\Delta} \pm 0.6^{\Delta}$ base out and range 4 - 7^{Δ} base out. The cohort requiring the biggest reduction in prism to regain fusion was cohort 40 - 49 years (7.3^{Δ}); and the cohort requiring the smallest reduction in prism to regain fusion was cohort 30 - 39 years (3.9^{Δ}). Again, cohort 50 - 59 years showed the least variability with a standard deviation of 4.6^{Δ}. In comparison, cohort 60 - 69 years showed the most variability with a standard deviation of 11.3^{Δ}.

Figure 5.6 shows that no cohort met the criteria for normal distribution of their data, with cohorts 20 - 29 years, 30 - 39 years, 50 - 59 years, 60 - 69 years, and 70 - 79 years showing positively skewed data, and cohorts 10 - 19 years and 40 - 49 years showing negatively skewed data. Cohorts 10 - 19 years, 40 - 49 years and 50 - 59 years all recorded the same median value (20^{Δ} base out), but with different distributions. Cohorts 20 - 29 years and 60 - 69 years recorded the same median value (12^{Δ} base out), but with different distributions. Cohort 70 - 79 years had the lowest median value for distance positive recovery (8^{Δ} base out). Cohort 50 - 59 years had the smallest boxplot, reflecting high level of agreement between participants. Cohort 40 - 49 years showed the longest upper and lower whiskers, indicating the cohort had the most variability in its IQR.

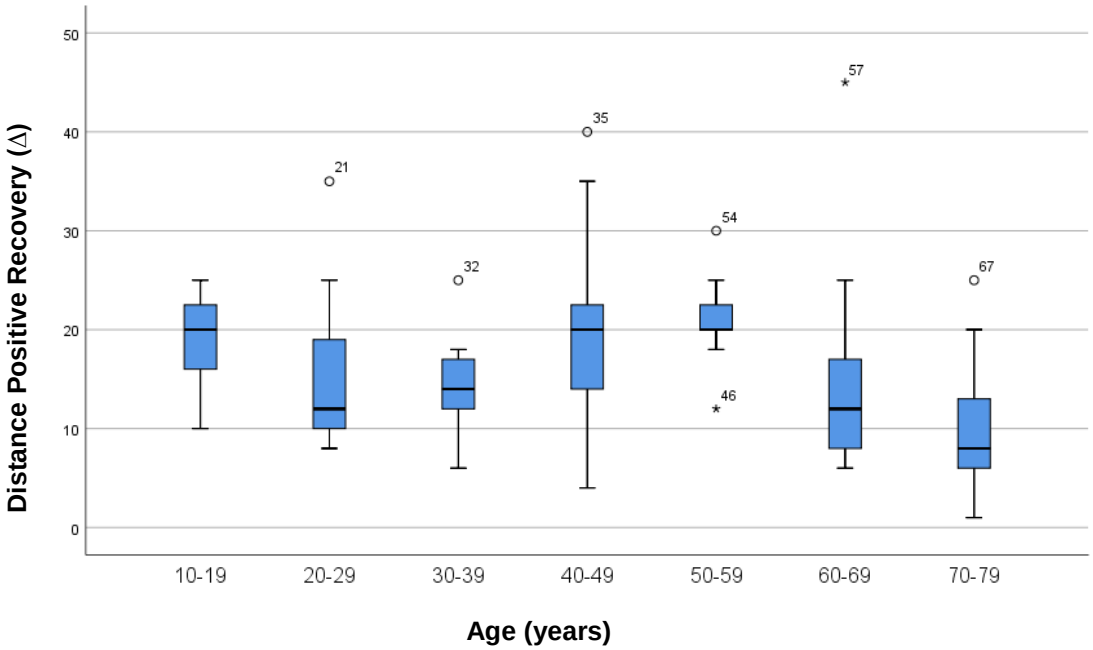


Figure 5.6 Box plot displaying the median, IQR, and the minimum and maximum measurements of the distance positive recovery. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohort were individually plotted (participants' ages: 24, 38, 40, 52, 54, 62 and 73 years).

Horizontal Motor Fusion- distance negative break point

The mean distance negative fusion for the total population was 9.2$^{\Delta}$ ± 3.8$^{\Delta}$base in, mode break point was 8$^{\Delta}$ base in (18 of 77 participants, 23.4%) and the range was 2 - 20$^{\Delta}$ base in. The mean near negative fusion was weakest for cohort 60 - 69 years (8.4$^{\Delta}$ base in) and strongest for cohort 20 - 29 years (10.2$^{\Delta}$ base in). The weakest mean near negative fusion (2$^{\Delta}$ base in) was recorded in five participants, aged 37 years, 46 years, 58 years, 63 years, and 76 years. No participant achieved the maximum negative fusion value of 45$^{\Delta}$ base in. Cohort 20 - 29 years showed the least variability with a standard deviation of 2.7$^{\Delta}$. In comparison, cohort 70 - 79 years showed the most variability, with a standard deviation of 4.8$^{\Delta}$.

Figure 5.7 showed that cohort 60 - 69 years had normally distributed data, cohorts 40 - 49 years, 50 - 59 years and 70 - 79 years had positively skewed data, and cohort 10 – 19 years had negatively skewed data. Cohorts 10 - 19 years, 20 - 29 years and 30 - 39 years all recorded the same median value (10$^{\Delta}$ base in), but with different distributions. Cohorts 40 - 49 years, 50 - 59 years, 60 - 69 years and 70 - 79 years also had same

median value (8$^{\Delta}$ base in), but with different distributions. Cohort 70 - 79 years had the largest boxplot reflecting low level of agreement between participants.

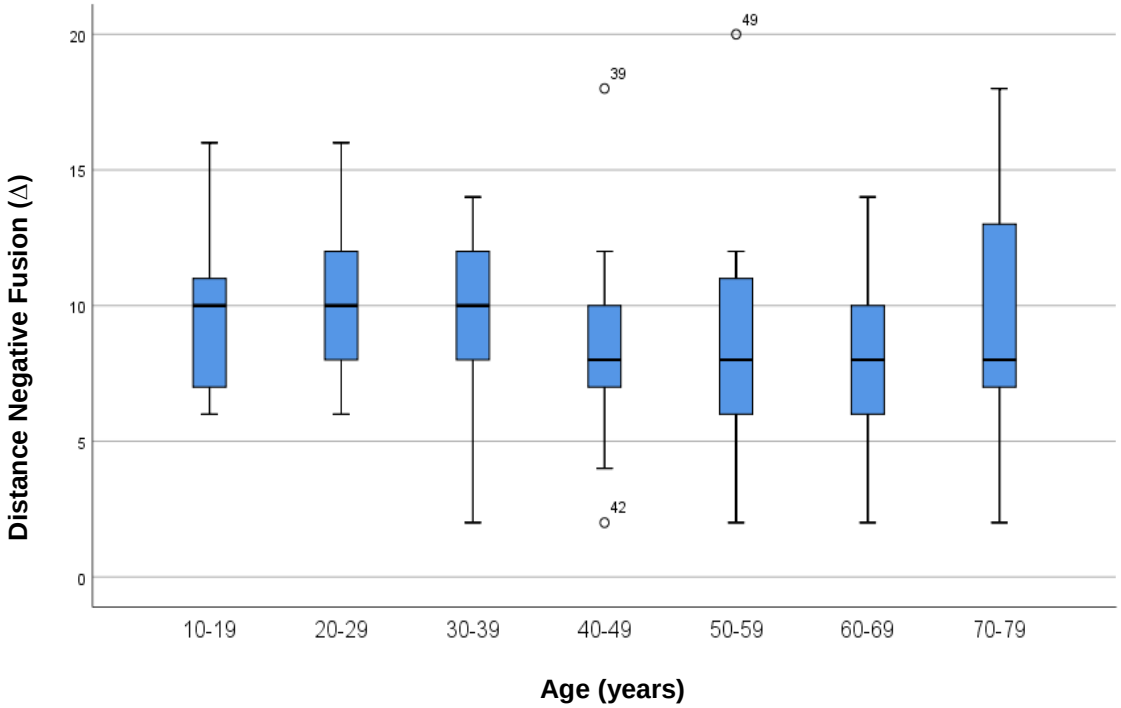


Figure 5.7 Box plot displaying the median, IQR, and the minimum and maximum measurements of the distance negative fusion. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers are individually plotted (participants' ages: 46 years, 48 years, and 54 years).

Horizontal Motor Fusion- distance negative recovery point

The mean distance negative recovery for the total population was 6.7$^{\Delta}$ ± 3.2$^{\Delta}$ base in and the range was 1 - 18$^{\Delta}$ base in. The difference from the mean break point to mean recovery point for the total population was 2.5$^{\Delta}$ base in (standard deviation 0.6$^{\Delta}$ and range 2 - 3$^{\Delta}$ base in). The cohort requiring the biggest reduction in prism to regain fusion was cohort 20 - 29 years (2.9$^{\Delta}$). The cohort requiring the smallest reduction in prism to regain fusion was cohort 50 - 59 years (1.9$^{\Delta}$). Cohort 20 - 29 years showed the least variability with a standard deviation of 2.2$^{\Delta}$. In comparison, cohort 50 - 59 years showed the most variability, with a standard deviation of 4.6$^{\Delta}$.

Figure 5.8 showed that no cohort had normally distributed data, cohorts 20 - 29 years, 50 - 59 years, and 70 - 79 years showed positively skewed data, and cohorts 10 - 19

years, 30 - 39 years, 40 - 49 years, and 60 - 69 years showed negatively skewed data. Cohorts 10 - 19 years and 30 - 39 years recorded same median value (8^{Δ} base in), but with different distributions. The remaining cohorts all recorded the same median value (6^{Δ} base in), but with different distributions. Cohort 20 - 29 years had the smallest boxplot, reflecting high level of agreement between participants. Cohort 70 - 79 years showed the longest upper and lower whiskers, indicating the greatest variability in the positive and negative quartile values of all the cohorts.

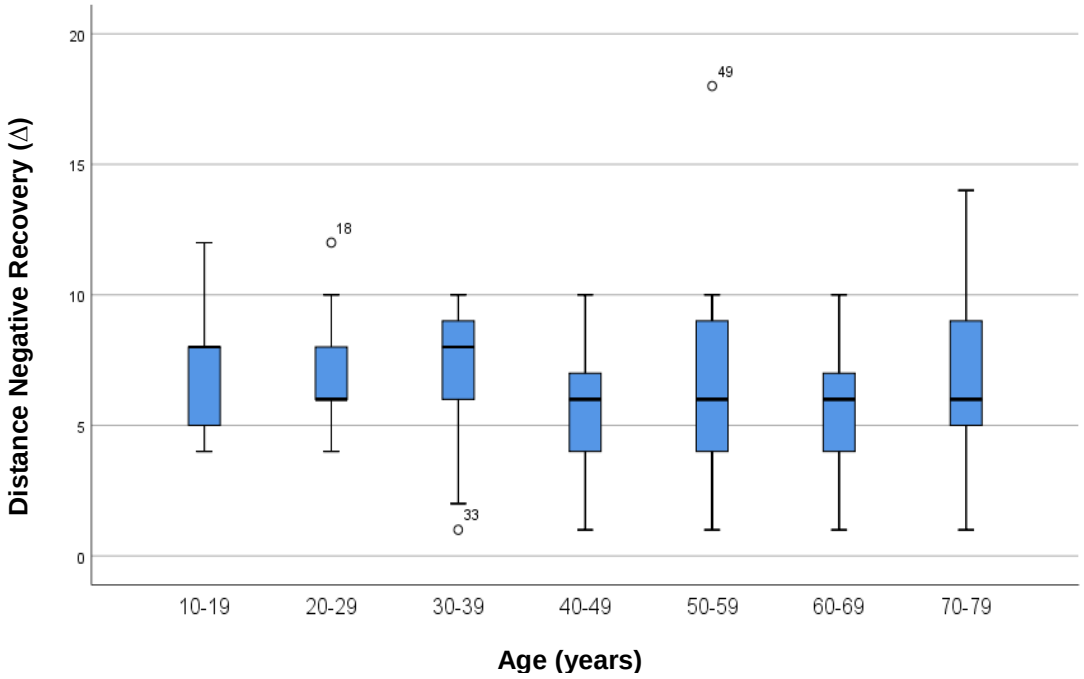


Figure 5.8 Box plot displaying the median, IQR, and the minimum and maximum measurements of the distance negative recovery point. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers are individually plotted (participants' ages: 29, 37 and 54 years).

Horizontal Fusion Recovery- Clinical presentation of findings

The prism steps on the Clement Clarke prism bar create an instrumental error; the prism steps increase by unequal prism power amounts (for example, 1 - 2 - 4 - 6 - 8 - 10 - 12 - 14 - 16 - 18 - 20 - 25 - 30 - 35 - 40 - 45^{Δ}). Consequently, fusional recovery data are presented both in terms of prism dioptres (referred to as raw score), and the number of prism steps required to regain fusion. When deciding whether a patient has good or poor fusion recovery, clinicians will often consider the question *how many steps it took to recover.* A high number of steps to regain fusion indicating weak binocular function.

Within the total population, the raw near recovery point for positive fusion was 2 - 10$^{\Delta}$ less than the break point, corresponding to 1 - 3 steps on the prism bar (mean 1.12 ± 0.90 steps) (see Table 5.2). Using the means for the total population and to the nearest whole prism and step, this corresponded to a 5$^{\Delta}$ change and one step on the prism bar (NB 1 step equals 5$^{\Delta}$ for magnitudes greater than 20$^{\Delta}$). There were 22 participants able to reach maximum near positive fusion and maintain it at 45$^{\Delta}$ Base Out, therefore, based on 55 of 77 participants (71.4%) who had to regain fusion (recover), 28 of 55 participants (40%) who regained binocularity in one prism step and 51 of 55 participants (93%) who regained binocularity within two prism steps. Cohort 60 - 69 years had the smallest mean number of steps because 9 of 11 participants reached and maintained fusion at 45$^{\Delta}$ base out.

Within the total population the raw near recovery point for negative fusion was 2 - 12$^{\Delta}$ less than the break point, corresponding to 1 - 5 steps on the prism bar (mean was 1.64 ± 0.89 steps) (see Table 5.2). Using the means for the total population and to the nearest whole prism and step, this corresponded to a 4$^{\Delta}$ change and two steps on the prism bar (see Table 5.2) (NB one step equals 2$^{\Delta}$ for magnitudes less than 20$^{\Delta}$). There were 43 of 77 participants (56%) who regained binocularity in one prism step, and 66 of 77 participants (86%) who regained binocularity within two prism steps. Cohort 60 - 69 years showed the smallest standard deviation because it was the only cohort that all participants recovered fusion within two steps.

Age cohort (years)	Mean positive recovery (Δ)	Difference between mean positive break & mean recovery (Δ)	Mean and standard deviation prism bar steps to regain fusion	Mean negative recovery (Δ)	Difference between mean negative break & recovery (Δ)	Mean and standard deviation prism bar steps to regain fusion
10 - 19	29.91	7.09	1.64 ± 0.92	11.73	3.91	1.82 ± 0.98
20 - 29	27.45	5.55	1.27 ± 0.90	10.73	3.36	1.55 ± 0.82
30 - 39	26.64	5.54	1.18 ± 0.60	10.91	3.54	1.64 ± 0.92
40 - 49	34.36	4.28	0.91 ± 0.70	10.73	3.82	1.82 ± 1.25
50 - 59	30.91	7.27	1.45 ± 0.69	13.45	4.91	1.73 ± 0.86
60 - 69	40.82	1.54	0.36 ± 0.92	13.45	3.46	1.36 ± 0.50
70 - 79	30.91	3.64	1.0 ± 1.04	8.91	3.09	1.55 ± 0.82
10 - 79	31.57	4.99	1.12 ± 0.90	11.42	3.72	1.64 ± 0.89

Table 5.2 Fusional recovery means and standard deviations for near binocular data recorded for each cohort and the calculated number of prism steps taken to regain fusion.

Within the total population the raw recovery point for positive distance fusion was 2 - 17$^{\Delta}$ less than the break point, corresponding to 1 - 9 steps on the prism bar (mean was 1.90 ± 1.29 steps) (see Table 5.3). Using the means for the total population and to the nearest whole prism and prism bar step, this corresponded to a 6$^{\Delta}$ change and two steps on the prism bar. There was one participant (aged 62 years) who was able to reach maximum distance positive fusion and maintain it at 45$^{\Delta}$ base out. Therefore, based on 76 participants who had to regain fusion (recover), 35 of 76 participants (46%) who regained binocularity in one prism step, and 51 of 76 participants (67%) who regained binocularity within two prism steps. This is a significantly lower percentage than for near positive recovery, where 93% recovered within two prism steps for both positive and negative near fusion; indicating a greater difficulty to regain positive fusion at 6 m. One participant (aged 70 years) required nine steps to recover positive distance fusion (fusion break point 18$^{\Delta}$ fusion recovery point 1$^{\Delta}$); this resulted in a much larger standard deviation for the cohort when compared to the other cohorts (see Table 5.3).

Within the total population the raw the distance recovery point for negative fusion was 1 - 8 $^{\Delta}$ less than the break point, corresponding to 1 - 4 steps on the prism bar (mean

1.31 ± 0.61 steps) (see Table 5.3). Using the means for the total population and to the nearest whole prism and prism bar step, this corresponded to a 3^{Δ} change and one step on the prism bar (see Table 5.3). There were 58 of 77 (75%) who regained binocularity in one prism step, and 72 of 77 participants (93%) who regained binocularity within two prism steps. Cohort 50 - 59 years had no standard deviation for prism bar steps as all participants in the cohort achieved recovery in one step.

Age cohort (years)	**Mean positive recovery (Δ)**	**Difference between mean positive break and mean recovery (Δ)**	**Mean and standard deviation prism bar steps to regain fusion**	**Mean negative recovery (Δ)**	**Difference between mean negative break and recovery (Δ)**	**Mean and standard deviation prism bar steps to regain fusion**
10 - 19	18.82	6.36	1.73 ± 1.01	7.09	2.55	1.27 ± 0.47
20 - 29	15.64	5.09	2.0 ± 1.18	7.27	2.91	1.45 ± 0.69
30 - 39	14.45	3.91	1.63 ± 0.81	7.0	2.45	1.27 ± 0.47
40 - 49	19.27	7.28	2.09 ± 1.04	5.73	2.82	1.45 ± 1.04
50 - 59	20.91	5.54	1.27 ± 0.47	6.82	1.91	1.0 ± 0
60 - 69	15.45	5.91	2.27 ± 1.49	5.73	2.63	1.45 ± 0.69
70 - 79	10.55	5.81	2.21 ± 2.28	7.18	2.46	1.27 ± 0.47
10 - 79	16.44	5.70	1.90 ± 1.29	6.69	2.53	1.31 ± 0.61

Table 5.3 Fusional recovery means and standard deviation for distance binocular data recorded for each cohort and the calculated number of prism steps taken to regain fusion.

Horizontal Motor Fusion Summary

The strongest mean fusion was near positive fusion, then distance positive fusion, then near negative fusion, with distance negative fusion the weakest horizontal fusion measurement. Table 5.4 shows that this horizontal fusion pattern was demonstrated across all cohorts and across the total population.

Age (years)	Near positive ($^{\Delta}$ base out)	Distance positive ($^{\Delta}$ base out)	Near negative ($^{\Delta}$ base in)	Distance negative ($^{\Delta}$ base in)
10 - 19	37 ± 12.0	25 ± 6.1	16 ± 5.9	10 ± 3.3
20 - 29	33 ± 9.6	21 ± 9.2	14 ± 5.0	10 ± 2.8
30 - 39	32 ± 10.3	18 ± 6.0	14 ± 5.5	9 ± 3.8
40 - 49	39 ± 9.0	27 ± 10.5	15 ± 3.8	9 ± 4.2
50 - 59	38 ± 6.8	26 ± 5.8	18 ± 8.6	9 ± 4.8
60 - 69	42 ± 8.7	21 ± 11.2	17 ± 5.7	8 ± 3.3
70 - 79	35 ± 12.5	16 ± 7.9	12 ± 3.7	10 ± 4.8
10 - 79	**37 ± 10. 2**	**22 ± 8.9**	**15 ± 5.8**	**9 ± 3.8**

Table 5.4 Mean and standard deviations for each horizontal motor fusion variable (near positive, distance positive, near negative and distance negative), for each age cohort and for total population. The final row ('10 – 79') is in bold to highlight that this is the data for the total cohort of participants.

A box outlier in the box plots figures was a result that differed significantly from other results, lying an abnormal distance from the other fusion values in the sample, in this study outside 95% of all the data values (± 2 standard deviation). From the box plots (Figures 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, and 5.8) descriptions it can be seen that some participants were identified as outliers. However, one participant (aged 54 years) was an outlier for all four distance variables box plots, (positive fusion and recovery and negative fusion and recovery), and recorded the highest near negative fusion and recovery in their cohort. Outliers are to be expected in larger sample sizes, and therefore, the data from all participants were included in the statistical analysis.

Association between horizontal motor fusion and age

Initially, an analysis of correlation between all fusion measurements with ungrouped age was performed. The analysis of correlation showed that there was no association between horizontal fusion and ungrouped age (near positive $p = 0.27$, near negative $p = 0.69$, distance positive $p = 0.19$, distance negative $p = 0.45$). The take away conclusion from this is that older adults had the same horizontal fusional reserves as younger adults.

Using ANOVA, distance positive fusion showed a statistically significant association with age cohorts ($p < 0.01$), with cohort 70 - 79 years having a significantly lower distance positive fusion in comparison to cohorts 10 - 19 years, 40 - 49 years, and 50 - 59 years. However, there was no statistical significance found between age cohorts and negative fusion near and negative fusion distance (near negative break $p = 0.21$, distance negative break $p = 0.92$). The non-parametric Kruskal Wallis test was used for near positive fusion as normality was not satisfied for an ANOVA analysis. This found that there was no statistically significant association between age cohorts and near positive fusion (near positive fusion $p = 0.08$).

Association between horizontal motor fusion recovery and age

Using the raw data in prism dioptres (not prism bar steps), an analysis of correlation between all recovery measurements with ungrouped age was performed. Only near negative fusion recovery was statistically significant ($p < 0.05$). There was no association between near positive recovery ($p = 0.21$), distance positive recovery ($p = 0.17$), or distance negative recovery ($p = 0.62$) and ungrouped age.

Using ANOVA, distance positive recovery showed a statistically significant association with age cohorts ($p < 0.01$). However, there was no statistical significance found between age cohorts and negative recovery for near and distance (near negative recovery $p = 0.31$, distance negative recovery $p = 0.83$). The non-parametric Kruskal Wallis test was used for near positive recovery as normality was not satisfied for an ANOVA analysis. This found a statistically significant association between age cohorts and near positive recovery (near positive fusion $p < 0.05$). Over the total population, older participants required a larger decrease in prism strength to regain binocularity than younger participants despite this not being reflected in the cohort mean scores (see Table 5.2).

Vertical Fusion

Near Vertical Fusion

The mean near vertical fusion (total fusion) for the total population was $4.2^{\Delta} \pm 1.4^{\Delta}$, the mode was 3^{Δ} (24 of 77 participants, 31.2%), and the range was 2 to 7^{Δ}. Across the population there were four participants who achieved only 2^{Δ} near vertical fusion (aged 10, 13, 29 and 73 years); whereas in comparison, there were seven participants who

achieved 7^{Δ} near vertical fusion (aged 34, 41, 48, 54, 69, 72 years); appearing to show an increase in the frequency of larger vertical fusion values in older age cohorts. From the participants that achieved 7^{Δ} near vertical fusion only 3 of 7 achieved maximum near positive horizontal fusion, 4 of 7 were mid-range for near positive horizontal fusion; therefore, within this population a strong vertical near fusion does not necessarily mean the participant will demonstrate the maximum horizontal near fusion of 45^{Δ} base out.

The mean vertical fusion was weakest for cohort 10 - 19 years (3.4^{Δ}), and strongest for cohort 60 - 69 years (4.9^{Δ}). Cohort 50 - 59 years showed the least variability, with a standard deviation of 1.0^{Δ}. In comparison cohort 40 - 49 years showed the most variability, with a standard deviation of 1.6^{Δ}. The difference between these measurements is unlikely to be of clinical significance.

Figure 5.9 shows that there was no IQR for cohort 50 - 59 years, this cohort had a high level of agreement with 8 of 11 participants recording 4^{Δ}. Cohort 60 - 69 years showed normally distributed data, while cohort 10 - 19 years showed positively skewed data, and cohorts 20 - 29 years, 30 - 39 years and 40 - 49 years showed negatively skewed data. Cohorts 40 - 49 years and 60 - 69 years recorded the same median value (5^{Δ}), but with different distributions. Cohorts 20 - 29 years, 30 - 39 years, 50 - 59 years, and 70 - 79 years all recorded the same median value (4^{Δ}), but with different distributions. Cohort 40 - 49 years had the largest boxplot, reflecting low level of agreement between participants in this cohort. Cohort 70 - 79 years showed long upper and lower whiskers indicating the greatest variability in both the positive and negative quartile values respectively.

There was one participant with a near vertical phoria, which measured 1^{Δ} Right over Left; their total vertical fusion range was greater than the cohort and population mean, measuring 6^{Δ} for both near and distance. A Bielschowsky head tilt test was performed; it confirmed the absence of a longstanding / congenital superior oblique palsy in this participant.

Interestingly, within cohort 10 - 19 years, only one participant achieved > 5^{Δ} vertical fusion, this participant had the smallest near horizontal fusion of their cohort, demonstrating that large vertical fusional amplitudes have no direct bearing or extrapolations applicable to horizontal fusional amplitudes..

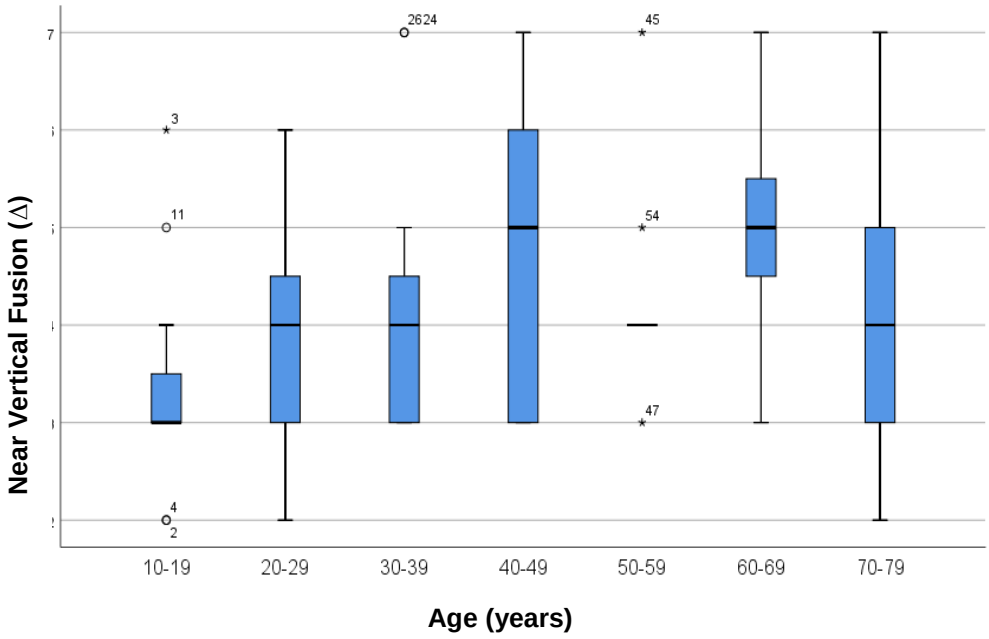


Figure 5.9 Box plot displaying the median, IQR, and the minimum and maximum measurements of the total near vertical fusion reserve. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohort were individually plotted.

Distance Vertical Fusion

The mean distance vertical fusion (total fusion) for the total population was 3.9$^{\Delta}$ ± 1.5$^{\Delta}$, mode 3$^{\Delta}$ (25 of 77 participants, 32.5%), and range 2 - 8$^{\Delta}$. Across the population there were 11 participants (14.3%), who achieved only 2$^{\Delta}$ distance vertical fusion (aged 13 years, 19 years, 26 years, 35 years, 46 years, 63 years, 66 years, 72 years, 73 years, and 74 years), indicating that age may not be a factor in predicting weaker distance vertical fusion. In comparison, there were seven participants (9.1%), who achieved ≥ 7$^{\Delta}$ near vertical fusion (aged 11 years, 29 years, 34 years, 44 years, 48 years, 66 years and 72 years), with one participant aged 72 years achieving 8$^{\Delta}$. Two participants aged 34 years and 48 years had 7$^{\Delta}$ of distance and near vertical fusion. Cohort 50 - 59 years was the only cohort to have a maximum distance vertical fusion of 6$^{\Delta}$.

The mean vertical fusion was weakest for cohort 10 - 19 years (3.4$^{\Delta}$), and strongest for cohort 40 - 49 years (4.6$^{\Delta}$). Cohort 50 - 59 years showed the least variability, with a standard deviation of 0.78$^{\Delta}$. In comparison, cohort 70 - 79 years showed the most variability, with a standard deviation of 1.79$^{\Delta}$.

Figure 5.10 showed that no cohort demonstrated normally distributed data, cohorts 10 - 19 years, 20 - 29 years, and 30 - 39 years showed positively skewed data, and cohorts 40 - 49 years, 60 - 69 years, and 70 - 79 years showed negatively skewed data. Cohorts 10 - 19 years, 20 - 29 years, and 30 - 39 years all recorded same median value (3^{Δ}), but with different distributions. Cohorts 50 - 59 years and 70 - 79 years both recorded the same median value (4^{Δ}), but with different distributions. There is no IQR for cohort 50 - 59 years, as this cohort had a high level of concordance with 9 of 11 participants recording 4^{Δ}. Cohorts 40 - 49 years and 60 - 69 years recorded same median value (5^{Δ}), but with different distributions. Cohort 70 - 79 years showed the longest upper whiskers indicating the greatest variability of the entire study population in positive quartile values.

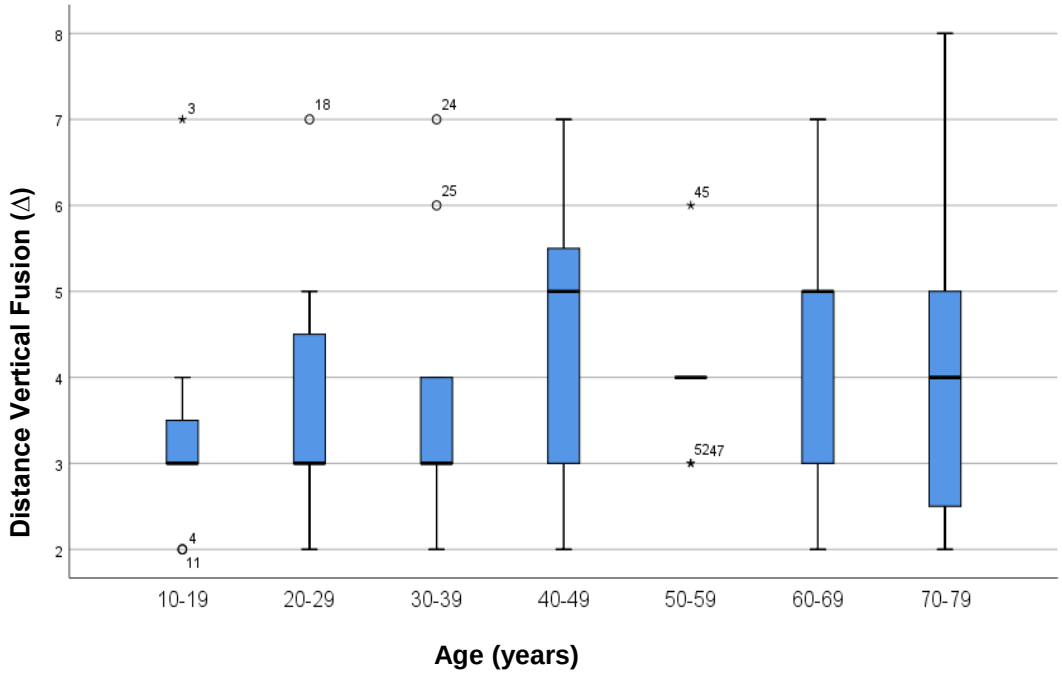


Figure 5.10 Box plot displaying the median, IQR, and the minimum and maximum measurements of the total distance vertical fusion reserve. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohort were individually plotted.

Vertical Fusion Summary

Vertical fusion was unaffected by test distance, with the mean total vertical fusion 4^{Δ} for both measurements taken at 1/3 m and 6 m. There were only 16 of 77 participants (21%) who achieved > 5^{Δ} of total vertical fusion, eight participants achieved for both

near and distance measurements, five participants for near only, and three participants for distance only. Within a similar population the total vertical fusion range is likely to be < 5^{Δ} and should be considered extended if > 7^{Δ}.

Association between age and vertical fusion

Initially, an analysis of correlation between near vertical fusion measurements with ungrouped age was performed. The Pearson's correlation coefficient analysis found a statistically significant correlation between near vertical fusion and increasing age ($p < 0.05$); older adults had a better vertical fusion reserve than younger adults. This analysis supports this study's results, of a higher frequency of larger vertical fusion values in older age cohorts. However, this correlation was not supported by the Kruskal-Wallis analysis test, which found no statistical significance between age cohorts and near vertical fusion ($p = 0.12$).

An analysis of correlation between distance vertical fusion measurements with ungrouped age was also performed. The Pearson's correlation coefficient analysis found no linear correlation between distance vertical fusion and increasing age ($p = 0.18$); older adults had the same vertical fusion reserve than younger adults. This analysis supports this study's results that a larger vertical fusion values occurred across the entire population. This correlation was also supported by the Kruskal-Wallis analysis test of age cohorts and distance vertical fusion, which found no statistical significance ($p = 0.41$).

NPC

For each participant, the value of NPC was the mean of three measurements taken using the RAF rule. The mean NPC for the total population was 6.5 ± 2.12 cm, mode 5 cm (30 of 77 participants, 39.0%), and range 5 - 16 cm. The majority of participants (55 of 77 participants, 71%) recorded a NPC of 6cm or better. All participants in cohort 20 - 29 years recorded NPC ≤ 6 cm. The best mean NPC was measured in cohort 20 - 29 years (5.2 cm) and the worst NPC was measured in cohort 70 - 79 years (7.3 cm). Cohorts 10 - 19 years and 20 - 29 years showed the least variability in mean NPC (standard deviation 0.82 cm and 0.42 cm respectively), whereas cohorts 40 - 49 years, 50 - 59 years, 60 - 69 years, and 70 - 79 years all showed a standard deviation > 2 cm.

Clinically, there were six participants who would have been diagnosed with a convergence insufficiency (NPC worse than 10 cm) although symptoms were not

present on initial screening. These participants were aged 46 years, 56 years, 63 years, 70 years, 74 years, and 75 years of age. The frequency of these potential convergence insufficiency diagnosis increases with age, 3 of 6 (50%) occurring in the 70 - 79 years cohort.

Figure 5.11 shows that no cohort had normally distributed data, with cohort 30 - 39 years showing negatively skewed data, and the remaining cohorts showing positively skewed data. Cohorts 30 - 39 years, 40 - 49 years, 50 - 59 years and 70 - 79 years all recorded the same median value (6 cm), but with different distributions. Cohorts 20 - 29 years and 60 - 69 years recorded the same median value (5 cm), but with different distributions. There was no IQR range for 20 - 29 years as this cohort had a high level of concordance, 9 of 11 participants having NPC at 5cms. Cohort 70 - 79 years had the largest boxplot reflecting low level of concordance between participants.

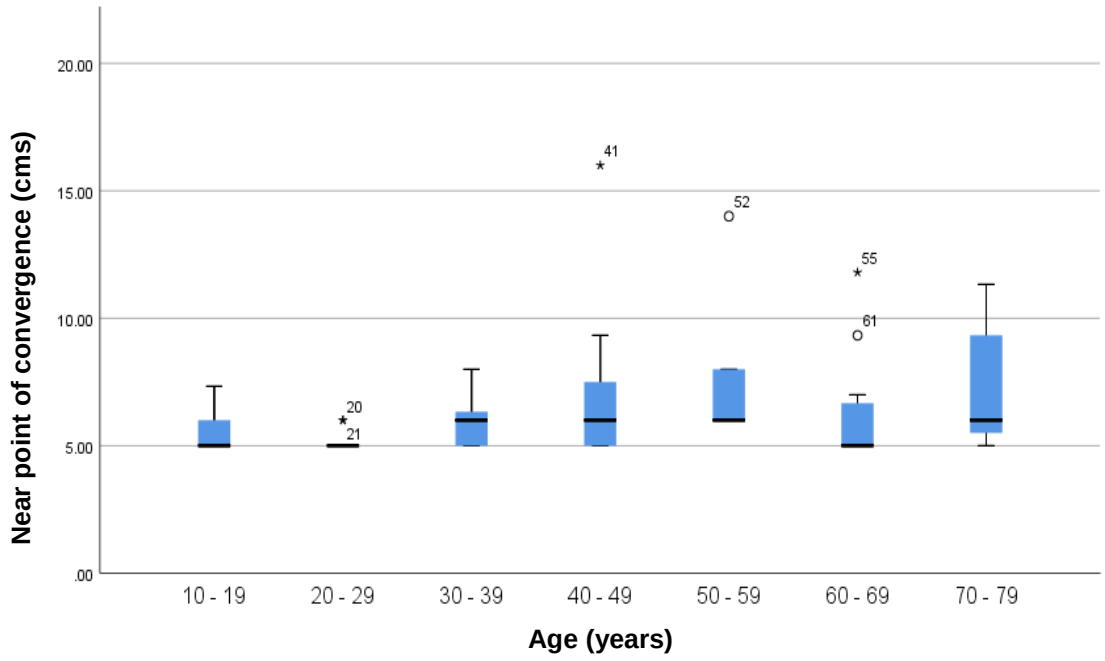


Figure 5.11 Box plot displaying the median, IQR, and the minimum and maximum measurements of NPC. Median is indicated by the black horizontal line, the edges of the blue boxes represent the IQR, and the whisker limits the 5th and 95th centile. The participants who were box outliers for the cohorts were individually plotted.

Association between Age and NPC

Initially, a correlation analysis was performed for the total population, which found a statistically significant linear correlation ($p \leq 0.01$) between ungrouped age and convergence. Therefore, as ungrouped age increases, the NPC declines.

The cohorts were tested for normality but this was not met in all cohorts, a log transformation was performed, but normality was again not achieved. The non-parametric Kruskal-Wallis test was performed to test the null hypothesis that all cohort medians are the same against the alternative hypothesis that not all cohort medians are equal. The Kruskal-Wallis test showed that there is a statistically significant difference between the cohorts ($p < 0.05$), as cohort age increases, the NPC declines. This supported the earlier observation from the results, as 3 of 6 participants met the criteria for a convergence insufficiency diagnosis were aged > 70 years. The statistical analysis therefore indicates that > 10 cm is in fact a 'normal' value of NPC in this age cohort, perhaps explaining why these patients did not manifest any symptoms of convergence insufficiency.

A correlation coefficient was calculated between actual age and NPC, this showed a significant linear correlation. Pearson correlation was $r = 0.295$ between age and NPC, as age increases the NPC numerical value increases (i.e. NPC declines) (see Appendix 20). To determine the effect of a year increase in age on NPC, a simple regression model was fitted. Assumptions for the regression model were checked and none seemed to be violated. The Pearson correlation analysis for the ungrouped age versus NPC showed a statistically significant correlation ($p < 0.05$). Additionally, a one year increase in age will yield a 0.032 cm decline in NPC.

	Parameter (NPC cms)	**P Value**
Ungrouped Age (years)	.032	.008

Table 5.5 The regression model analysis shows a statistically significant positive relationship between age and NPC ($p < 0.05$). A value in purple indicates statistical significance. A one year increase in age will yield a 0.032 cm decline in NPC.

Ocular movements

With regard to ocular movements, 76 of 77 participants (99%) showed a full range of eye movements, with one participant (aged 76 years) showing mild limitation of both

lateral recti (i.e. reduction in abduction of each eye). Three participants (aged 10, 68, 74 years) showed mild bilateral inferior oblique over-action. All participants had smooth non-jerky eye movements. No participant showed any motility dependent change in their globe nor lid position (i.e. narrowing of the palpebral aperture or globe retraction on attempted ocular movement), although one participant (age 76 years) was observed to have bilateral mild aponeurotic ptosis from outset.

There were seven participants (aged 32 years, 40 years, 62 years, 69 years, 72 years, 73 years, and 75 years) who showed end point nystagmus on horizontal versions. There appears to be an increased frequency of end-point nystagmus in older cohorts compared to younger cohorts as 5/7 participants were aged 60 - 79 years. As end point nystagmus was only ocular movement variable to show a change it underwent statistical analysis.

Association between age and the presence of end-point nystagmus

Initially a logistic regression was performed to determine the effect of age cohort on the presence of end point nystagmus. The logistic regression model predicts the log odds of getting end point nystagmus, which can be used to predict the probability of getting end point nystagmus within an age cohort. The results for the logistic regression model between end point nystagmus occurrence and age cohort showed no statistically significant difference between cohorts.

To determine the effect of a unit increase in age on the presence of end point nystagmus, a logistic regression model was fitted with end point nystagmus presence as an outcome and ungrouped age as a predictor. There was a statistically significant association between ungrouped age and end point nystagmus ($p < 0.05$). The odds of having end point nystagmus are 0.057 greater per increasing year of age (see Table 5.6). In a nutshell, the older you get the more likely you are to show end point nystagmus on ocular motility testing. Though clinically detectable, endpoint nystagmus is not a specific sign of disease; however, may indicate changes in central motor coordination of ocular movements outside of the habitually used range of eye movements (i.e. change of head position to effect lateral gaze may be used to a greater degree than purely ocular movements in younger, i.e. children, and older i.e. >~65 year age cohorts).

	P Value	Exponentiation of the B coefficient
Age	.040	1.057

Table 5.6 A logistic regression model was fitted with the presence of end point nystagmus as an outcome and ungrouped age as a predictor. There was a significant association between age and end point nystagmus ($p < 0.05$). Values in purple indicate statistical significance.

Summary of ocular motility

Participants within this population showed full smooth eye movements, without age related restrictions evident, however it does appear that increasing age may increase the likelihood of end point nystagmus on eye movement.

Ocular alignment

Near Heterophoria

Mean heterophoria for near fixation across the population was 2.2 ± 4.1$^{\Delta}$ base in (range 14$^{\Delta}$ base in to 6$^{\Delta}$ base out). A total of 28 participants (36%) were orthophoric, 34 participants (44%) were exophoric, and 15 participants (19%) were esophoric. The overall mean ocular alignment for every cohort was minimal exophoria, with cohort 60 - 69 years having the largest exophoria with 3.7 ± 4.3$^{\Delta}$ base in, and cohort 10 - 19 years having the smallest exophoria with 0.6 ± 3.0$^{\Delta}$ base in. Despite every cohort showing exophoria as their mean ocular alignment, all cohorts measured participants who had orthophoria or esophoria (see Figure 5.12). There were 6 of 77 participants (8%) who had a heterophoria > 10$^{\Delta}$ for near fixation, in all cases this was exophoria. Cohort 10 - 19 years showed the least variability in standard deviation (3.0$^{\Delta}$). In comparison, cohort 70 - 79 years showed the most variability in standard deviation (5.4$^{\Delta}$).

Figure 5.12 showed that orthophoria predominated for cohorts 10 - 19 years and 40 - 19 years. Exophoria was the predominant alignment for near fixation for the total population, and for cohorts 20 - 29 years, 30 - 39 years, 50 - 59 years and 60 - 69 years. Esophoria was the least common heterophoria measured across the population. The eldest cohort (70 - 79 years) was almost equally divided between orthophoria (n = 4), esophoria (n = 4), and exophoria (n = 3) for near fixation.

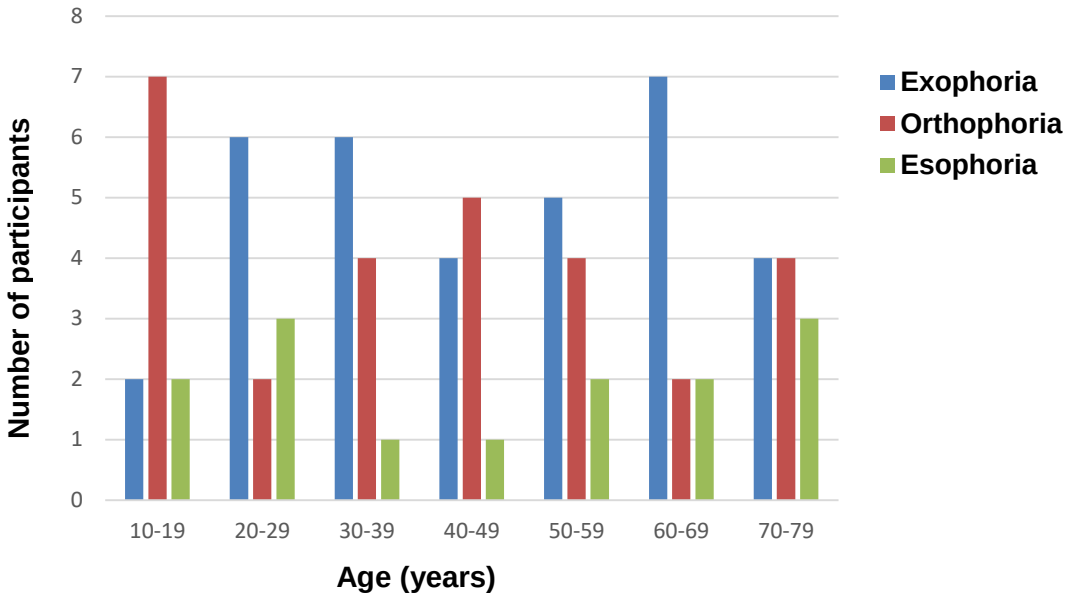


Figure 5.12 Bar chart demonstrating the near ocular alignment in each cohort.

Distance Heterophoria

Mean heterophoria for distance fixation across the population was 0.4 ± 1.2$^{\Delta}$ base in (range 6$^{\Delta}$ base in to 1$^{\Delta}$ base out). A total of 60 participants had orthophoria, 13 had exophoria and 4 had esophoria. The lower age cohorts (10 - 19 years, 20 - 29 years and 30 - 39 years) do not have any participants with an esophoria at 6 metres (see Figure 5.13). The overall mean ocular alignment for all cohorts was minimal exophoria, except for cohort 40 - 49 years, which was minimal esophoria. Cohort 10 - 19 years was the most exophoric (0.9 ± 2.0$^{\Delta}$ base in). Cohort 50 - 59 years was the least exophoric (0.1 ± 0.8$^{\Delta}$ base in). Cohort 60 - 69 years showed the least variability, with a standard deviation of 0.6$^{\Delta}$. In comparison, cohort 10 - 19 years showed the most variability, with a standard deviation of 2.0$^{\Delta}$.

Figure 5.13 shows that orthophoria predominated in all cohorts. Exophoria was recorded in all cohorts except cohort 40 - 49 years. Esophoria was the least common heterophoria measured, and was found only in cohorts 40 - 49 years, 50 - 59 years, and 70 - 79 years.

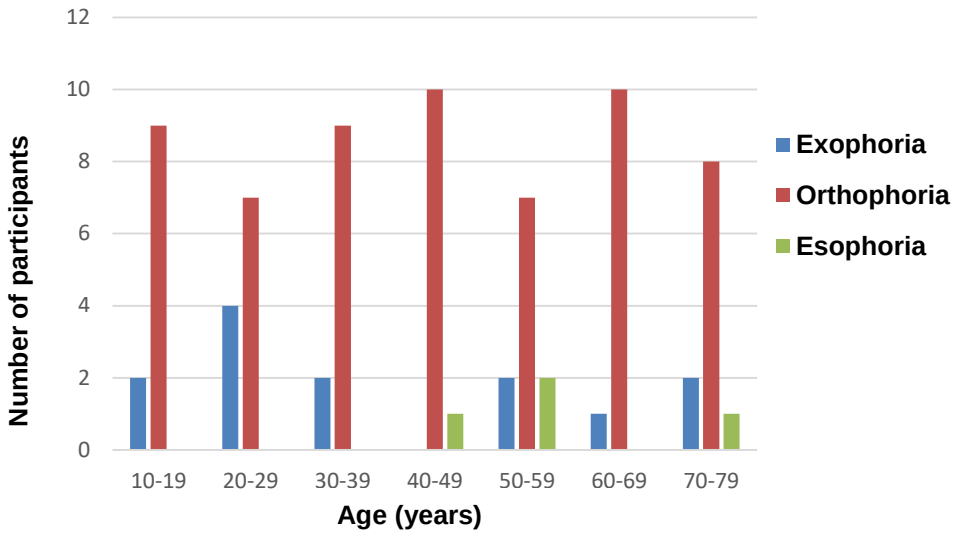


Figure 5.13 Bar chart demonstrating the distance ocular alignment in each age cohort.

Association between age and ocular alignment

To determine if there were any association between age and heterophoria, the Fisher's exact test was performed. The Fisher's exact test is used to determine if there is an association between two categorical variables when the cell sizes are small. The Fisher's exact tests showed no association between ungrouped age and heterophoria, for both near and distance alignment (near $p = 0.637$; distance $p = 0.496$). Therefore, older adults had the same ocular alignment as younger adults.

Normality tests were then performed in order to determine if it was appropriate to use ANOVA to compare near and distance alignment between age cohorts; this analysis showed a skew of values to the lower prism strengths and therefore normality was not satisfied in all the age cohorts for both near and distance alignment. The non-parametric Kruskal-Wallis test was then performed since ANOVA assumptions were not met. The Kruskal-Wallis test is a non-parametric procedure that does not depend on parametric distribution of the data. The results from the Kruskal-Wallis analysis showed that there were no significant differences by age cohorts for both near ($p = 0.80$) and distance alignment ($p = 0.41$). This again suggested that older adults had the same ocular alignment (near and distance) as younger adults.

Ocular alignment summary

Within this population, the overall mean ocular alignment was a minimal exophoria for both near and distance. A larger exophoria (< 10^{Δ} base in) is more likely for near than

for distance, and an esophoria is an uncommon finding in the distance. There was no association between increasing age and ocular alignment.

5.5 Discussion

In this study, motor fusion, ocular motility, ocular alignment and NPC were measured with standard clinical techniques, as used by UK trained orthoptists. This study confirmed that there is a reduction in NPC and distance positive fusion with increasing age in a population with normal visual acuity and normal ocular health. Conversely, this study did not find any association between age and near fusion (positive horizontal, negative horizontal, and vertical), distance negative fusion and distance vertical fusion. It was a surprising finding that near positive fusion was not associated with increasing age; as the researcher is a hospital based orthoptist her prior clinical experience of patients which convergence insufficiency having weaker near positive fusion reserves, but this did not translate when the decrease in NPC is associated with age. Within this population the overall mean ocular alignment was a minimal exophoria for both near and distance, with a larger exophoria (> 10^{Δ} base in) more likely to occur for near fixation than for distance fixation, and that an esophoria was an uncommon finding for distance fixation. Finally, participants showed full smooth eye movements without any evidence of age related restrictions; however, it does appear that increasing age may increase the likelihood of end point nystagmus being present on eye movement.

There was a high degree of compatibility between fusion break points for the youngest and oldest age cohorts in this study for all fusion variables except distance positive fusion. Across every age cohort and across the total population, this population of participants demonstrated the expected motor fusion pattern. The expected motor fusion strength pattern (from strongest to weakest fusion measurement) is: positive fusion for near, positive fusion for distance, negative fusion for near, negative fusion for distance, and finally, vertical fusion. Strangely, increasing age was associated with poor positive recovery but not with negative recovery, and this finding was independent of fixation distance; clinically, this means that older patients will require a greater decrease in base out prism to regain fusion than younger patients.

When the mean near positive fusion value for this population was compared to the seven publications detailed in Table 1.5, a similar mean near positive fusion was found. Using the seven publications/populations that reported a mean near positive fusion value (99, 126-128, 130, 131), there was a total population of 1314 participants for near

fusion, and the mean near positive fusion was 27^{Δ} base out (range 17 - 45^{Δ} base out). However, if the study with 390 children aged 10 - 12 years was excluded (127), the mean near positive fusion increases to 31^{Δ} base out (range 26 - 45^{Δ} base out, n = 924). If the study of 561 participants, which used a synoptophore rather than prisms is excluded (99); then the mean near positive fusion based on five publications again increases to 37^{Δ} base out (range 31 - 45^{Δ} base out, n = 363). This mean near positive fusion value (from five publications), is exactly the same result for mean near positive fusion as in the present study, 37 ± 10^{Δ} base out. This validates the primary researcher's decision not to use the synoptophore in the study methodology as this has a clear effect on measured outcomes for fusion (in addition to its limitation: being unable to quantify stereopsis); using the same parameters, the researcher has been able to replicate findings of other groups, while expanding this to equally divided regularly grouped age cohorts as well as looking at a wider range of parameters.

When the mean near negative fusion value for this population was compared to the seven publications detailed in Table 1.5 (99, 126-128, 130, 131), a similar mean near negative fusion was found. Using the seven publications/populations, there was a total population of 1314 participants for near fusion, the mean near negative fusion was 14^{Δ} base in (range 10 - 16^{Δ} base in). However, if the study with 390 children aged 10 - 12 years (127) is excluded, the mean near negative fusion increases to 15^{Δ} base in (range 13 - 16^{Δ} base in, n = 924). This mean near negative fusion value is exactly the same result as the mean near positive fusion as this present study (15^{Δ} ± 6^{Δ} base in). If, again, the study of 561 participants which used a synoptophore is excluded (99), then the mean near negative fusion increases to 16^{Δ} base in (range 13 - 16^{Δ} base in, n = 363). As the negative fusion value is approximately half of the near positive fusion value, the exclusion of studies with dissimilar methods/populations does not have the same dramatic effect, as it did for mean near positive fusion; though only including studies with similar methodologies remains important when comparing data across different populations.

When the mean distance positive fusion value for this population was compared to the six publications detailed in Table 1.5 (99, 127, 128, 130, 131), a larger mean distance positive fusion was found than in this present study. Considering the six publications, there was a total population of 1286 participants with distance fusion data, the mean distance positive fusion was 18^{Δ} base out (range 14 - 27^{Δ} base out). When the study with 390 children aged 10 - 12 years is excluded (127), the mean distance positive fusion remains 18^{Δ} base out (range 14 - 27^{Δ} base out, n = 896). However, if the study on 561 participants using a synoptophore is excluded (99) then the mean distance

positive fusion increases to 19^{Δ} base out (range 18 - 27^{Δ} base out, n = 335). This value for mean distance positive fusion is less than the value measured in this present study ($22^{\Delta} \pm 9^{\Delta}$ base out). Interestingly, the study most similar in design to the present study, performed by a single experienced American orthoptist, based on 50 participants aged 20 - 70 years, found the highest mean distance positive fusion of 27^{Δ} base out (130).

When the mean distance negative fusion value for this population was compared to the six publications detailed in Table 1.5 (99, 127, 128, 130, 131), a similar mean distance negative fusion was found. Using these six publications, there was a total population of 1286 participants for distance fusion, and the mean distance negative fusion was 7^{Δ} base in (range 5^{Δ} - 10^{Δ} base in) (99, 127, 128, 130, 131). This is a slightly lower (worse) result than the mean distance negative fusion in this present study ($9^{\Delta} \pm 4^{\Delta}$ base in). The numerical values of the mean and range of distance negative fusion are so low that the inclusion or exclusion of individual studies does not change the comparison. The normal range of amplitudes of vertical fusion are very low and, using whole prism dioptre increments, is unable to be expanded into larger units. The lack of a commercially available vertical prism bar with smaller increments suggests an incredibly low prevalence of symptomatic low-amplitude vertical phorias, and thus further statistical analysis of past and present publications is unlikely to yield clinical or academically interesting/useful results.

The findings of this present study concur with a similarly designed study (Moorfields study) which measured motor horizontal fusion over a wide age range (113); both studies found no statistically significant association between these near fusion variables (positive and negative) and age. Additionally, both the present study and the Moorfields study found no statistically significant association between negative distance fusion and age (113). Unfortunately, the Moorfields study's authors did not specify their median or mean fusion for each cohort to facilitate a direct comparison (113). This present study also supported the Moorfields study's finding of a small decline in positive distance fusion with increasing age; this was a statistically significant finding (113).

The fusional recovery point was reported to be 2^{Δ} - 6^{Δ} less than the break point (35, 99, 125). However, a study of 50 participants aged 20 - 65 years (mean age 37 years), found the median recovery point was 10^{Δ} base out less than the break point for distance (130). This study of 50 participants had a greater range of ages and an older mean age than the previous studies (130). Consequently, a subsequent publication by the same author on 99 participants age 20 - 70 years found the change was 4.3^{Δ} base

out for near positive, 3^{Δ} base in for near negative, 7.3^{Δ} base out for distance positive and 2.2^{Δ} base in for distance negative (228). Whilst this study appears comparable in method to the present study, they had five age cohorts with unequal numbers of participants (228). In this present study, a wider range of fusional recovery values was found. For near positive, near negative and distance positive, the recovery point range was 2^{Δ} - 10^{Δ} less than the break point. For distance negative, the recovery point range was 1^{Δ} - 8^{Δ} less than the break point. The larger range of recovery points may reflect studies with a larger age range of participants. The main finding from this present study, was an association between age and positive fusional recovery (near and distance), and although this is not a new finding, it adds to the existing volume of evidence in this area, which is currently sparse. Senile changes in the fusion system could be explained by ageing effects in the EOMs; however, there must be a multifactorial cause (i.e. central control, neuromuscular junction, sustained activity of binocular functions vs transient of ocular movements), as the fusional break points and ocular motility showed stability across the population. As NPC does decrease with age, there are greater demands on motor fusion for near, so perhaps fusion recovery is more sensitive to acquired abnormalities of binocular function than motor fusion break.

The present study found a smaller mean vertical fusion range for near and distance of 4^{Δ} (to nearest whole prism value) relative to the previous publications which reported 3^{Δ} - 9^{Δ} (130, 132-136). The study by Rowe that stated large values of vertical fusion (9^{Δ} for near and 7^{Δ} for distance, range not reported) was performed on 22 university students aged 19 - 23 years (125). Rowe's data are almost double the vertical fusion value recorded in the present study cohort aged 20 - 29 years (125); in this present study the near vertical fusion was 3.91^{Δ} for near (range 2^{Δ} - 6^{Δ}) and 3.64^{Δ} for distance (range 2^{Δ} - 7^{Δ}). This difference in vertical prism range may be a reflection of differences in the populations recruited, different target size used or errors from small sample sizes. To the author's knowledge, this current study is the first study to assess vertical fusion over a seven decade age range and so comparisons cannot be made; however, there was no change in vertical fusion with increasing age.

The findings for NPC in this present study support other studies, there was a statistically significant decline in the NPC with increasing age (112, 114, 225). In this present study, the change was 5.64 ± 0.82 cm to 7.36 ± 2.33 cm, from the youngest to the eldest cohorts. This present study found a one year increase in age yielded a 0.032 cm decline in NPC. The change in NPC from youngest to eldest cohort was not as large as the NPC change reported in a previous study; the authors described a decline in NPC from 6.95 ± 3.87 cm in cohort 10 - 19 years, to 13.06 ± 5.2 cm cohort >

70 years (114). However, their method to measure NPC was a Gulden fixation stick and a ruler, which may have been subject to measurement variability or error (114). This present study conflicts with the statistical analysis from a large population based cross-sectional study performed in Iran on 1784 participants aged over 60 years (mean age 65.9 ± 4.6 years) (115). The Iran study found no statistically significant change in NPC with increasing age, despite reporting a 1 cm decline in NPC between the youngest cohort (60 - 64 years) and the eldest cohort (≥ 80 years) (115).

This present study does not support prior studies which found a limitation of elevation with increasing age; this may relate to the methodologies of the previous studies utilized, for example a hand held perimeter (227), fusion slides on a synoptophore (112), and the lateral version light reflex test of Urist (67). The researcher would agree with their discussion comment that qualitative asymmetry in EOMs remains the best clinical tool for identifying muscle weakness rather than absolute quantitative measurements (67). A potential limitation of this present study was the method of assessing ocular movements, as this could be considered to be a subjective test with potential bias; however, this is the technique endorsed by BIOS for use by orthoptists in the UK and Ireland. This present study aimed to use common clinical methods available to all eye care professionals in order to have the most relevance to the normal eye clinic scenario (hospital, community or private practice), maximizing applications of routine orthoptic, optometric or ophthalmic clinical practice. More objective measures of motility assessment could have been used, including the Goldmann perimeter for kinetic recording or the Lee/Hess screen for static recording. These testing modalities were available within the Hospital department; however, these tests are not often available in standard optometric practices and the Goldmann perimeter is no longer manufactured (63). While these perimetric or Lee/Hess screen methods provide standardization and fixed quantification of degree of ocular motility, they also come with significant limitations. The techniques are time consuming, require continuous supervision by skilled personnel, restrict the researcher from observing the eye muscles (for example, to observe any changes in globe or lid position with eye movement, end point nystagmus, fluidity of motility (i.e. jerky or smooth) and any variability between ductions and versions). Other potential errors with the Goldmann perimeter include, transposing errors when the researcher records what she sees to the Hess record sheet, any compensatory head movement (which may not be detected behind the dome of the perimeter), will result in eye movements appearing normal when they are reduced/limited, and participant fatigue may affect the performance of other binocular functions.

There are conflicting publications on whether ocular alignment changes with increasing age. A publication comparing 150 participants aged 10 - 35 years found that the near alignment became more divergent (exophoria) with increasing age whilst distance alignment remained unchanged (111), versus a publication with a larger number of participants and a wider age range (271 participants aged 21 - 80 years) found no statistically significant relationship between distance heterophoria and increasing age (144). This present study did not find any statistically significant relationship between increasing age and ocular alignment for near or distance fixation. Within this present study's population only one participant demonstrated a vertical phoria for near, and no participant demonstrated a vertical phoria in the distance. Therefore, supporting a previous publication concluding that vertical phorias are uncommon (144).

5.6 Strengths and limitations of current study

There were 22 participants (29%) with an unknown positive fusion break point and recovery point (as a result of participants maintaining fusion at 45^{Δ} base out). Potentially for both the total population and particularly cohort 60 - 69 years, (this cohort had a high level of agreement with 10/11 participants achieving 45^{Δ} base out positive fusion), the mean positive fusion was potentially higher than 45^{Δ} base out. The use of two prism bars (placing one in front of each eye) would have facilitated measuring a larger positive fusion break point in those participants. However, it was decided in the study design stage to only use one prism, as a second prism bar can induce unknown degree of measurement error (see Chapter 1.6.4).

As the measurement of fusion break point, fusion recovery and NPC were not automated there is the potential for examiner bias. Potentially, as the researcher had an expectation/approximation from prior clinical knowledge of the measurement's end point, it may have influenced how the test was performed, and thereby the results e.g. slowing down the target speed towards end-point of test. The researcher was aware of this potential bias ahead of commencing the research and demonstrated mindfulness during data collection.

The researcher did not record the 'blur point' of fusion; this is because this measurement is not routinely recorded in clinical practice nor does it appear in the publications the author used in literature review. Some publications noted that they recorded it but did not present the results, analyse or discuss fusion blur point, therefore, the author decided to not include it in the data collection.

The method of measuring and recording of NPC used in the present study may be considered by others as subjected to recording error. It was decided during the design stage that the RAF rule would be used to measure NPC and recorded as per the last completed cm on the rule, for example, if the participant's NPC was between 6 and 7 cm it was recorded as 7 cm. Other studies may have recorded this as 6 or 6.5 cm which would have given them a better NPC value.

The main strengths of this research chapter findings are firstly that the study was performed by a single clinically experienced orthoptist so the recorded raw data is a true reflection of the participants' fusion, ocular alignment, ocular motility and NPC without inter-observer variability, and secondly, that this research has confirmed findings in a similarly designed study whilst having more age cohorts and cohorts based on decades of life. The study has added to the researcher's clinical knowledge, and will add to the evidence base when published new information on the association between age and vertical fusion.

5.7 Conclusions

The results of the study add to the literature on binocular functions by providing normative data on ocular alignment, ocular motility, NPC, and fusion ranges for a large spectrum of ages. This study has found that in keeping with previously published findings in the literature a vertical heterophoria and esophoria for distance were uncommon in a general population. Clinicians should maintain a high index of suspicion for acquired pathology when reduced EOMs and reduced fusion reserves are detected regardless of patient age. These abnormalities may indicate new pathology arising from a myogenic, neuromuscular synaptic junction or neurological origin. These aetiologies should be excluded in older adults before these abnormalities are attributed to 'old- age'.

5.8 Summary of key findings applicable to clinical practice

1. There was no association between horizontal fusion and increasing age, therefore all adult patients, irrespective of age, should have the same horizontal fusional reserves.
2. Positive motor fusion (base out measurements) is greater than negative motor fusion (base in measurements) for both near and distance. From this

population, the normative data were: $37^{\Delta} \pm 10^{\Delta}$ base out and $15^{\Delta} \pm 6^{\Delta}$ base in for near, $22^{\Delta} \pm 9^{\Delta}$ base out and $9^{\Delta} \pm 4^{\Delta}$ base in for distance.

3. 80% of patients will regain horizontal binocularity within two prism bar steps from the break point.
4. Older patients may require a larger decrease in prism strength, particularly base out prism, to recover binocularity than younger patients.
5. Patients of all ages should be expected to have 3^{Δ} or 4^{Δ} of vertical fusion; fusion ranges beyond 7^{Δ} would indicate an extended vertical fusion range and support the diagnosis of a longstanding vertical misalignment.
6. Older adults have reduced NPC. This study found a one year increase in age will yield a 0.032 cm decline in NPC.
7. There is no association between changes in EOMs and increasing age, therefore, all adult patients irrespective of age should have a full range of EOMs.
8. Distance esophoria and vertical heterophorias are not common; they warrant further investigations (for example Hess/Lee screen) to rule out an EOM weakness/limitation.

Chapter 6:
General conclusions

Chapter 6: General conclusions

6.1 Aims

The aims of this chapter are to summarize and contextualise the clinical implications of the study's findings, to assess what this research has contributed to the literature, to identify and discuss the strengths and limitations of the present research, and finally to discuss suggestions for future research.

6.2 Summary of thesis

The principal aim of this research was to examine for the presence of any associations between increasing age and changes in binocular functions (i.e. motor fusion, ocular alignment, ocular movements, NPC, and stereoacuity).

Chapter 1 began with describing the anatomical and physiological features of eye muscles, eye movements and cortical functioning which allows for binocular functions to be performed. The grades of binocular functions (i.e. simultaneous perception, motor fusion, and stereopsis), and the clinical methods used to assess them were described. Finally, the literature on the associations between increasing age and binocular functions were discussed. Chapter 1 concluded that there was either a lack of published evidence or conflicting reports, to answer the question *do binocular functions change as we get older?*

Chapter 2 reported the preliminary questionnaire survey of orthoptists and optometrists that was performed as an initial research step to gauge general knowledge and understanding of binocular functions with age among practitioners involved with assessing these conditions (i.e. scoping exercise). The aim of the preliminary research was to explore whether a clinical need existed, and to identify areas of uncertainty in the field of binocular vision, which did and did not need to be investigated further. The research questions were:

- What are the views of practicing British and Irish optometrists and orthoptists' on the association between age and binocular functions?
- Is there a gap in current knowledge on the association between age and binocular functions?

The survey results showed there was a lack of definitive understanding of how binocular functions relate to age. Orthoptists frequently gave a definitive response to

more questions than optometrists (there was a higher frequency of 'Don't know' responses from optometrists); this is probably a reflection that the typical primary clinical role of an orthoptist is the assessment of ocular motility, ocular alignment, strabismus and binocular functions. This knowledge gap represents a void in the evidence base for a very commonly encountered clinical entity. In practical terms, if a patient is having a test of binocular function(s) as part of an ophthalmic assessment (whether as part of a routine optometric examination or for a pre-operative cataract or refractive surgery assessment), well-defined age-matched normative data should be available to determine appropriate cases for further investigations; orthoptists, optometrists and ophthalmologists should be familiar with this. Lack of this knowledge could incite or prevent relevant investigations, with significant cost implications for public and private health services (i.e. from unnecessary expensive investigations in a patient within the normal age limits for binocular functions, or from increased morbidity- and mortality-related health costs from an central nervous system malignancy that was not investigated and treated an early stage when the only manifestation was impaired binocular functions). Therefore, the ambiguity highlighted that others like myself, did not know the answer to what seems like a straightforward clinical question, and confirmed the need for this research. The information gained from the survey was then generalised to form a series of hypotheses for the main doctorate study (see Chapter 4.3 and Chapter 5.3). Based on these hypotheses a prospective, non-randomised, cohort study was designed to answer the following research questions:

- Is there a decline in near and distance stereoacuity with increasing age as measured by commercially available stereoacuity tests?
- Is there a decline in positive fusion (near and distance) associated with increasing age?
- Is there a decline in negative fusion (near and distance) associated with increasing age?
- Is there a decline in vertical fusion (near and distance) associated with increasing age?
- Is there a decline in NPC associated with increasing age?
- Is there a decline in ocular motility associated with increasing age?
- Is there a change in ocular alignment associated with increasing age?

Chapter 3 described the method of how the main study would be performed, and how the results would be analysed. It detailed the method by which patients were recruited (i.e. via advertisements), the inclusion and exclusion criteria (potential participants were

screened by phone in advance of booking a study appointment), and the specific details of how each test of binocular function was carried out. This took into account the methodologies of the prevailing canon of studies in the scientific literature with a view to addressing significant knowledge gaps and facilitating inter-study comparisons with this present study's data.

Chapter 4 investigated the association between age and stereoacuity using four commercially available stereotests (i.e. the Frisby stereotest (crossed and uncrossed disparity), the TNO stereotest, the Titmus stereotest, and the FD2 stereotest), and revealed a number of clinically-relevant insights. All the stereotests showed that increasing age was associated with a decline in stereoacuity, with TNO and Frisby stereotests being more sensitive for detecting age-related changes in stereoacuity. Therefore, the choice of stereoacuity test is important, and highlights that they are not interchangeable between visits, a conclusion already reported in the literature (94). Choice of stereotest may be impacted by local practice, preference, and availability. This data adds to the weight that more precise tests (for example, the Frisby stereotest and the TNO stereotest), are more accurate and less susceptible to monocular clues; in particular, wider adoption of the Frisby stereotest is supported by the primary researcher, as no special glasses are required for viewing (unlike the TNO stereotest and the Titmus stereotest). This is significant as these glasses may induce measurement error if damaged, and render the test unusable if lost (a common occurrence in a busy ophthalmology department). The presence of stereo-negative results for distance stereoacuity within this normal asymptomatic population, suggests that the routine testing of distance stereoacuity in older adults may lead to false referrals, unnecessary anxiety to patients, and, as mentioned above, increased cost to the health service.

There was an unexpected finding in the stereoacuity results, with cohorts 10 - 19 years and 20 - 29 years having a weaker mean near stereoacuity value than cohort 30 - 39 years on the Titmus stereotest, the TNO stereotest and the Frisby stereotest; although, the finding was not statistically significant. As 3 of 11 participants in cohort 10 - 19 years were aged 10 years, 10 years, and 11 years, it could be argued that perhaps stereoacuity is still developing in the 2nd decade of life, and these young participants influenced the overall mean stereoacuity for the cohort. However, the researcher is unclear as to why participants aged 20 - 29 years would not have same level of stereoacuity as participants aged 30 - 39 years. Presbyopia could be used as an explanation for those aged > 40 years, that presbyopia influences near stereoacuity measurements (NB 41 participants in this study (53.2%) were presbyopic), but could

not be used as an explanation of the findings. Repeating the study with a larger cohort only of 20 - 29 year olds, may support or reject the findings; it may be that there is no difference between cohorts 20 - 29 years and 30 - 39 years and the finding was as a result of a bias within the population sampled.

Chapter 5 investigated the association between age and other aspects of binocular vision (for example, fusion, ocular alignment, and ocular motility); the chapter highlighted several normative values across all age cohorts within the population. The results of this chapter give a greater evidence base to determine abnormal, possibly pathologic findings, regardless of a patient's age. Particularly relevant is the finding of the same mean vertical fusion across the entire population, which has immediate clinical applications (i.e. if a patient complains of vertical diplopia symptoms, age can be ruled out as a likely cause and a definitive pathology sought). The only age-related change in motor fusion identified was in positive distance fusion. The relevance and clinical implications of this are, if there is a weakness in one or both lateral recti that an older patient will not have same reserves as a younger patient to control the resulting ocular misalignment and will experience diplopia. The overall mean ocular alignment was a minimal exophoria for both near and distance; distance esophoria and vertical phoria (at any distance) are uncommon ocular alignments, and therefore, would give the clinician suspicion of a VI or IV nerve palsy contributing to primary ocular misalignments. A one-year increase in age yielded a 0.032 cm decline in NPC, therefore clinicians should apply caution when diagnosing convergence insufficiency in elderly patients.

6.3 Contribution of this research to the literature

This research adds to the knowledge base of ocular motility, NPC, fusion, ocular alignment, and stereopsis by using an even distribution of age cohorts, which are each composed of 10 year intervals.

Ocular motility was shown to be grossly unaffected by age, thus supporting the clinical trend that all motility disturbances need to be investigated.

As previously reported by other authors, NPC declines with increasing age despite adequate presbyopic refractive correction; however, the data presented here, shows that the rate of this deterioration is very gradual (0.032 cm / year); thus, it would take 31.25 years for NPC to worsen by 1 cm. Though a reduction in NPC is expected with

age, significant changes (i.e. > 2cm) should be considered pathological and be investigated and treated. None of the age cohorts in this study had a mean (or IQR) NPC ≥ 10 cm, thus this value should be considered pathologic/abnormal in clinical practice.

Fusion was largely unaffected by age with the exception of horizontal positive distance fusion, with the clinical take away that older people are more subject to developing binocular diplopia at distance from a decompensated horizontal heterophoria, while their younger counterparts may be better equipped to control a latent deviation, potentially masking significant acquired pathology.

Across the total age range of the population, mean ocular alignment was minimal near and distance exophoria, with distance esophoria and vertical phoria (at near or distance) being infrequent ocular alignments. This was not significantly attributable to advancing age; either of these findings should raise clinical suspicion of a cranial nerve VI or IV nerve palsy, respectively, with appropriate investigations being instigated.

The most significant and relevant findings to clinical practice are those found from assessment of stereopsis. The technique employed in this study was to use four commercially available stereotests on every participant; this allows direct extrapolations to clinical practice. The researcher showed that there was further improvement in stereopsis in the second decade of life. Older adults (> 70 years) showed reduction in near and distance stereoacuity with all test types; and those > 70 years are most likely to score stereo-negative responses on distance testing. There is debate that all distance (beyond 6 m) assessment of depth relies on monocular clues, and this is not disrupted until vision or VA is significantly reduced, so this study's finding may not have any significant functional impact on distance-based activities of daily living (e.g. driving), for this age group with normal VA. Different stereotests give different stereoacuity results for the same participant (and clinically the same patient) due to test design (for example, the Frisby stereotest is a real depth stereotest, while the Titmus stereotest is a Randot simulated stereotest), and degree of stereoacuity measurable (for example, upper limit of the Frisby stereoacuity is 5 arcsec versus 40 arcsec for the Titmus stereotest). Thus, younger patients in particular are better served by using a stereotest with numerically lower stereoacuity measurements (i.e. 5 arcsec). In addition, as the Northern Ireland school-children study (94) showed, Frisby stereotest is a simple and suitable for use in children aged 6 or older. Like past studies, the data in this present study demonstrated that crossed disparity (circle forward projection) and uncrossed disparity (circle backward projection) for the Frisby stereotest were

equivocal, and thus only one option needs to be assessed in clinical practice, though the choice should be consistently used between the three plates so as not to confuse patients. This makes using the Frisby stereotest simple for inexperienced practitioners while maintaining accuracy.

The researcher feels that these findings have helped to fill some of the gaps in the literature regarding the effect of age on binocular functions, and it is the intention of the researcher to publish these outcomes in peer-reviewed scientific journals to officially add this data to the knowledge base for clinical application, as well as for comparison with future and existing studies, as discussed in the preceding chapter.

6.4 Strengths and limitations of the study

Strengths of study

A thorough literature review was performed and sub-analyses of the data available were made, where possible. This allowed for meticulous planning of the study parameters. The study aims and hypotheses were clearly stated; the inclusion and exclusion criteria were detailed and adhered to. The author has no conflict of interest or vested interests in the commercially available equipment used. The author designed and produced, with the assistance of a mechanical engineering student from the local university the Frisby stereotest plate holding gantry table. This table ensured that the correct stereoacuity could be calculated based on accurate measurement of testing distance and elimination of measurement error from head movement.

A further strength of this experimental study is that it objectively evaluated all components of a typical orthoptic examination (for example, ocular alignment, ocular motility, fusion, NPC and stereoacuity), measured aspects not always routinely assessed (for example, vertical fusion and distance stereoacuity), and additionally measured near stereoacuity on three commercially available tests to maximise the applicability of the results to clinicians depending on which stereotest(s) were available to them, as well as to allow unbiased comparison of these widely adopted test modalities. An additional strength, all participants completed all aspects of the experiment, so there was a comprehensive data set of outcomes to analyse.

The analysis did not make any assumptions regarding binocular functions; instead each outcome measurement was a direct reflection of the participant's binocular functions. To the researcher's knowledge, she avoided all possible misinterpretations

of the data, and applied the question ‘is this clinically significant’ when commenting on the statistical significance, in an attempt to maximise the clinical practice take-aways applicable to an everyday clinical setting. Additionally, following the analysis, the researcher presented the appropriate measure for the type of variable (for example, when the data was not normally distributed the median stereoacuity was presented instead of the mean stereoacuity). However, when comparing this study to previously published papers, the same comparators were used (for example, mean with mean, median with median) in order to facilitate direct comparisons.

As mentioned in previous chapters, the researcher struggled with data collection on two occasions; however, the author adapted to this situation and found alternative methods to recruit participants to ensure the sample size number was reached for the main research project to achieve the desired statistical power. For the online survey the researcher received no online responses from optometrists, this issue was resolved by delivering the survey in a person-to-person fashion at a UK optometry educational event. Again, for the main study the researcher had difficulty recruiting sufficient participants older than 60 years through advertisement posters; however, when the researcher targeted members of public via personal appearances at ‘active retirement’ clubs, the remaining participants were recruited to fulfil the required cohort criteria. While people who volunteer to participate in a study may not be representative of the general population, and the researcher has no way to qualify or quantify the effect of volunteer bias, the application of the inclusion and exclusion criteria ensures that the included participants are within the desired demographic of ‘ophthalmologically normal’ individuals. However, as the volunteers in the main study were not patients of the ophthalmology department or optometric/orthoptic students, the sample is quite representative of a general population, naïve to the equipment and expected outcomes; this is a strength in comparison to many of the studies referenced, which were predominantly performed on university optometry/orthoptic staff and students.

The population had shared common characteristics (i.e. standardized inclusion and exclusion criteria), and each cohort shared a further common characteristic (i.e. each cohort was aged in same decade). Finally, the generalizability of the study results can be applied to the racial and ethnic composition of county Galway, Ireland, with the results extrapolated to the description “small urban Irish population”. Previous studies from the UK (Moorfields study and Newcastle study) may have had a more diverse ethnic background, although neither study described their racial and ethnic compositions; however, a wider diversity may infer the bias of genetic influences on ophthalmic health and binocular functions. This study is comprised of 97% white Irish

people and thus largely removes these potential genetic modifying factors from the outcome analysis.

Limitations of study

Whilst no ethical issues were identified on completion of the research, there were several potential causes of bias inherent in the experimental design. There was a gender bias as 78% of the participants were female; and although the author is not aware of any influence this could have had on the results, a 50/50 gender distribution would be the ideal representation of the population. Potentially, female reproductive hormones (for example, oestrogen and progesterone) could have an effect on EOM actions or binocular functions, which may change as participants become menopausal. Assessment of serum oestrogen and progesterone synchronous with the clinical assessments performed in this study could help to clarify the role of these hormones with regard to binocular functions; however, this is beyond the scope of the present study. This issue may not be easily rectifiable as, statistically, women have a longer lifespan. As the numbers were skewed towards women, gross analyses of outcomes for the studied binocular functions were not compared between the genders in this study.

This study was performed with one unmasked examiner, so there was the potential for observer bias, for example, the ages of the participants were not masked from the researcher, which may have had an effect on fusion measurements and endpoint of NPC. The researcher could have unknowingly applied their expectation of the approximate NPC and fusion measurements from prior clinical experience, and then influenced the measurement (for example, slowing down target speed with NPC or giving increased time to see if prism could be overcome). However, the researcher mitigated this bias by following previously published methods (as described in Chapter 3). However, measurement error may have occurred with the measurement of NPC. The NPC was measured using the RAF rule (a mean of three measurements), when a measurement was between two values, the last completed value was recorded (for example, if the NPC was between 6 and 7 cm, it was recorded as 7 cm). This technique may have decreased the mean NPC value slightly; however, it did not overestimate best NPC and, as seen from the data, NPC was only minimally impacted by age. Finally, age cohorts may have been too wide for the older age cohorts; perhaps associations would have been more accurately identified with 5 year rather than 10 year cohort age ranges.

The maximum value obtained from a test (referred to as the ceiling effect in the thesis) may have affected a number of outcomes in this research (for example, positive fusion, NPC, TNO and Titmus). The maximum fusion recorded was 45^{Δ}, with 22 participants (29%) achieving this maximum value; if testing technique allowed larger measurements to be made, these 22 participants may have been able to achieve greater values of fusion. This would have increased the overall mean fusion (particularly positive near fusion) measurement for both the total population and the individual cohorts. Other studies have used two prism bars to allow for measurements greater than 45^{Δ}; however, as discussed in Chapter 1.6.3, the introduction of a second prism bar in front of the fixating eye does induce a degree of measurement error. Whilst, the maximum achievable NPC value with the RAF rule was achieved by 25 participants (32%), the use of a free space measurement with a fixation stick and a ruler would allow measurements < 5 cm. However, the researcher followed the RCOphth guidelines and measured NPC with the RAF rule, and discussed the literature supporting this measurement method in Chapter 1. As concluded in Chapter 4.8, the researcher recommends the use of the Frisby stereotest for the measurement of near stereoacuity; this recommendation is partly based on the evidence that 55 participants (71%) were able to reach the ceiling effect with Titmus stereotest, 2 participants (3%) were able to reach the ceiling effect with TNO stereotest, and no participant in this study reached the ceiling effect using Frisby stereotest (crossed or uncrossed disparity).

Phorias ≤ 15^{Δ} were included, there is the potential that this latent ocular misalignment influenced the fusion measurements. Whilst, no participant had a distance phoria > 10^{Δ}, there were three participants with a near exophoria > 10^{Δ} base in. The researcher does not believe that this impacted the results and the volume of these participants precludes and statistical analysis for significance.

6.5 Presentation of thesis

The researcher was due to present the investigation detailed in chapter 4 at the American Association of Pediatric Ophthalmology and Strabismus conference in Texas, USA in March 2020 (see Appendix 21 for abstract). Unfortunately, as the COVID-19 pandemic gripped the world, the conference was cancelled in the week preceding the conference. The researcher presented a poster at the virtual American Academy of Ophthalmology conference in November 2020 (see Appendix 22 for electronic poster). The researcher was due to present oral presentations of the thesis at the Irish Association of Dispensing Opticians conference on 23rd May 2021 (4

General Optical Council continuous education and training points had been approved), but unfortunately Ireland remains at level 5 COVID-19 restrictions with all such live events prohibited, and the conference now cancelled until May 2022. However, the researcher has been invited to present the research and findings at the Canadian Orthoptic Society conference in Halifax, Canada in June 2022.

6.6 Future work

This may not be a generalizable study; it is unusual for a population ≥ 50 years and especially ≥ 70 years to have 'normal' vision, and to be as healthy as the population selected in this study. Although, it becomes increasing difficult to recruit participants without ocular or general health conditions aged ≥ 70 years, it would be beneficial to expand the study to a greater number of participants aged ≥ 70 years. Further recruitment of healthy individuals with good vision in this age cohort would allow multivariate analyse of factors influencing changes to ocular alignment and motility, thus impacting binocular vision. This data would reduce variability in measurements and better represent the age group (≥ 70 years) more likely to suffer eye disease, including intermittent and/or variable diplopia. Considering the difficulty experienced to identify healthy patients without pre-existing eye disease, a study investigating the same parameters (i.e. binocular functions) in a group of cohorts with set categories of eye disease and set levels of visual acuity could be informative as some studies demonstrate retained stereoacuity in states of reduced vision/VA up to LogMAR 0.7 (229). If a significant difference in binocular functions were not found, this pool of participants could be included in the total dataset, thus expanding the robustness/veracity of the dataset in establishing normative values; this may also help to identify the missing proportion of males from the cohort ≥ 70 years. The findings for ocular alignment found a drift 'inwards' with increasing age, and this could suggest a lateral recti underaction with increasing age; perhaps there is an orthoptic therapy which could be developed to help maintain or improve binocular functions in the older population, as an alternative or adjunct to prism therapy.

Six participants in cohorts 60 - 69 years and 70 - 79 years were stereo-negative for distance despite normal vision, no significant heterophoria and demonstrating near stereoacuity (Titmus range 40 - 140 arcsec, TNO range 60 - 480 arcsec, Frisby range 40 - 110 arcsec). This high number of stereo-negative distance stereoacuity in the 70 - 79 years cohort is a most interesting finding, especially from adding to the literature on driving safety (230). A further study with a larger cohort of participants and multiple

distance stereoacuity tests (e.g. non commercially available psychophysical research tests) would establish if this is a true reflection of the general population aged over 70 years, but direct applications to clinical practice remain difficult. One study, which matched 20 participants for age and driving experience (10 with normal stereoacuity and 10 with absent or defective stereoacuity) found that a lack of stereoacuity affected dynamic driving situations at intermediate distances (231). It is possible, that the participants in cohorts 60 - 69 years and 70 - 79 years did not fully understand the FD2 instructions, but the researcher (as an experienced clinician), feels that this is unlikely, and these results represent a new finding worth investigating in more depth.

All participants in this study had normal vision (≥ 0.10 LogMAR). A study of 30 participants with amblyopia (amblyopia defined as interocular acuity difference of ≥ 0.2 logMAR) found that participants with amblyopia performed significantly slower on bead threading tasks than those without amblyopia (n= 96) (217). As touched on previously, by repeating the present study methods with participants from only older cohorts (50+ years) with differing visual acuity levels as covariant cohorts (for example, differing degree of cataract or AMD, causing a reduction in the visual acuity), we may be able to establish how significant the impact of increasing age plus reducing vision acuity is on stereoacuity. Additionally, repeating all the measurements on participants over 60 years who are known to have conditions which effect ocular alignment and ocular motility (for example, neurological conditions (i.e. diabetes, hypertension, cerebrovascular events, intracranial mass lesions), mechanical conditions (i.e. thyroid eye disease, trauma) and neuromuscular/myogenic conditions (i.e. myasthenia gravis)), but who do not currently have symptoms of diplopia, would provide data for another comparison study.

6.7 Future goals

It would be the endeavour of this researcher to design and perform a randomised clinical trial to establish the effectiveness of orthoptic therapy (for example, fusion exercises, stereograms, convergence exercises) in older adults at preventing age associated changes in binocular functions (i.e. not attributable to acute events, e.g. stroke). This could highlight the utility of the above-mentioned orthoptic exercises therapy, as practiced in a healthy ageing population (i.e., without acquired ocular motility disease, for example, cranial nerve palsies, thyroid eye disease, etc.). Considerable organization and a large population would be required, as follow up would have to be maintained at regular specified intervals over decades (i.e. as

participants graduate from one age bracket to the next). Otherwise, these exercises would look at recovery of lost binocular functions due to age rather than prevention of acquired non-pathological loss of range of binocular functions. If an effect were proven, and shown to be functionally beneficial to patients, this data could be used to develop 'orthoptic exercise aids' either manual or electronic to facilitate the practice of such exercises. This would have commercial and public health implications.

By continuing to expand the population recruited and taking on board the outcomes of a study comparing differing levels of visual acuity in older adults (i.e. ≥ 65 years), the outcomes of this study could be validated, particularly if performed to the same specifications in other jurisdictions with similar and disparate ethnic and racial populations. Such a large dataset could help to establish a definitive database of normative values for the various binocular functions. This would help to establish 'gold standard' of clinical techniques for assessing and recording binocular functions, particularly ocular motility, across all eye care professionals, which can be unanimously used as standardized clinical management guidelines. If the recommendations of BIOS and the RCOphth were used by all orthoptists and optometrists trained and practicing in the UK and Ireland, multicentre data collection and interpretation would help to validate this set of recommended investigations, and allow confident application of these binocular vision techniques in clinical practice. The lack of a standard technique for assessment and documentation of binocular functions internationally leads to an inability to compare epidemiological and therapeutic data between centres, and between differing eye care professionals. Standard nomenclature, as used in other areas of ophthalmology (for example, the early treatment of diabetic retinopathy grading system and LogMAR visual acuity), have allowed collaboration, research, and the development of collective knowledge, for the benefit of patients and the service. Logically, a similar approach to the assessment and documentation of binocular functions would be beneficial. For example, if the BIOS guidelines for the assessment and documentation of eye movements (60), were universally used by all eye care professionals, both nationally and internationally, then it would allow more effective comparison of data between clinical centres, without making excessive unsubstantiated assumptions, and improve the flow of patient referral pathways between professionals working in different clinical locations/settings (for example, the optometrist working in primary care to the hospital based orthoptist). The above action plan for validating this technique would facilitate international and national collaborations, streamline local referral systems, and develop knowledge of binocular functions among all eye care professionals.

6.8 Conclusion

Stereoacuity measured by four commercially available stereotests was affected by age; but this study challenges the view that other aspects of a binocular vision examination (for example motor fusion, ocular alignment and ocular motility) are similarly influenced by increasing age. The data on normative values will provide a baseline from which to compare outcomes in clinical situations.

As a researcher, the process of conducting this doctorate level research project has taught me many new skills, from designing a study, applying for ethical approval from a university and from a hospital, methods for recruiting participants (and adapting when recruitment is challenging), performing two different types of studies, rigidity in gathering the data, performing a statistical analysis and then interpreting the statistical analysis, comparing newly acquired data to pre-existing published studies, interpreting all the data (raw and analysed) to form clinical relevant conclusions.

As a clinician, I have gained a better understanding of binocular vision assessments, developed a greater depth of knowledge on how to interpret clinical data, and, most importantly, improved the standard of care that I provide my patients with the aid of this new clinical information and depth of understanding. I look forward to publishing the thesis and developing further projects to drive progress in the field of binocular vision. I would hope to see independent confirmation of my experimental findings by other researchers. International presentation and publication of this data will drive such confirmation, many of which are planned in the coming months.

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Appendices

Appendix 1 Ethics approval for the preliminary research from Aston University.

Aston University

Aston Triangle

Birmingham

B4 7ET

0121 204 3000

Date: 08/11/2016

Dr Leon Davies

Life and Health Sciences

Study title:	Do binocular functions change as we age?
REC REF:	Ethics application - #922

Confirmation of Ethical Opinion

On behalf of the Committee, I am pleased to confirm a favourable opinion for the amendment to this research:

Addition of a questionnaire exploring professionals views on whether binocular vision changes with age – as described in you e-mail of 7th November 2016

Documents approved

Document	*Version*	*Date*
OD survey questionnaire	1	November 2016

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Nichola Seare

Chair of the University Research Ethics Committee

Appendix 2 PIL questionnaire exploring professionals views on binocular functions

Title of Project: Do binocular functions change as we age?

Project Team: Geraldine McBride, University Hospital Galway and Aston University

Ms. Deirdre Townley, University Hospital Galway and Professor Leon Davies, Aston University

Invitation

You are invited to take part in a doctorate research project. Before you decide, it is important that you understand why the research is being done and what will be involved. This *Participant Information Leaflet* tells you about the purpose, risks and benefits of the research study. If there is anything which is unclear I am happy to answer any questions that you may have. Please take your time to read this information sheet before deciding. You should only consent to participate in this research project when you feel you understand what is being asked of you and if you have sufficient free time to complete the research.

What is the purpose of the study?

The purpose of this questionnaire is to investigate professional opinions on whether there are changes in binocular functions with increasing age. The questionnaire will identify if there is a need for further research to provide normative data on motor fusion, near point of convergence and stereoacuity. Taking part in this study will not have any direct benefits to you, the participant. The data collected will only be accessible by the researcher and supervisors. This study will be completed by September 2019.

Why have I been chosen?

You have been chosen to partake in the study because you have volunteered to complete a questionnaire survey on the association between age and binocular functions. Additionally, you are a registered and practicing optometrist or orthoptist in the UK or Ireland.

Appendix 2 PIL questionnaire exploring professionals views on binocular functions

What will happen to me if I take part?

If you chose to take part in the research project via the online questionnaire you will tick the consent boxes before commencing the survey. If you are completing the paper version of the survey you will be asked to sign and date a consent form (i.e. the top sheet on the paper version of the questionnaire). You will then be asked to complete the questionnaire provided by the research team. The questionnaire will take less than 10 minutes to complete.

What are the possible benefits in taking part in the study?

From participating in this study, the research team will be able to establish eye care professionals' views on the association of increasing age on binocular functions. There will be no monetary compensation for participating in this research project.

What are the possible disadvantages and risks of taking part in the study?

Other than the use of your time there are no known disadvantages or risks.

Do I have to take part?

Participation in this study is voluntary, if you do decide to take part, please retain the *Participant Information Sheet* in case you would like to contact us regarding any issue. If you decide to take part you are still free to withdraw at any time and without giving a reason, and your submitted questionnaire will be excluded.

Expenses and payments

No compensation will be provided for taking part in this study.

Will my taking part in this study be kept confidential?

All work pertaining to this study will be stored in a password protected computer. The information will be stored securely for 5 years following the award of Doctorate in Ophthalmic Science for Geraldine McBride. Confidentiality will be ensured by the recording of only your professional background. No other personal data such as your name or email address will be required.

Appendix 2 PIL questionnaire exploring professionals views on binocular functions

What will happen the results of the research study?

When the project is completed, the information obtained will undergo analysis and conclusions will be made. The information will be used as part of a Doctorate of Ophthalmic Science thesis. The thesis will be published in peer reviewed journals. The confidentiality of individuals will be protected as no personal data (i.e. participant identifiers) is documented. Volunteers can obtain a copy of the published research from the researcher after final submission 1st September 2020.

Who is organizing and funding the research?

The researcher is Geraldine McBride, senior orthoptist, UHG as part of her Doctorate in Ophthalmic Science with Aston University, UK. No funding for this research has been obtained.

What happens if I change my mind during the Study?

You are entitled to change your mind about participating in this study at any time without disadvantage or penalty. You can withdraw by contacting Geraldine McBride on the email address below. All your data will then be destroyed and will not be used in the study.

Who do I contact for more information or if I have concerns?

If you have any queries or would like more information, please do not hesitate to contact the researcher, Geraldine McBride at her email address geraldine.mcbride@hse.ie or you can contact the UHG supervising Consultant Ophthalmic Surgeon Ms Deirdre Townley at her email address deirdre.townley2@hse.ie

Ethical Permission

This questionnaire study has been approved by the Research Ethics Committees of Aston University.

Who do I contact if I wish to make a complaint about the way in which the research is conducted?

If you have any concerns about the way in which the study has been conducted, you can contact the secretary of Aston University Ethics Committee on j.g.walter@aston.ac.uk or telephone 00441212044869.

Appendix 3 Adult participant consent form for the preliminary research assessing the current professional understanding of binocular functions as affected by age

ADULT PARTICIPANT CONSENT FORM

Please read the accompanying participant information sheet before you sign this form

Title of Project: Do binocular functions change with age?

Researcher: Geraldine McBride, senior orthoptist, University Hospital Galway
Supervisors: Deirdre Townley, University Hospital Galway and Leon Davies, Aston University

Date: 21/06/2016 Version Number: 1

		Initial Box
1	I confirm that I have read and understand the information sheet for the above study.	
2	I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.	

_____ _____

Signature Date

Geraldine McBride

_____ _____ _____

Researcher Date Signature

Appendix 4 Ethical approval from the Research Ethics Committee at Aston University.

Aston University

Aston University
Aston Triangle
Birmingham
B4 7ET
0121 204 3000

Date: 21/06/2016

Life and Health Sciences

Dear Dr Leon Davies

Study title:	Do binocular functions change as we age?
REC REF:	Ethics application #922

Confirmation of Ethical Opinion

On behalf of the Committee, I am pleased to confirm a favourable opinion for the above research based on the basis described in the application form, protocol and supporting documentation listed below.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
OD June 2016 Response to Dr Seare		17/06/2016
OD JUNE 2016 Version 4 participant information sheets and consents	4	21/06/2016

With the Committee's best wishes for the success of this project.
Yours sincerely

Dr Nichola Seare
Chair of the University Research Ethics Committee

Appendix 5 Ethical approval from the Research Ethics Committee at UHG.

Saolta
Grúpa Ollscoile Cúram Sláinte
University Health Care Group

Ospidéal na h-Ollscoile, Páirc Mheirlinne
Merlin Park University Hospital
GALWAY UNIVERSITY HOSPITALS

Clinical Research Ethics Committee
Room 59
1st Floor
HR Building
Merlin Park Hospital
Galway.

10th December, 2015.

Ms. Geraldine McBride
Senior Orthoptist
Department of Ophthalmology
Eye OPD
University College Hospital
Galway.

Ref: C.A. 1403 - How do binocular functions change with age?

Dear Ms. McBride,

I have considered the above project, and I wish to confirm that I am happy to grant Chairman's approval to proceed.

Yours sincerely,

p.p. Colette Collins

Dr. Shaun T. O'Keeffe
Chairman Clinical Research Ethics Committee.

Ospidéal na h-Ollscoile, Páirc Mheirlinne, MERLIN PARK UNIVERSITY HOSPITAL,
Galway, Ireland. Tel: 00 353 (0)91 757631

Appendix 6 Advertisement poster for recruiting main study participants.

Do eyes function differently as we age?

There will be a research project undertaken within the Eye OPD by the senior orthoptist Geraldine McBride from September 2016.

The aim of the research is to see whether *how our* eyes function together change as we get older?

Geraldine will be looking to voluntarily recruit people who

1. Aged over 10 years old but younger than 80 years!
2. Have normal eyesight (with or without glasses)
3. Have eyes that are healthy and without any eye diseases

The research will probably only require one visit and will last 45minutes.

You can be a patient, a relative, a member of the public, a hospital volunteer or a hospital staff member.

Following a few questions to ensure you are eligible a range of orthoptic tests looking at your eye movements and how your eyes function together will be undertaken. There is no pain, discomfort or touching of your eyes!! NO eye drops are used!

For an informal chat or further information about participating in the study, contact Geraldine in the Orthoptic room 091-544105, or email Geraldine.mcbride@hse.ie

Appendix 7 Adult Participant information Leaflet- Main study.

Title of Project: Do binocular functions change as we age?

Project Team:

Geraldine McBride, University Hospital Galway and Aston University

Deirdre Townley, University Hospital Galway

Leon Davies, Aston University

Invitation

You are invited to take part in a doctorate research project. Before you decide, it is important that you understand why the research is being done and what will be involved. This *Participant Information Leaflet* tells you about the purpose, risks and benefits of the research study. If there is anything which is unclear I am happy to answer any questions that you may have. Please take your time to read this information sheet before deciding. You should only consent to participate in this research project when you feel you understand what is being asked of you and if you have sufficient free time to complete the research.

What is the purpose of the study?

The purpose of this study is to investigate whether there are changes in how the eyes function 'as a team' (known as binocular functions) as we age. This research will further our understanding on eye movements and eye functions but will not have any direct benefits to you the participant. The data collected will only be accessible by the researcher and supervisors. This study will be completed by September 2019.

Why have I been chosen?

You have been chosen to partake in the study because you have volunteered to undergo an extended orthoptic assessment with the UHG eye department's senior orthoptist. There are certain criteria for enrolment in this research and Geraldine McBride will be able to identify your suitability with some basic initial tests, if you are eligible then with your consent a full extended orthoptic examination will be performed.

Appendix 7 Adult Participant information Leaflet- Main study.

What will happen to me if I take part?

If you chose to take part in the research project you will be asked to sign and date a consent form. You will be asked to complete an orthoptic assessment with Geraldine McBride. Following a period of data analysis, you may also be asked to participate in one further short assessment. The purpose of the second visit will be to confirm repeatability of the data. The orthoptic assessment will take 45 minutes to complete and will take place in the eye clinic at UHG, at a mutually agreeable date.

What are the possible benefits in taking part in the study?

From participating in this study, the research team will be able to establish normative data of binocular functions, per decade of life, depending on which test the clinician chooses to use. There will be no monetary compensation for participating in this research project.

What are the possible disadvantages and risks of taking part in the study?

Other than the use of your time there are no known disadvantages or risks.

Do I have to take part?

Participation in this study is voluntary, if you do decide to take part, please retain the *Participant Information Sheet* in case you would like to contact us regarding any issue. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect your care/ your relative's care within the ophthalmology department at UHG.

Expenses and payments

There are no expenses available for travel, meals, child-care, compensation for loss of earnings etc.

Will my taking part in this study be kept confidential?

All work pertaining to this study will be stored in a password protected computer. The information will be stored securely for 5 years following the award of Doctorate in Ophthalmic Science for Geraldine McBride. Confidentiality will be ensured by the recording of only your age; no other personal data such as your name or address will be required.

Appendix 7 Adult Participant information Leaflet- Main study.

What will happen the results of the research study?

When the project is completed, the information obtained will undergo analysis and conclusions will be drawn. The information will be used as a Doctorate of Ophthalmic Science thesis and published in a peer reviewed Journal. The confidentiality of individuals will be protected as no personal data is documented. Volunteers can obtain a copy of the published research from the researcher after final submission 1st September 2020.

Who is organizing and funding the research?

The researcher is Geraldine McBride, senior orthoptist, UHG as part of her Doctorate in Ophthalmic Science with Aston University, UK. No funding for this research has been obtained.

What happens if I change my mind during the Study?

You are entitled to change your mind about participating in this study at any time without disadvantage or penalty. You can withdraw by contacting me on the email address below. All your data will then be destroyed and will not be used in the study.

Who do I contact for more information or if I have concerns?

If you have any queries or would like more information, please do not hesitate to contact the researcher, Geraldine McBride at her email address geraldine.mcbride@hse.ie or you can contact the UHG supervising Consultant Ophthalmic Surgeon Ms Deirdre Townley at her email address deirdre.townley2@hse.ie

Ethical Permission

This study has been given a favourable opinion from the Research Ethics Committees of Aston University and University Hospital Galway.

Who do I contact if I wish to make a complaint about the way in which the research is conducted?

If you have any concerns about the way in which the study has been conducted, you can contact the secretary of Aston University Ethics Committee on j.g.walter@aston.ac.uk or telephone 00441212044869.

Appendix 8 Parent Information Leaflet (Child aged 10 – 16 years).

Title of Project: Do binocular functions change as we age?

Project Team: Geraldine McBride, University Hospital Galway and Aston University, Deirdre Townley, University Hospital Galway and Leon Davies, Aston University

Invitation

Children over 10 years old are being invited to take part in a doctorate research project. Before you decide whether you wish your child to be involved, it is important that you understand why the research is being done and what will be involved. This *Participant Information Leaflet for parents* tells you about the purpose, risks and benefits of the research study. If there is anything which is unclear I am happy to answer any questions that you may have. Please take your time to read this information sheet before deciding. You should only consent to participate in this research project when you feel you understand what is being asked of your child and if you have sufficient free time to bring your child to complete the research. Your consent will be required before undertaking the initial screening tests which identify whether your child will be a suitable participant.

What is the purpose of the study?

The purpose of this study is to investigate whether there are changes in how the eyes function 'as a team' as we age. This research will further our understanding on eye movements and eye functions but will not have any direct benefits to you or your child. The data collected will only be accessible by the researcher and supervisors. This study will be completed by September 2019.

Why have my child been chosen?

Your child has been chosen to partake in the study because you are happy to volunteer them to undergo an extended orthoptic assessment with the UHG eye department's senior orthoptist. There are certain criteria for enrolment in this research and Geraldine McBride will be able to identify your child's suitability with some basic initial tests, for example a test of their distance vision. If your child is eligible, and with your continued consent, a full extended orthoptic examination will be performed. If your child does not match all the enrolment requirements, no further assessment will be performed. If your child is not suitable to participate, no data about your child will be stored, with the exception of your signed consent form.

Appendix 8 Parent Information Sheet (Child aged 10 – 16 years)

What will happen to me if I take part?

If you chose to consent to your child participating to take part in the research project you will be asked to sign and date a consent form. Your child will be asked to complete an orthoptic assessment with Geraldine McBride.

The orthoptic assessment will include:

1. A measurement of your child's vision (near and distance).
2. A measurement of your child's current glasses/ glasses requirement.
3. An assessment of the position of your child's eyes (i.e. checking for a squint).
4. An observation of your child's eye movements, including the ability to move them together to view objects close to their nose.
5. A measurement of the strength of your child's muscles using prisms. Prisms bend the light going into your child's eyes forcing the muscles to work, this can cause temporary blurring and diplopia whilst prism is in front of the eye. This is relieved immediately following prism removal.
6. An assessment of your child's ability to see 3D using four different stereoacuity tests.

Following a period of data analysis, you may also be asked to participate in one further short assessment. The purpose of the second visit will be to confirm repeatability of data.

The orthoptic assessment will take 45 minutes to complete and will take place in the eye clinic at UHG, at a mutually agreeable date.

What are the possible benefits in taking part in the study?

This research will not benefit you or your child. However, by participating in this study, the researcher will be able to establish what the normal measurements of binocular functions are as we age. There will be no monetary compensation for participating in this research project.

Appendix 8 Parent Information Leaflet (Child aged 10 – 16 years).

What are the possible disadvantages and risks of taking part in the study?

Other than the use of you and your child's time there are no known disadvantages or risks.

Do I have to take part?

Participation in this study is voluntary, if you do decide to allow your child to take part, please retain the *Participant Information Sheet* in case you would like to contact us regarding any issue. If you decide to consent to your child taking part you are still free to withdraw your child at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect current/future care or your child's current/future care within the ophthalmology department at UHG.

Expenses and payments

There are no expenses available for travel, meals, child-care, compensation for loss of earnings etc.

Will my child's taking part in this study be kept confidential?

All work pertaining to this study will be stored in a password protected computer. The information will be stored securely for 5 years following the award of Doctorate of Ophthalmic Science to Geraldine McBride. Confidentiality will be ensured by the recording of only your child's age. No other personal data such as your name, your child's name or your address will be required.

What will happen the results of the research study?

When the project is completed, the information obtained will undergo analysis and conclusions will be drawn. The information will be used as a Doctorate of Ophthalmic Science thesis and published in a peer reviewed Journal. The confidentiality of all individuals will be protected as no personal data is documented. Volunteers can obtain a copy of the published research from the researcher after final submission 1st September 2020.

Who is organizing and funding the research?

The researcher is Geraldine McBride, senior orthoptist, UHG as part of her Doctorate in Ophthalmic Science with Aston University, UK. No funding for this research has been obtained.

Appendix 8 Parent Information Leaflet (Child aged 10 – 16 years).

What happens if I change my mind during the Study?

You are entitled to change your mind about allowing your child to participate in this study at any time without disadvantage or penalty. You can withdraw your child by contacting me on the email address below. All your data will then be destroyed and will not be used in the study.

Who do I contact for more information or if I have concerns?

If you have any queried or would like more information, please do not hesitate to contact the researcher, Geraldine McBride at her email address geraldine.mcbride@hse.ie or you can contact the UHG supervising Consultant Ophthalmic Surgeon Ms Deirdre Townley at her email address deirdre.townley2@hse.ie

Ethical Permission

This study has been given a favourable opinion from the Research Ethics Committees of Aston University and University Hospital Galway.

Who do I contact if I wish to make a complaint about the way in which the research is conducted?

If you have any concerns about the way in which the study has been conducted, you can contact the secretary of Aston University Ethics Committee on j.g.walter@aston.ac.uk or telephone 00441212044869.

Appendix 9 Child Participant Information Leaflet.

Title of Project: Do binocular functions change as we age?

Invitation

Would you like to take part in a study which looks at how well your eyes work together as a team.

What is the purpose of the study?

This eye test will show us how well your eyes work as a team and compare them to older people.

Why have I been chosen?

I want to see HOW WELL your eyes work together. I will use this information to help me with my university work.

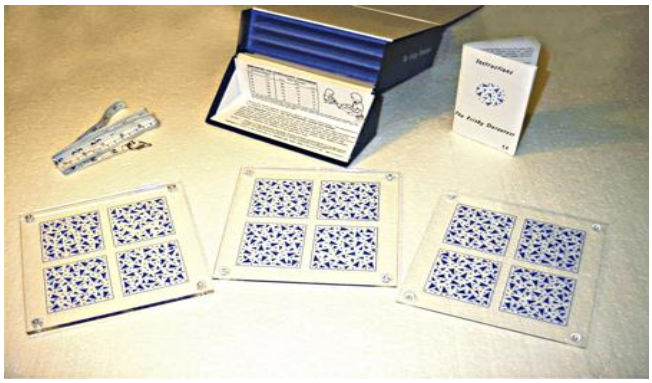
What will happen during the test?

You will come to the eye clinic at the hospital. You will be asked to do some games with Geraldine, such as following a light and reading letters on the vision chart. No eye drops, medicines or needles will be used. These are pictures of most of the games that we will be doing:

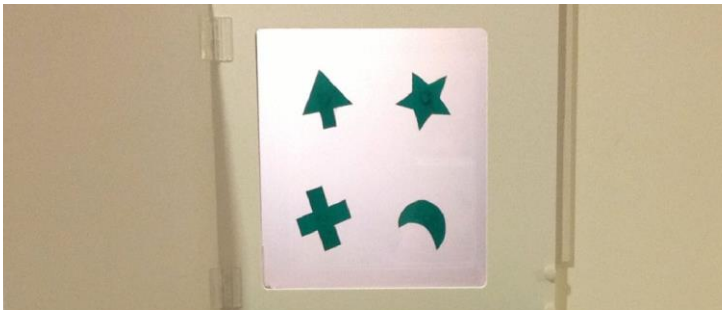
1. You will read letters from the vision chart which is far away (like the whiteboard in school) and up close (like your school books).

Appendix 9 Child Participant Information Leaflet.

2. You will be asked to find the circle inside one of the four boxes.



3. You will be asked which shape is coming towards you



4. You will be asked to point to where is the second butterfly is hiding and then find the missing piece in a circle whilst wearing the coloured glasses

5. You will be asked to point to which circle in the box of four circles is coming towards you whilst wearing a special sunglasses.

Do I have to take part?

No, this is only if you want to. Neither Geraldine nor your parent/guardian will make you do the eye tests. If you decide to withdraw from the study at any point, you do not have to be part of the study.

Will my taking part in this study be kept confidential?

Yes apart from your age and how your eyes work together I don't record anything else about you.

What happens if I change my mind during the Study?

If you decide you don't want to be part of the study, tell your parent/guardian, and they will contact me and let me know, you changed your mind and I won't use any of the answers or measurements which you gave me. It's ok to change your mind about being part of the study.

Appendix 10 Adult participant consent form- main study.

ADULT PARTICIPANT CONSENT FORM

Please read the accompanying participant information sheet before you sign this form

Title of Project: Do binocular functions change with age?

Researcher: Geraldine McBride, senior orthoptist, University Hospital Galway

Supervisors: Deirdre Townley, University Hospital Galway and Leon Davies, Aston University

Name: Date: 21/06/2016 Version Number: 4

		Initial Box
1	I confirm that I have read and understand the information sheet for the above study.	
2	I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	

Name of participant	Date	Signature
Geraldine McBride		
Researcher	Date	Signature

Appendix 11 Parent/ Guardian consent form.

PARENT/GUARDIAN CONSENT FORM

Please read the accompanying participant information sheet before you sign this form

Title of Project: Do binocular functions change with age?

Researcher: Geraldine McBride, senior orthoptist, University Hospital Galway
Supervisors: Deirdre Townley, University Hospital Galway and Leon Davies, Aston University

Date: 21/06/2016 Version Number: 4

Name of participant

		Initial Box
1	I confirm that I have read and understand the information sheet for the above study.	
2	I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
3	I understand that my child's participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
4	I understand that my child's participation for this study may be required on a second visit.	

_____ _____ _____

Name of Person consenting to the participation in the research Geraldine McBride

Date

Signature

_____ _____ _____

Researcher

Date

Signature

Appendix 12 Child assent form.

Child/ young person assent form

Title of Project: Do binocular functions change with age?

Name: **DOB:**

Date: 21/06/2016 Version Number: 4

Child to circle all they agree with

Have you read (or had read to you) information about this project?	Yes/ No
Has somebody else explained this project to you?	Yes/ No
Do you understand what this project is about?	Yes/ No
Have you asked the questions you want?	Yes/ No
Have you had your questions answered in a way you understand?	Yes/ No
Do you understand it is ok to stop taking part at any time?	Yes/ No
Do you understand that it is ok to not take part in this project?	Yes/ No
Are you happy to begin this study?	Yes/No

If any answers are “no” and you don’t want to take part, do not sign your name.

If you do want to take part in this study, please write your name and write today’s date.

Your name **Date**

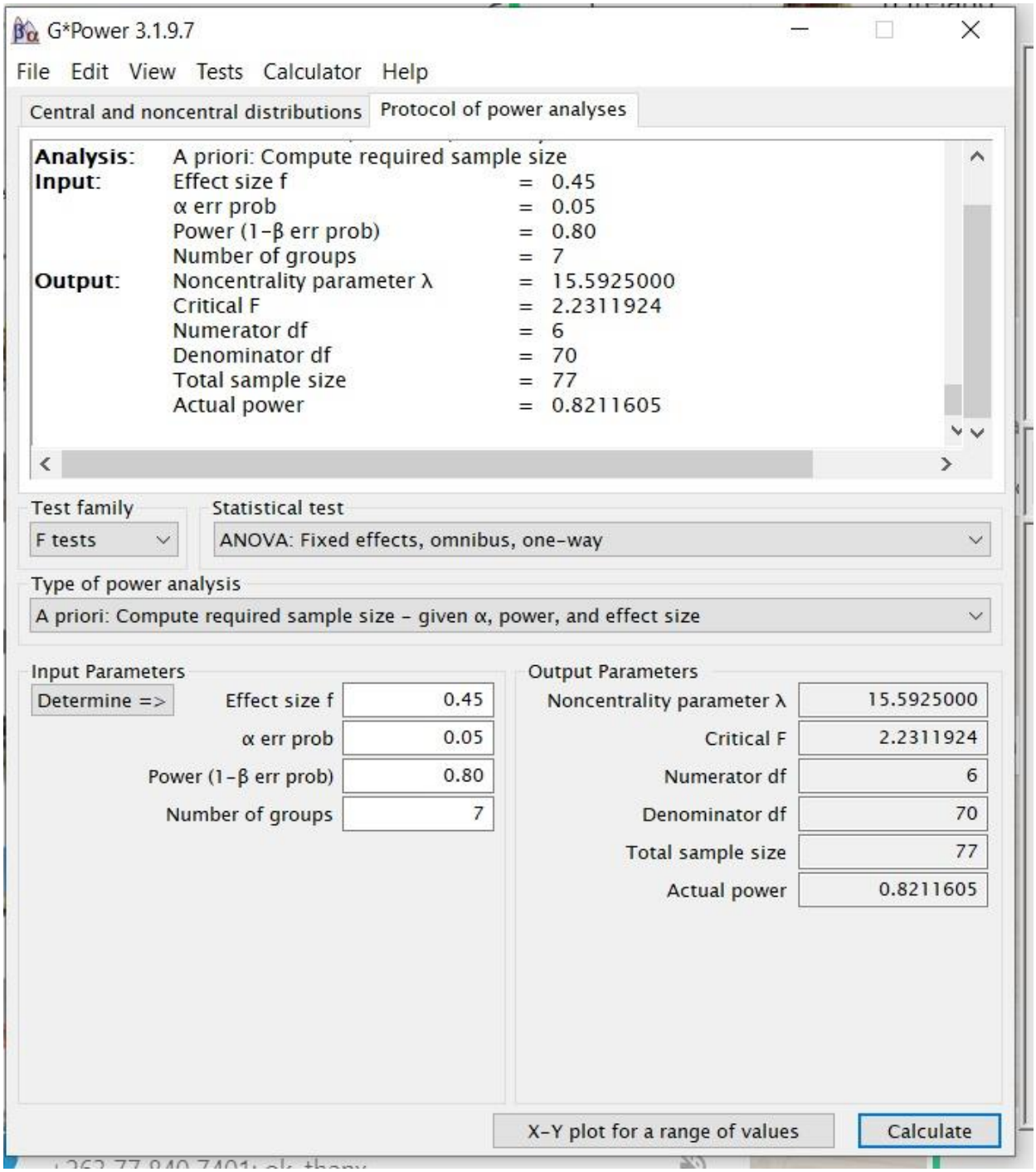
The researcher who explained this project to you needs to sign here too:

Researcher Signature **Date**

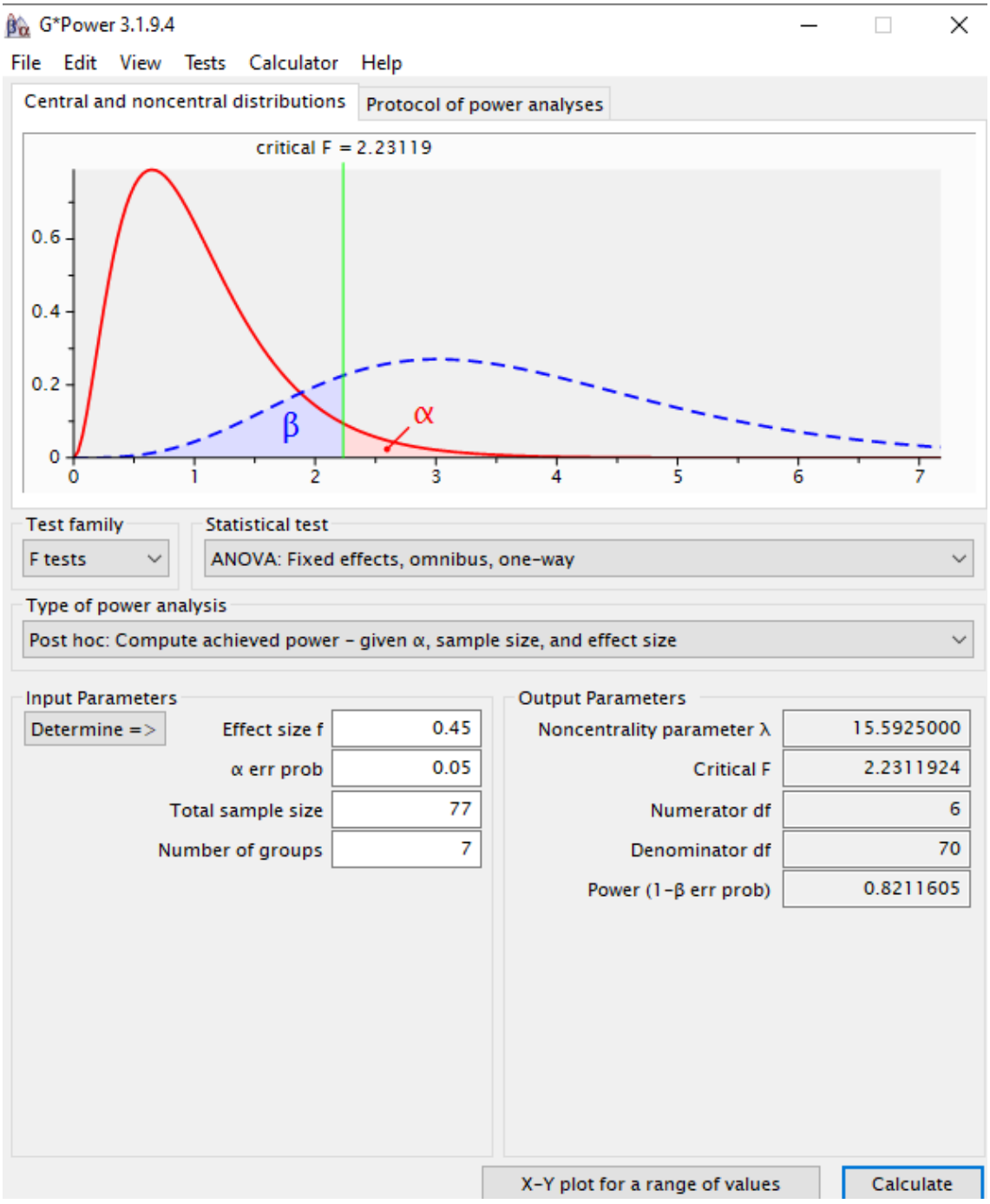
Geraldine McBride, Researcher

Thank you for helping!!

Appendix 13 Screenshot from G*Power sample size calculation and G*Power post-hoc power calculation



Appendix 13 Screenshot from G*Power sample size calculation and G*Power post-hoc power calculation



Appendix 14 Data collection record.

Research Project: Do binocular functions change as we age?

Researcher: Geraldine McBride **Consent form** ☐

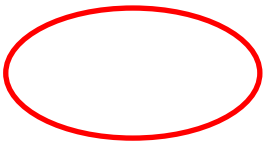
Participant Initials: ***Age:*** ***Participant No:***

Glasses Prescription		R			Add	
		L				
Auto-refraction		R		L		
POH:						
GH:					FH:	
Vision		R		L		
Visual Acuity		R		L		
Near VA		R		L		BEO
Cover Test	cgls	N			PCT	cgls N
		D				D
	sgls	N				sgls N
		D				D

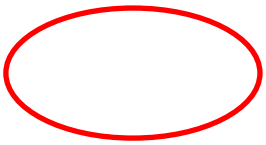
Appendix 14 Data collection record.

Participant Initials: ***Age:*** ***Participant No:***

OM



Right



Left

☐ Ductions = Versions

☐ Smooth ☐ Jerky

☐ End point nystagmus

☐ Lid position changes

☐ Globe position changes

RAF NPC

Prism Fusion Range	Break	N	BI	BO
	Recovery	N	BI	BO
	Break	D	BI	BO
	Recovery	D	BI	BO
	Vertical (Total)			

Titmus

TNO

Frisby Uncrossed Crossed

FD2 Binocular Monocular

Appendix 15 Participant current and previous general health details and ophthalmic family history.

Information regarding current and previous general health:

- One participant was taking an anti-depressant medication.
- One participant was taking aspirin on alternative days (participant was unclear as to reason).
- One participant was taking irritable bowel syndrome medication.
- One participant was taking a blood pressure reducing medication.
- Two participants use anti-histamine during summer months.
- Three patients had a history of previous surgery to remove cancer, all of whom were in remission and on no treatment for cancer (location of cancer: bowel, breast and skin).
- One participant had a history of vertigo, which required pharmacology treatment during historical vertigo episodes.
- One participant had regular migraines pre-menopause (now aged 75), same participant had unilateral deafness from a childhood ear injury but no vestibular imbalance.

Information regarding ophthalmic family history

With a first degree relative was considered for a child, sibling or parent of the participant, and a second degree relative was considered for a cousin or grandparent of the participant.

- Eight x 1st degree relative having a refractive error which required spectacles (six for myopia, one for astigmatism and one for childhood hypermetropia).
- Two x 1st degree relative with strabismus.
- One x 1st degree relative with amblyopia (same relative was also described as having hypermetropia and strabismus).
- One x 2nd degree relative with amblyopia.
- Four x 1st degree relative with age related macular degeneration (AMD) (three wet and one dry).
- One x 2nd degree relative with dry AMD.
- Eight x 1st degree relative having glaucoma (six were mother).

Appendix 16: Descriptive Statistics for Chapter 4

Titmus Stereotest

Age (years)	Mean	N	Std. Deviation	Median	Minimum	Maximum
10 - 19	45.45	11	9.342	40.00	40	60
20 - 29	48.18	11	18.340	40.00	40	100
30 - 39	40.00	11	.000	40.00	40	40
40 - 49	45.45	11	12.933	40.00	40	80
50 - 59	49.09	11	16.404	40.00	40	80
60 - 69	49.09	11	15.783	40.00	40	80
70 - 79	69.09	11	38.067	50.00	40	140
Total	49.48	77	20.255	40.00	40	140

TNO Stereotest

Age (years)	Mean	N	Std. Deviation	Median	Minimum	Maximum
10 – 19	70.91	11	62.961	60.00	15	240
20 – 29	95.45	11	58.200	60.00	30	240
30 – 39	43.64	11	15.667	30.00	30	60
40 – 49	114.55	11	124.287	60.00	60	480
50 – 59	79.09	11	33.602	60.00	30	120
60 – 69	125.45	11	129.951	60.00	60	480
70 – 79	130.91	11	58.899	120.00	60	240
Total	94.29	77	82.081	60.00	15	480

Frisby Stereotest (UNCROSSED)

Age (years)	Mean	N	Std. Deviation	Median	Minimum	Maximum
10 – 19	48.18	11	39.766	30.00	20	150
20 – 29	25.91	11	19.598	20.00	20	85
30 – 39	20.00	11	.000	20.00	20	20
40 – 49	25.45	11	12.933	20.00	20	55
50 – 59	37.73	11	22.401	30.00	20	85
60 – 69	71.82	11	77.533	55.00	20	300
70 – 79	83.18	11	35.936	85.00	30	150
Total	44.61	77	42.780	20.00	20	300

Frisby Stereotest (CROSSED)

Age (years)	Mean	N	Std. Deviation	Median	Minimum	Maximum
10 – 19	44.55	11	38.500	30.00	20	150
20 – 29	31.82	11	39.196	20.00	20	150
30 – 39	20.00	11	.000	20.00	20	20
40 – 49	27.27	11	13.484	20.00	20	55
50 – 59	37.27	11	26.397	20.00	20	85
60 – 69	55.91	11	42.768	40.00	20	150
70 – 79	89.09	11	39.358	85.00	40	150
Total	43.70	77	37.735	20.00	20	150

FD2 stereotest

Age (years)	Mean	N	Std. Deviation	Median	Minimum	Maximum
10 – 19	21.36	11	6.742	20.00	10	30
20 – 29	19.55	11	11.716	20.00	5	45
30 – 39	20.00	11	5.916	20.00	10	30
40 – 49	17.73	11	9.318	20.00	5	30
50 – 59	24.55	11	7.891	25.00	15	40
60 – 69	28.50	10	12.483	27.50	10	50
70 – 79	35.83	6	17.440	42.50	10	50
Total	23.03	71	11.003	20.00	5	50

Appendix 17 SPSS outputs for Chapter 4

SPSS output for Titmus against ungrouped age (Ordinal regression)

Parameter Estimates

Parameter		B	Std. Error	95% Wald Confidence Interval Lower	95% Wald Confidence Interval Upper	Hypothesis Test Wald Chi-Square	Hypothesis Test df	Hypothesis Test Sig.
Threshold	[Titmus=40]	2.362	.7250	.941	3.783	10.613	1	.001
	[Titmus =50]	2.722	.7414	1.269	4.175	13.479	1	.000
	[Titmus =60]	3.388	.7794	1.860	4.915	18.892	1	.000
	[Titmus =80]	4.732	.9317	2.906	6.558	25.799	1	.000
	[Titmus =100]	5.159	1.0203	3.159	7.159	25.564	1	.000
AGE		.031	.0136	.004	.058	5.120	1	.024
(Scale)		1[a]						

Dependent Variable: WORTHS

Model: (Threshold), AGE

a. Fixed at the displayed value.

Appendix 17 SPSS outputs for Chapter 4

SPSS output for Titmus against cohort ages (Ordinal regression)

Parameter Estimates

Parameter		B	Std. Error	95% Wald Confidence Interval Lower	95% Wald Confidence Interval Upper	Hypothesis Test Wald Chi-Square	Hypothesis Test df	Hypothesis Test Sig.
Threshold	[Titmus=40]	-.562	.5741	-1.687	.563	.957	1	.328
	[Titmus =50]	-.172	.5726	-1.294	.950	.090	1	.764
	[Titmus =60]	.523	.5902	-.634	1.680	.784	1	.376
	[Titmus =80]	1.906	.7385	.458	3.353	6.658	1	.010
	[Titmus =100]	2.346	.8376	.705	3.988	7.848	1	.005
[Age = 10-19 years]		-1.597	.8677	-3.298	.104	3.387	1	.066
[Age = 20-29 years]		-1.553	.8753	-3.268	.163	3.147	1	.076
[Age = 30-39 years]		-21.981	13499.9443	-26481.385	26437.424	.000	1	.999
[Age = 40-49 years]		-2.020	.9632	-3.908	-.132	4.398	1	.036
[Age = 50-59 years]		-1.442	.8765	-3.160	.275	2.708	1	.100
[Age = 60-69 years]		-1.210	.8255	-2.828	.408	2.147	1	.143
[Age = 70-79 years]		0[a]	.	.	.	.	.	.
(Scale)		1[b]						

Dependent Variable: Titmus

Model: (Threshold), Age cohort

a. Set to zero because this parameter is redundant.

b. Fixed at the displayed value.

Appendix 17 SPSS outputs for Chapter 4

SPSS output for TNO against ungrouped age (Ordinal regression)

Parameter Estimates

Parameter		B	Std. Error	95% Wald Confidence Interval Lower	95% Wald Confidence Interval Upper	Hypothesis Test Wald Chi-Square	Hypothesis Test Df	Hypothesis Test Sig.
Threshold	[TNO=15]	-2.192	.8408	-3.840	-.544	6.797	1	.009
	[TNO=30]	-.295	.5671	-1.407	.816	.271	1	.603
	[TNO=60]	2.301	.6320	1.062	3.540	13.257	1	.000
	[TNO=120]	4.166	.7546	2.687	5.645	30.486	1	.000
	[TNO=240]	5.507	.9680	3.610	7.404	32.370	1	.000
AGE		.037	.0118	.013	.060	9.548	1	.002
(Scale)		1[a]						

Dependent Variable: TNO

Model: (Threshold), AGE

a. Fixed at the displayed value.

Appendix 17 SPSS outputs for Chapter 4

SPSS output for TNO against cohort ages (Ordinal regression)

Parameter Estimates

Parameter		B	Std. Error	95% Wald Confidence Interval Lower	95% Wald Confidence Interval Upper	Hypothesis Test Wald Chi-Square	Hypothesis Test df	Hypothesis Test Sig.
Threshold	[TNO=15]	-6.368	1.0360	-8.398	-4.337	37.781	1	.000
	[TNO=30]	-4.247	.7702	-5.756	-2.737	30.408	1	.000
	[TNO=60]	-.978	.5630	-2.081	.126	3.017	1	.082
	[TNO=120]	1.055	.5611	-.044	2.155	3.538	1	.060
	[TNO=240]	2.413	.8129	.820	4.006	8.810	1	.003
[Age = 10-19 years]		-3.093	.9547	-4.964	-1.222	10.499	1	.001
[Age = 20-29 years]		-1.277	.7996	-2.844	.290	2.550	1	.110
[Age = 30-39 years]		-4.259	.9281	-6.077	-2.440	21.056	1	.000
[Age = 40-49 years]		-1.345	.7983	-2.910	.220	2.839	1	.092
[Age = 50-59 years]		-1.697	.8086	-3.282	-.112	4.403	1	.036
[Age = 60-69 years]		-1.208	.8090	-2.793	.378	2.229	1	.135
[Age = 70-79 years]		0[a]	.	.	.	.	.	.
(Scale)		1[b]						

Dependent Variable: TNO Model: (Threshold), Age cohort

a. Set to zero because this parameter is redundant.

b. Fixed at the displayed value.

Appendix 17 SPSS outputs for Chapter 4

SPSS outputs for Frisby (uncrossed) against cohort ages (Kruskal Wallis test)

Ranks

	Age (years)	N	Mean Rank
FRISBY UNCROSSED	10 – 19	11	43.73
	20 – 29	11	24.82
	30 – 39	11	20.50
	40 – 49	11	26.95
	50 – 59	11	39.41
	60 – 69	11	53.59
	70 – 79	11	64.00
	Total	77	

Test Statistics[a,b]

	FRISBY UNCROSSED
Kruskal-Wallis H	39.762
Df	6
Asymp. Sig.	.000

a. Kruskal Wallis Test

b. Grouping Variable: Age cohort

SPSS output for Frisby (uncrossed) against ungrouped age (simple linear regression)

Parameter Estimates

Dependent Variable: FRISBY UNCROSSED

					95% Confidence Interval	
Parameter	B	Std. Error	t	Sig.	Lower Bound	Upper Bound
Intercept	9.368	11.385	.823	.413	-13.313	32.048
AGE	.791	.234	3.380	.001	.325	1.257

Appendix 17 SPSS outputs for Chapter 4

SPSS outputs for Frisby (crossed) against cohort ages (Kruskal Wallis test)

Ranks

	Age (years)	N	Mean Rank
FRISBY CROSSED	10 – 19	11	41.86
	20 – 29	11	27.27
	30 – 39	11	22.50
	40 – 49	11	31.23
	50 – 59	11	38.41
	60 – 69	11	47.00
	70 – 79	11	64.73
	Total	77	

Test Statistics[a,b]

	FRISBY CROSSED
Kruskal-Wallis H	32.623
Df	6
Asymp. Sig.	.000

a. Kruskal Wallis Test

b. Grouping Variable: Age cohort

SPSS output for Frisby (crossed) against ungrouped age (simple linear regression)

Parameter Estimates

Dependent Variable: FRISBY CROSSED

					95% Confidence Interval	
Parameter	B	Std. Error	T	Sig.	Lower Bound	Upper Bound
Intercept	11.505	9.987	1.152	.253	-8.390	31.400
AGE	.722	.205	3.520	.001	.314	1.131

Appendix 17 SPSS outputs for Chapter 4

SPSS output for Frisby (uncrossed) cohort 30 - 39 years against other cohorts (Ordinal regression)

		Estimate	Std. Error	P-value
1	(Constant)	20.000	7.448	.009
	Age = 10 – 19 years	28.182	10.532	.009
	Age = 20 – 29 years	5.909	10.532	.577
	Age = 40 – 49 years	5.455	10.532	.606
	Age = 50 – 59 years	17.727	10.532	.097
	Age = 60 – 69 years	29.000	10.793	.009
	Age =70 – 79 years	63.182	10.532	.000

SPSS output for Frisby (crossed) cohort 30 - 39 years against other cohorts (Ordinal regression)

		Unstandardized Coefficients		
Model		Estimate	Std. Error	p-value
1	(Constant)	20.000	9.720	.043
	Age = 10 – 19 years	24.545	13.747	.079
	Age = 20 – 29 years	11.818	13.747	.393
	Age = 40 – 49 years	7.273	13.747	.598
	Age = 50 – 59 years	17.273	13.747	.213
	Age = 60 – 69 years	35.909	13.747	.011
	Age = 70 – 79 years	69.091	13.747	.000

Appendix 17 SPSS outputs for Chapter 4

SPSS output for FD2 against ungrouped age (simple linear regression)

Parameter Estimates

Dependent Variable: FD2

Parameter	B	Std. Error	T	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Intercept	14.119	3.064	4.608	.000	8.006	20.232
AGE	.211	.066	3.174	.002	.078	.344

SPSS output for FD2 cohort 40 - 49 years against other cohorts (Ordinal regression)

Model		Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	T	Sig.
1	(Constant)	17.727	3.060	5.793	.000
	Age = 10 – 19 years	3.636	4.327	.840	.404
	Age = 20 – 29 years	1.818	4.327	.420	.676
	Age = 30 – 39 years	2.273	4.327	.525	.601
	Age = 50 – 59 years	6.818	4.327	1.576	.120
	Age = 60 – 69 years	10.773	4.434	2.429	.018
	Age = 70 – 79 years	18.106	5.151	3.515	.001

Appendix 17 SPSS outputs for Chapter 4

SPSS output for FD2 pairwise comparison:

(I) Age (years)	(J) Age (years)	Mean Difference (I-J)	Std. Error	P-value
10 – 19	20 – 29	1.818	4.327	.676
	30 – 39	1.364	4.327	.754
	40 – 49	3.636	4.327	.404
	50 – 59	-3.182	4.327	.465
	60 – 69	-7.136	4.434	.112
	70 – 79	-14.470*	5.151	.007
20 – 29	10 – 19	-1.818	4.327	.676
	30 – 39	-.455	4.327	.917
	40 – 49	1.818	4.327	.676
	50 – 59	-5.000	4.327	.252
	60 – 69	-8.955*	4.434	.048
	70 – 79	-16.288*	5.151	.002
30 – 39	10 – 19	-1.364	4.327	.754
	20 – 29	.455	4.327	.917
	40 – 49	2.273	4.327	.601
	50 – 59	-4.545	4.327	.297
	60 – 69	-8.500	4.434	.060
	70 – 79	-15.833*	5.151	.003
40 – 49	10 – 19	-3.636	4.327	.404
	20 – 29	-1.818	4.327	.676
	30 – 39	-2.273	4.327	.601
	50 – 59	-6.818	4.327	.120
	60 – 69	-10.773*	4.434	.018
	70 – 79	-18.106*	5.151	.001
50 – 59	10 – 19	3.182	4.327	.465
	20 – 29	5.000	4.327	.252
	30 – 39	4.545	4.327	.297
	40 – 49	6.818	4.327	.120
	60 – 69	-3.955	4.434	.376

	70 – 79	-11.288*	5.151	.032
60 – 69	10 – 19	7.136	4.434	.112
	20 – 29	8.955*	4.434	.048
	30 – 39	8.500	4.434	.060
	40 - 49	10.773*	4.434	.018
	50 - 59	3.955	4.434	.376
	70 - 79	-7.333	5.241	.167
70 – 79	10 - 19	14.470*	5.151	.007
	20 - 29	16.288*	5.151	.002
	30 - 39	15.833*	5.151	.003
	40 - 49	18.106*	5.151	.001
	50 - 59	11.288*	5.151	.032
	60 - 69	7.333	5.241	.167

SPSS output for FD2 Kolmogorov-Smirnov[a] Shapiro-Wilk and tests for normality:

Tests of Normality

	Age	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	(years)	Statistic	Df	p-value	Statistic	Df	p-value
FD2	10 – 19	.217	11	.157	.905	11	.211
	20 – 29	.139	11	.200*	.937	11	.484
	30 – 39	.165	11	.200*	.947	11	.609
	40 – 49	.160	11	.200*	.914	11	.275
	50 – 59	.160	11	.200*	.909	11	.239
	60 – 69	.152	10	.200*	.968	10	.872
	70 – 79	.292	6	.121	.827	6	.101

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Appendix 17 SPSS outputs for Chapter 4

SPSS output for FD2 test for variance within cohorts and between cohorts (ANOVA)

FD2

	Sum of Squares	Df	Mean Square	F	p-value
Between Groups	1882.429	6	313.738	3.046	.011
Within Groups	6591.515	64	102.992		
Total	8473.944	70			

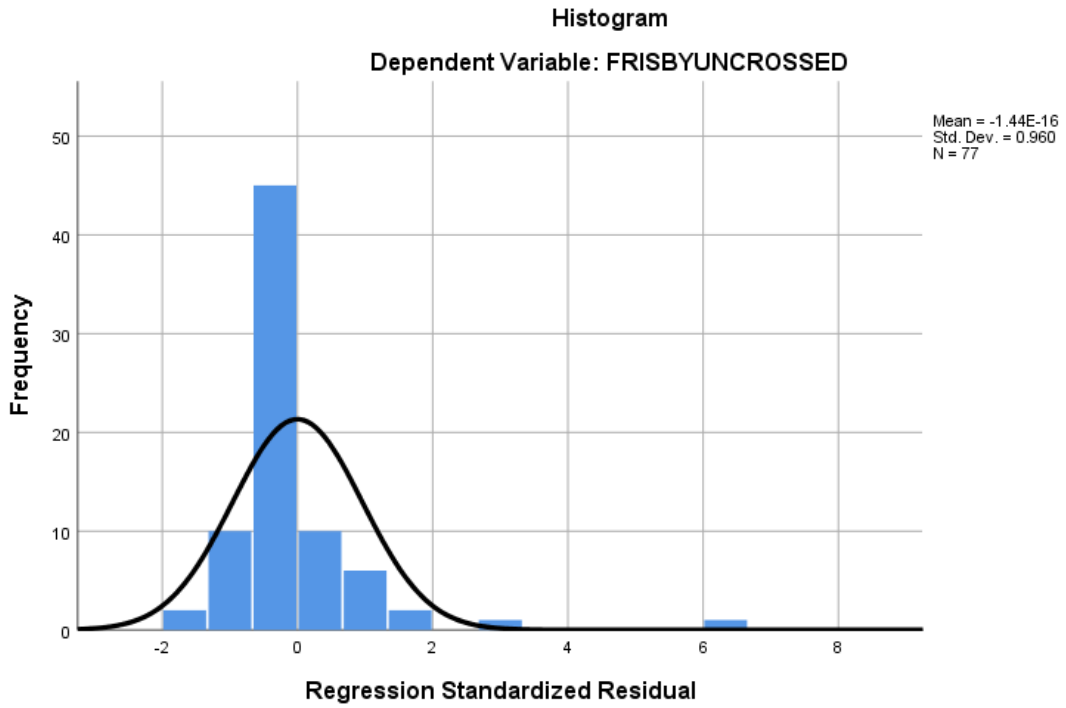
SPSS output for FD2 and Frisby against ungrouped age (Pearson Correlation coefficient)

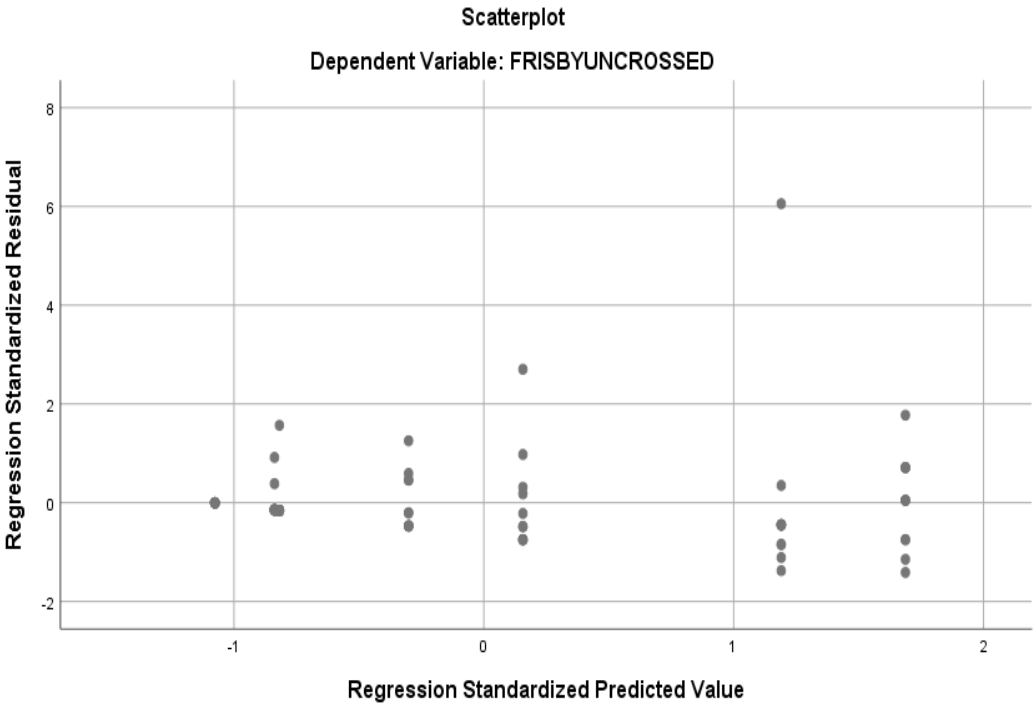
Correlations

		AGE	FRISBY UNCROSSED	FRISBY CROSSED	FD2
AGE	Pearson Correlation	1	.364**	.377**	.357**
	Sig. (2-tailed)		.001	.001	.002

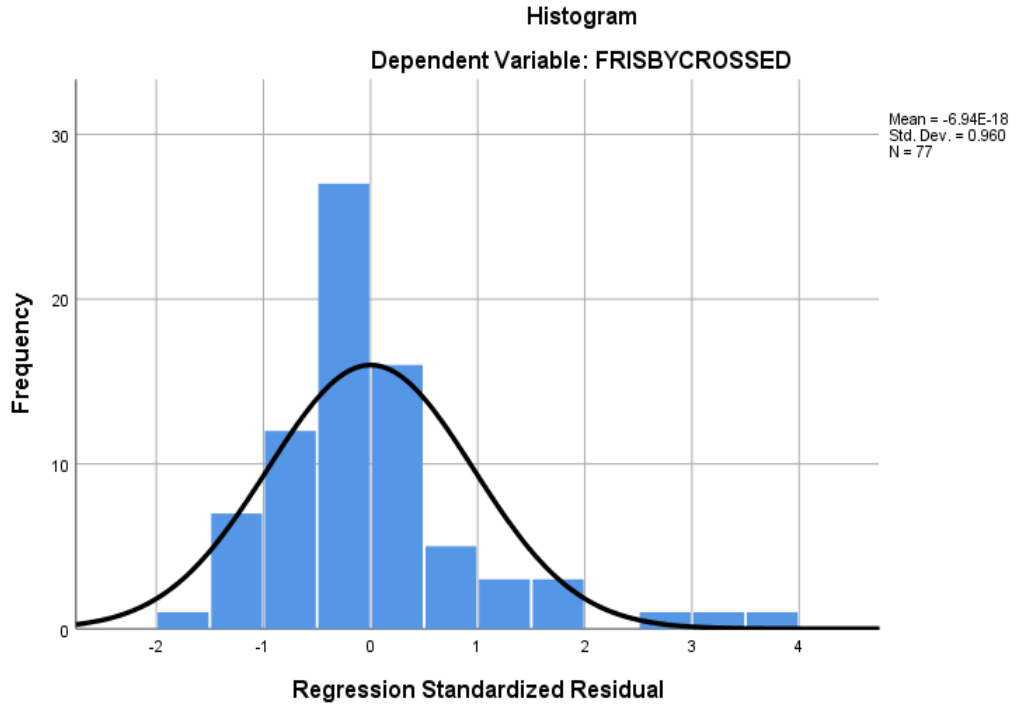
**. Correlation is significant at the 0.01 level (2-tailed).

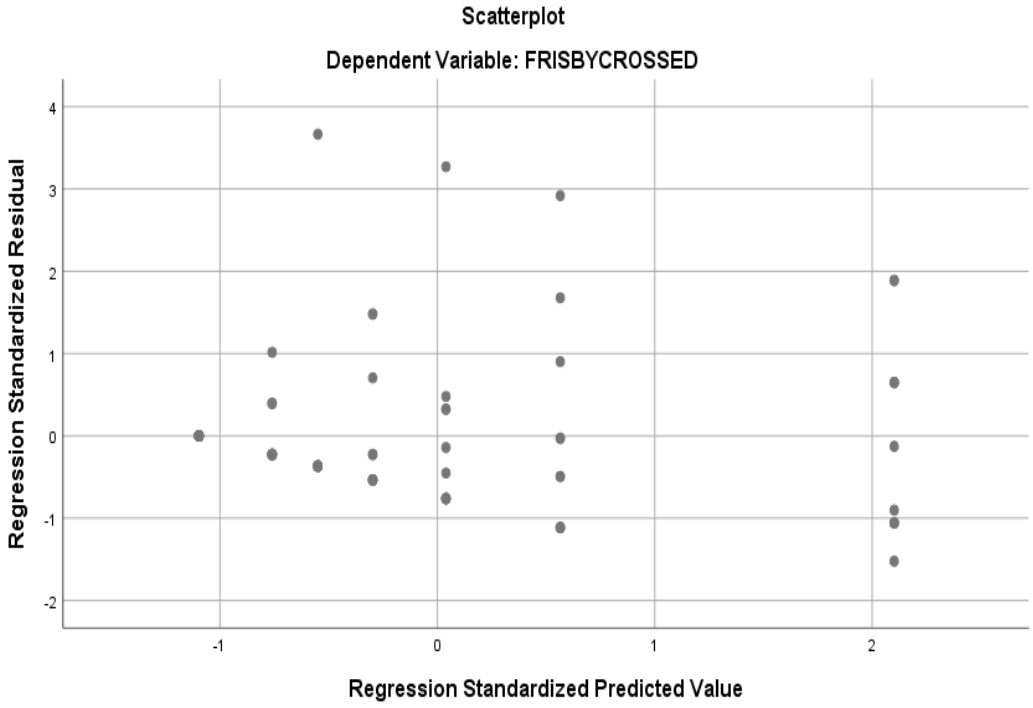
Appendix 18 Histogram and scatterplots for regression analysis assumptions (Frisby and FD2 data).



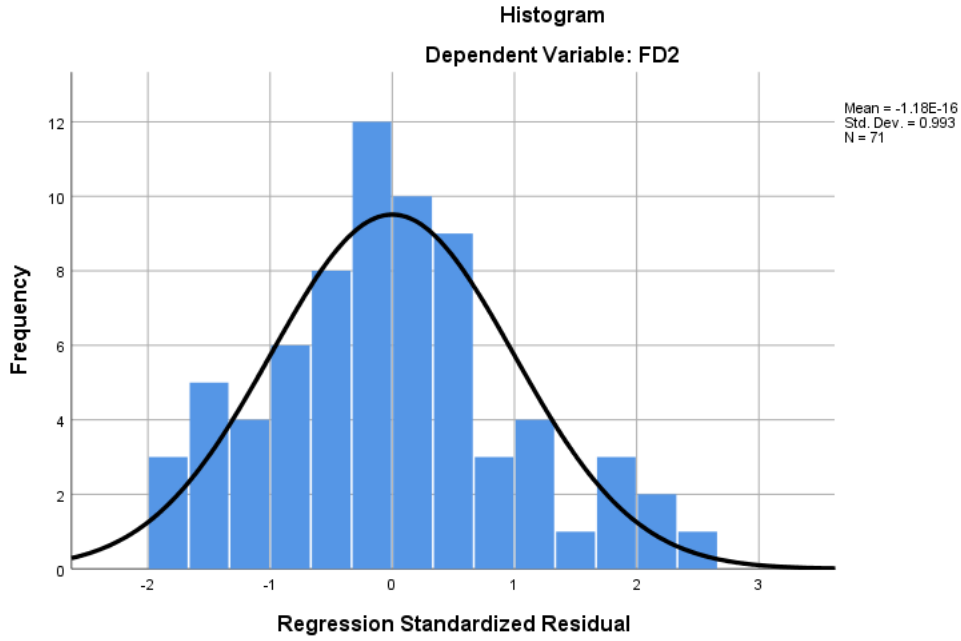


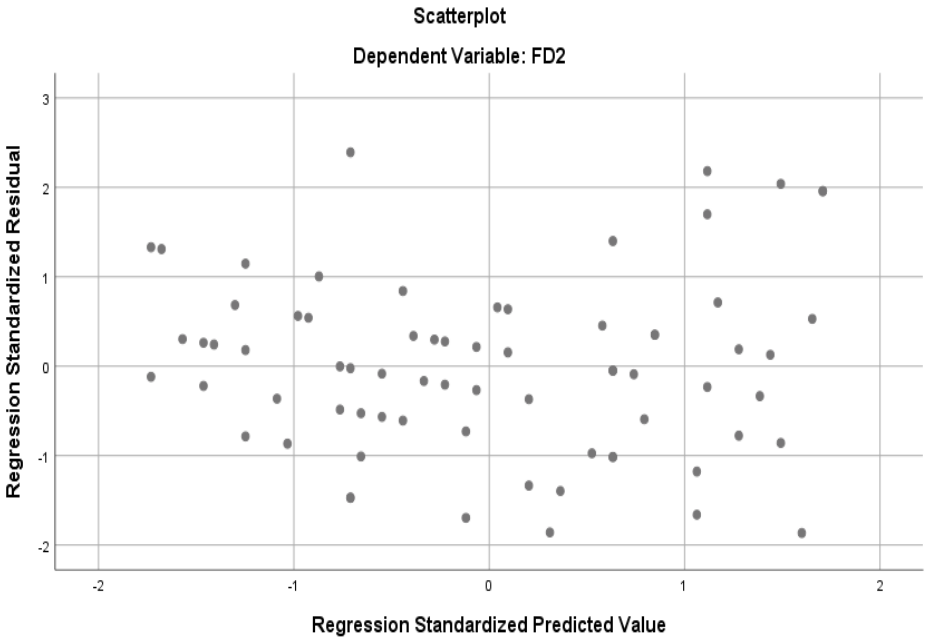
Appendix 18 Histogram and scatterplots for regression analysis assumptions (Frisby and FD2 data).





Appendix 18 Histogram and scatterplots for regression analysis assumptions (Frisby and FD2 data).





Appendix 19 Descriptive Statistics for Chapter 5

Fusion	Age (years)	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean Lower Bound	95% Confidence Interval for Mean Upper Bound	Minimum	Maximum
Near Positive Break	10 - 19	37.00	11.950	3.603	28.97	45.03	16	45
	20 - 29	33.00	9.592	2.892	26.56	39.44	18	45
	30 - 39	32.18	10.265	3.095	25.29	39.08	14	45
	40 - 49	38.64	8.970	2.704	32.61	44.66	25	45
	50 - 59	38.18	6.809	2.053	33.61	42.76	25	45
	60 - 69	42.36	8.744	2.636	36.49	48.24	16	45
	70 - 79	34.55	12.549	3.784	26.12	42.98	14	45
	Total	36.56	10.165	1.158	34.25	38.87	14	45
Near Positive Recovery	10 - 19	29.91	10.634	3.206	22.76	37.05	10	45
	20 - 29	27.45	11.308	3.410	19.86	35.05	14	45
	30 - 39	26.64	10.462	3.154	19.61	33.66	10	45
	40 - 49	34.36	10.414	3.140	27.37	41.36	18	45
	50 - 59	30.91	7.687	2.318	25.74	36.07	20	45
	60 - 69	40.82	9.968	3.006	34.12	47.51	14	45
	70 - 79	30.91	14.577	4.395	21.12	40.70	8	45
	Total	31.57	11.366	1.295	28.99	34.15	8	45
Near Negative Break	10 - 19	15.64	5.921	1.785	11.66	19.61	8	30
	20 - 29	14.09	5.029	1.516	10.71	17.47	8	25
	30 - 39	14.45	5.538	1.670	10.73	18.18	4	25
	40 - 49	14.55	3.804	1.147	11.99	17.10	6	20
	50 - 59	18.36	8.605	2.595	12.58	24.14	4	30
	60 - 69	16.91	5.665	1.708	13.10	20.71	8	25
	70 - 79	12.00	3.688	1.112	9.52	14.48	6	18
	Total	15.14	5.774	.658	13.83	16.45	4	30

Near	10 - 19	11.73	5.798	1.748	7.83	15.62	6	25
Negative	20 - 29	10.73	4.407	1.329	7.77	13.69	6	20
Recovery	30 - 39	10.91	5.319	1.604	7.34	14.48	2	20
	40 - 49	10.73	3.133	.945	8.62	12.83	4	16
	50 - 59	13.45	6.393	1.928	9.16	17.75	2	20
	60 - 69	13.45	4.741	1.429	10.27	16.64	6	20
	70 - 79	8.91	3.618	1.091	6.48	11.34	4	16
	Total	11.42	4.935	.562	10.30	12.54	2	25
Near	10 - 19	3.36	1.206	.364	2.55	4.17	2	6
Vertical	20 - 29	3.91	1.136	.343	3.15	4.67	2	6
	30 - 39	4.18	1.537	.464	3.15	5.21	3	7
	40 - 49	4.73	1.618	.488	3.64	5.81	3	7
	50 - 59	4.27	1.009	.304	3.59	4.95	3	7
	60 - 69	4.91	1.221	.368	4.09	5.73	3	7
	70 - 79	4.18	1.401	.423	3.24	5.12	2	7
	Total	4.22	1.354	.154	3.91	4.53	2	7
Distance	10 - 19	25.18	6.080	1.833	21.10	29.27	14	35
Positive	20 - 29	20.73	9.188	2.770	14.55	26.90	12	40
Break	30 - 39	18.36	5.988	1.805	14.34	22.39	8	30
	40 - 49	26.55	10.539	3.178	19.47	33.63	12	45
	50 - 59	26.45	5.768	1.739	22.58	30.33	16	40
	60 - 69	21.36	11.183	3.372	13.85	28.88	10	45
	70 - 79	16.36	7.941	2.394	11.03	21.70	8	30
	Total	22.14	8.863	1.010	20.13	24.15	8	45
Distance	10 - 19	18.82	5.173	1.560	15.34	22.29	10	25
Positive	20 - 29	15.64	8.441	2.545	9.97	21.31	8	35
Recovery	30 - 39	14.45	5.241	1.580	10.93	17.98	6	25
	40 - 49	19.27	10.974	3.309	11.90	26.64	4	40
	50 - 59	20.91	4.571	1.378	17.84	23.98	12	30
	60 - 69	15.45	11.343	3.420	7.83	23.08	6	45
	70 - 79	10.55	6.919	2.086	5.90	15.19	1	25
	Total	16.44	8.309	.947	14.56	18.33	1	45

Distance Negative Break	10 - 19	9.64	3.325	1.002	7.40	11.87	6	16
	20 - 29	10.18	2.750	.829	8.33	12.03	6	16
	30 - 39	9.45	3.804	1.147	6.90	12.01	2	14
	40 - 49	8.55	4.204	1.268	5.72	11.37	2	18
	50 - 59	8.73	4.756	1.434	5.53	11.92	2	20
	60 - 69	8.36	3.325	1.002	6.13	10.60	2	14
	70 - 79	9.64	4.802	1.448	6.41	12.86	2	18
	Total	9.22	3.813	.435	8.36	10.09	2	20
Distance Negative Recovery	10 - 19	7.09	2.587	.780	5.35	8.83	4	12
	20 - 29	7.27	2.240	.675	5.77	8.78	4	12
	30 - 39	7.00	3.066	.924	4.94	9.06	1	10
	40 - 49	5.73	2.901	.875	3.78	7.68	1	10
	50 - 59	6.82	4.622	1.394	3.71	9.92	1	18
	60 - 69	5.73	2.453	.740	4.08	7.38	1	10
	70 - 79	7.18	4.070	1.227	4.45	9.92	1	14
	Total	6.69	3.172	.361	5.97	7.41	1	18
Distance Vertical	10 - 19	3.36	1.362	.411	2.45	4.28	2	7
	20 - 29	3.64	1.502	.453	2.63	4.65	2	7
	30 - 39	3.73	1.489	.449	2.73	4.73	2	7
	40 - 49	4.55	1.695	.511	3.41	5.68	2	7
	50 - 59	4.00	.775	.234	3.48	4.52	3	6
	60 - 69	4.27	1.618	.488	3.19	5.36	2	7
	70 - 79	4.00	1.789	.539	2.80	5.20	2	8
	Total	3.94	1.481	.169	3.60	4.27	2	8

Appendix 19 Descriptive Statistics for Chapter 5

Near point of convergence cms

Age (years)	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean Lower Bound	95% Confidence Interval for Mean Upper Bound	Minimum	Maximum
10 – 19	11	5.6364	.82239	.24796	5.0839	6.1889	5.00	7.33
20 – 29	11	5.2000	.42164	.13333	4.8984	5.5016	5.00	6.00
30 – 39	11	5.9973	1.13749	.34297	5.2331	6.7614	5.00	8.00
40 – 49	11	7.2118	3.23937	.97671	5.0356	9.3881	5.00	16.00
50 – 59	11	7.2727	2.41209	.72727	5.6523	8.8932	6.00	14.00
60 – 69	11	6.4055	2.23673	.67440	4.9028	7.9081	5.00	11.80
70 – 79	11	7.3627	2.32502	.70102	5.8008	8.9247	5.00	11.33
Total	77	6.4572	2.11874	.24304	5.9731	6.9414	5.00	16.00

Appendix 19 Descriptive Statistics for Chapter 5

Age (years)		Phoria Near	Phoria distance
10-19	Mean	-.64	-.91
	N	11	11
	Std. Deviation	3.042	2.071
20-29	Mean	-2.09	-.55
	N	11	11
	Std. Deviation	3.700	.820
30-39	Mean	-2.91	-.45
	N	11	11
	Std. Deviation	4.323	1.214
40-49	Mean	-1.55	.09
	N	11	11
	Std. Deviation	4.034	.302
50-59	Mean	-2.27	-.09
	N	11	11
	Std. Deviation	4.474	.831
60-69	Mean	-3.73	-.18
	N	11	11
	Std. Deviation	4.245	.603
70-79	Mean	-1.91	-.45
	N	11	11
	Std. Deviation	4.867	1.368
Total	Mean	-2.16	-.36
	N	77	77
	Std. Deviation	4.072	1.157

Appendix 20 SPSS outputs for Chapter 5

SPSS output for NPC against ungrouped age (Pearson Correlation coefficient)

Correlations

		AGE	Near point of convergence cms
AGE	Pearson Correlation	1	.295**
	Sig. (2-tailed)		.010
	N	77	77
Near point of convergence cms	Pearson Correlation	.295**	1
	Sig. (2-tailed)	.010	
	N	77	77

**. Correlation is significant at the 0.01 level (2-tailed).

SPSS output for NPC Kolmogorov-Smirnov[a] Shapiro-Wilk and tests for normality

Tests of Normality

	Age	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	(years)	Statistic	df	Sig.	Statistic	Df	Sig.
Near point of convergence cms	10 – 19	.326	11	.002	.780	11	.005
	20 – 29	.482	11	.000	.509	11	.000
	30 – 39	.226	11	.121	.813	11	.014
	40 – 49	.253	11	.047	.710	11	.001
	50 – 59	.337	11	.001	.595	11	.000
	60 – 69	.281	11	.016	.709	11	.001
	70 – 79	.267	11	.028	.869	11	.075

Appendix 20 SPSS outputs for Chapter 5

SPSS outputs for NPC against cohort ages (Kruskal Wallis test)

Ranks

	Age (years)	N	Mean Rank
Near point of convergence cms	10 – 19	11	30.95
	20 – 29	11	21.40
	30 – 39	11	37.14
	40 – 49	11	43.23
	50 – 59	11	51.64
	60 – 69	11	35.86
	70 – 79	11	47.73
	Total	77	

Test Statistics[a,b]

	Near point of convergence cms
Kruskal-Wallis H	15.156
Df	6
Asymp. Sig.	.019

a. Kruskal Wallis Test

b. Grouping Variable: Age cohort

Appendix 20 SPSS outputs for Chapter 5

SPSS output for Fusion variables against ungrouped age (Pearson Correlation coefficient)

		AGE
Near Positive Break	Pearson Correlation	.129
	Sig. (2-tailed)	.265
Near Negative Break	Pearson Correlation	-.046
	Sig. (2-tailed)	.692
Near Positive Recovery	Pearson Correlation	.211
	Sig. (2-tailed)	.066
Near Vertical	Pearson Correlation	.225*
	Sig. (2-tailed)	.049
Near Negative Recovery	Pearson Correlation	-.029
	Sig. (2-tailed)	.802
Distance Positive Recovery	Pearson Correlation	-.168
	Sig. (2-tailed)	.144
Distance Positive Break	Pearson Correlation	-.151
	Sig. (2-tailed)	.190
Distance Negative Break	Pearson Correlation	-.087
	Sig. (2-tailed)	.450
Distance Vertical	Pearson Correlation	.154
	Sig. (2-tailed)	.180
Distance Negative Recovery	Pearson Correlation	-.062
	Sig. (2-tailed)	.594

Appendix 20 SPSS outputs for Chapter 5

SPSS output for fusion variables for variance within cohorts and between cohorts (ANOVA)

		Sum of Squares	df	Mean Square	F	P-value
Log Distance Positive Recovery	Between Groups	5.689	6	.948	3.164	.008
	Within Groups	20.975	71	.300		
	Total	26.665	77			
Log Distance Positive Break	Between Groups	2.878	6	.480	3.182	.008
	Within Groups	10.552	71	.151		
	Total	13.429	77			
Near Negative Break	Between Groups	281.065	6	46.844	1.456	.206
	Within Groups	2252.364	71	32.177		
	Total	2533.429	77			
Near Negative Recovery	Between Groups	174.883	6	29.147	1.217	.308
	Within Groups	1675.818	71	23.940		
	Total	1850.701	77			
Distance Negative Break	Between Groups	30.338	6	5.056	.329	.919
	Within Groups	1074.909	71	15.356		
	Total	1105.247	77			
Distance Negative Recovery	Between Groups	29.792	6	4.965	.473	.826
	Within Groups	734.727	71	10.496		
	Total	764.519	77			

Appendix 20 SPSS outputs for Chapter 5

SPSS output for fusion variables against cohorts (Kruskal Wallis test)

	Near Positive Recovery	Near Positive Break	Near Vertical	Distance Vertical
Kruskal-Wallis H	12.828	11.343	10.154	6.123
Df	6	6	6	6
Asymp. Sig.	.046	.078	.118	.410

SPSS output for near ocular alignment against ungrouped age (Fisher's exact test)

	Value	Df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	9.845[a]	10	.630	.656		
Likelihood Ratio	10.355	10	.585	.689		
Fisher's Exact Test	9.910			.637		
Linear-by-Linear Association	.142[b]	1	.706	.736	.368	.028
N of Valid Cases	77					

SPSS output for distance ocular alignment against ungrouped age (Fisher's exact test)

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	12.160[a]	10	.433	.445		
Likelihood Ratio	14.181	10	.289	.448		
Fisher's Exact Test	10.302			.496		
Linear-by-Linear Association	1.849[b]	1	.174	.197	.098	.020
N of Valid Cases	77					

Appendix 20 SPSS outputs for Chapter 5

SPSS outputs for near and distance ocular alignment variables against cohorts (Kruskal Wallis test)

	Near alignment	Distance alignment
Kruskal-Wallis H	3.095	6.144
Df	6	6
Asymp. Sig.	.797	.407

a. Kruskal Wallis Test

b. Grouping Variable: Age group

SPSS output for near ocular alignment variance within cohorts and between cohorts (ANOVA)

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	63.766	6	10.628	.622	.712
Within Groups	1196.364	70	17.091		
Total	1260.130	76			

Appendix 20 SPSS outputs for Chapter 5

SPSS output for distance ocular alignment variance within cohorts and between cohorts (ordinal regression)

		Estimate	Std. Error	P-value
Threshold	[Phoria distance = -6]	-4.547	1.244	.000
	[Phoria distance = -4]	-3.111	.892	.000
	[Phoria distance = -2]	-2.212	.807	.006
	[Phoria distance = -1]	-1.764	.782	.024
	[Phoria distance = 0]	3.164	.933	.001
Location	[Age 10 – 19 years]	-.574	1.031	.578
	[Age 20 – 29 years]	-1.038	.995	.297
	[Age 30 – 39 years]	-.397	1.047	.705
	[Age 40 – 49 years]	1.282	1.156	.267
	[Age 50 – 59 years]	.734	1.146	.522
	[Age 60 – 69 years]	.115	1.098	.917
	[Age 70 – 79 years]	0[a]	.	.

SPSS output to determine the effect of cohorts on the presence of endpoint nystagmus (logistic regression model)

	Estimate	S.E.	Test Statistics	P-value
Age (years)			1.740	.942
10 – 19	-20.222	12118.636	.000	.999
20 – 29	-20.222	12118.636	.000	.999
30 – 39	-1.322	1.248	1.121	.290
40 – 49	-1.322	1.248	1.121	.290
50 – 59	-20.222	12118.636	.000	.999
60 – 69	-.523	1.034	.256	.613
70 – 79	-.981	.677	2.099	.147

Appendix 20 SPSS outputs for Chapter 5

SPSS outputs for presence of endpoint nystagmus as an outcome and ungrouped age as a predictor (logistic regression model)

		B	S.E.	Wald	Sig.
	AGE	.055	.027	4.214	.040
	Constant	-5.200	1.643	10.015	.002

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	AGE	.055	.027	4.214	1	.040	1.057
	Constant	-5.200	1.643	10.015	1	.002	.006

a. Variable(s) entered on step 1: AGE.

Appendix 21 American Academy of Pediatric Ophthalmology and Strabismus conference Texas, USA, March 2020. Abstract (Submitted 01/12/2019)

Does Stereotest Selection and Age Alter Stereoacuity Achieved?

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Introduction: The study aimed to investiage whether there is a change in stereoacuity with age using commerically available steroacuity tests.

Methods: Stereoacuity was measured and analysed in 77 healthy participants who had a visual acuity of at least 0.10 LogMAR in each eye for near and distance and did not have a history of amblyopia treatment, childhood or acquired manifest strabismus and were naive to an orthoptist assessment. The 7 age groups were 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years and 70-79 years. Stereotests included Titmus, TNO, Frisby (crossed and uncrossed) and the Frisby-Davies (FD2) distance stereotest.

Results: There was a decrease in the level of stereoacuity with all stereotests with increasing age. Using ordinal regression analysis a statisically significant result was achieved for all stereotests: Titmus p-value= 0.0236; TNO p-value= 0.0019; Frisby crossed p-value= 0.0003; Frisby uncrossed p-value= 0.0003 and FD2 p-value <0.001. The 30-39 years group achieved the highest level of stereoacuity in all near stereotests whereas 40-49 years group achieved the highest level of far distance stereoacuity. Forty-five percent of participants in the 70-79 years group exhibited stereo negative results at far distance. With Titmus stereotest 71.4% of the study population achieved the maximum stereoacuity demonstrable by this test (40 seconds of Arc) whereas only 2.6% of participants achieved the maximum 15 seconds of Arc with TNO. There was correlation between the similarly designed free space stereotests, Frisby and FD2 (Pearson correlation p-value = 0.0004).

Discussion: The results of this study suggest that stereoacuity decreases with age. This reduction in stereoacuity begins in the 60-69 years group and is most visible in 70-79 years group with TNO, Frisby and FD2 stereotests, whereas a reduction was only detected in the 70-79 years group with Titmus. The results support a similar study which also found a decline in stereoacuity with age from 50+ years with TNO and 70+ years with Titmus[1].

Conclusions: The decrease in the mean values of stereoacuity should be considered when undertaking a binocular vision assessment in older patients. The high percentage of participants with normal visual acuity yet far distance stereo-negative aged 70-79 years needs further investigation due to the potential to impact on daily activities e.g. driving. The high percentage of 'best' stereoacuity findings with Titmus across the total population may suggest that it may not be useful measure of stereoacuity clinically.

References: Lee SY, Koo NK (2005) Change of Stereoacuity with Aging in Normal Eyes. *Korean Journal of Ophthalmology.* **19** (2):136-139

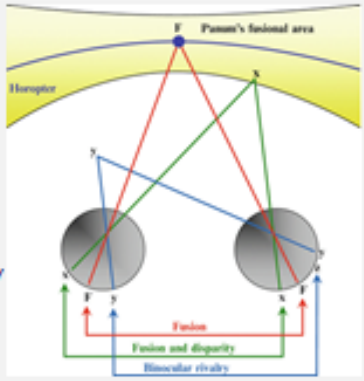
Appendix 22 American Academy of Ophthalmologists, virtual conference. November 2020. E Poster 349

Appendix 22 American Academy of Ophthalmologists, virtual conference. November 2020. E Poster 349

BACKGROUND/OBJECTIVE

Background

- Stereoacuity is the smallest threshold disparity that can be discriminated between two adjacent surfaces.[1]
- Disparate retinal images must fall within Panum's fusional area to be viewed as a binocular single image. [1-3]
- Stereopsis is present from age 3 - 6 months. [1, 3-5]
- Commercially available stereotests show variability as to when stereoacuity reaches adult level, but reported to be by age 9 years. [1, 6-9]
- Conflicting reports as to whether stereoacuity changes with age, possibly related to methodology (clinically-used stereotests versus research-based stereotests)



- Study formed part of presenting author's Doctorate in Ophthalmic Science research project.

Objective-

To test the hypothesis that measured **stereoacuity decreases as a function of age** when using commercially available stereotests when visual acuity is controlled.

METHODS AND MATERIALS

Methods

- **Prospective single-centre study measuring stereoacuity in participants aged 10 - 79 years.**
- Ethical approval from University Hospital Galway (UHG), Ireland and Aston University Birmingham, UK.
- Voluntary recruitment of healthy participants
- Participant origins:
  - Public, parents of children attending the orthoptic clinic at UHG
  - non-ophthalmic trained staff of the hospital/health centre
  - Members of 2 'active retirement clubs'
- Inclusion criteria:
  - 10 - 79 years, male or female, any ethnic group.
  - Minimum visual acuity 0.10 LogMAR, each eye (near and distance)
  - Naïve to orthoptic assessments
- Exclusion Criteria:
  - History of amblyopia treatment,
  - Childhood/acquired manifest strabismus,
  - Latent strabismus greater than 15 prism dioptres.
  - Previous eye surgery.
  - Extraocular muscle pathology -neurological, mechanical or myogenic

Equipment and Procedure

Stereotests

1. Frisby stereotest (Crossed and uncrossed)

2. TNO stereotest

3. Titmus stereotest

4. Frisby Davis distance stereotest

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RESULTS

- 77 participants aged 10 - 79 years old, stratified into 7 age categories (see Table 1). 78% female
- Using ordinal regression analysis all five tests showed that increasing age had a statistically significant effect on stereoacuity at a 5% significance level (Table 2)
- Real depth stereotests (i.e. Near: Frisby, Distance: FD2) showed the strongest statistical significance (Table 2).

- **Titmus Stereotest**
  - 55 participants (71%) achieved maximum stereoacuity.
  - Only 3 participants achieved 100-140" of Arc; with the 'worst' stereoacuity level of 140" of Arc value only found in the 70-79 year group.
- **TNO Stereotest**
  - 38 participants (49%) achieved 60" of Arc.
  - 100% of 30-39 year group achieved 'best' level of stereoacuity (≤ 60" of Arc)
  - 9/11 participants in 70-79 year group scored the 'worst' (≥120" of Arc).
  - Only 2 participants of the total population achieved maximum stereoacuity (15" of Arc)
- **Frisby Stereotests (Uncrossed and Crossed)**
  - Both uncrossed and crossed results were comparable (Pearson correlation p-value = 0.0004)
  - 42 participants (55%) achieved maximum stereoacuity (20" of Arc)
  - All participants in 30-39 year group achieved 'best' stereoacuity (20" of Arc - crossed &uncrossed)
  - 7/11 participants in 70-79 year group scored the 'worst' stereoacuity (≥85"of Arc)
- **FD2 stereotest**
  - 52 participants (68%) scored stereoacuity between 15" & 30" of Arc
  - 5/11 (46%) of 70-79 year group scored the 'worst' (stereo-negative results)
  - Statistical significant correlation between the **Frisby** and the **FD2** (p-value = 0.004)

Age Group (years)	Mean age (years) ± standard deviation	Range (years)
10-19	15 ± 3.6	10-19
20-29	26.6 ± 2.7	22-29
30-39	34.2 ± 2.9	30-39
40-49	43.8 ± 2.6	40-49
50-59	54.9 ± 2	52-58
60-69	64.4 ± 2.5	62-69
70-79	73.2 ± 2	70-76

Table 1: Mean age with standard deviation and the range of ages for each age cohort

Stereotest	P-value
Titmus	0.0236
TNO	0.0019
Frisby crossed	0.0003
Frisby uncrossed	0.0003
FD2	<0.001

Table 2: The statistical outcomes for each stereotest versus age

CONCLUSION/DISCUSSION

Conclusions

- This study has confirmed that there is a **statistical significant relationship between age and stereoacuity**.
- There is a **reduction in stereoacuity from the age of 60+ years** but is most evident from 70+ years.
- It has shown that **stereotest selection is important,** as the deterioration was more evident with the 'real depth' stereoacuity test (Frisby).

Additional comments

- The **results from this study support previous studies** that also found a deterioration in stereoacuity with age [1, 10, 11, 12]

Further research

- A high number of stereo-negative results for distance stereoacuity in the Group 70-79 years is interesting from the perspective of Traffic Medicine/ Vehicle safety. A further study of a larger cohort of participants aged 70+ years with multiple distance stereoacuity tests (e.g. non commercially available psychophysical research tests) could establish if this is a true reflection of the general population of over 70s.