An Evaluation of the accuracy of the Moorfields Motion Displacement Test

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1.0 Preface and declaration

Declaration:

I, Keshia Chetty, declare that this work has been done by me under the supervision of Professor Kovin Naidoo, Ms Pirindhavellie Govender and Professor James Loughman, and has not previously been submitted to UKZN or another tertiary institution for purposes of obtaining a degree or any other academic qualification.

Signature:

Dedication:

This work has been dedicated to all patients who have been affected by glaucoma, and to all the participants who volunteered for the study. I would also like to dedicate this study to the developers of the Moorfields Motion Displacement Test, who, by developing this instrument, have aided with mass screening projects in developing countries.

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Table of contents

Contents

List of tables, figures, and acronyms

List of acronyms

ARMD	Age Related Macular Degeneration
HVFA	Humphreys Visual Field Analyser
MDT	Motion Displacement Test
SAP	Standard Automated Perimetry
MMDT	Moorfield's Motion Displacement Test
ONH	Optic Nerve Head
IOP	Intra Ocular Pressure
POAG	Primary open angle glaucoma
GON	Glaucomatous optic neuropathy
PACG	Primary angle closure glaucoma
PCG	Infantile primary congenital glaucoma
CCT	Central corneal thickness
JAMA	Journal of American Medical Association
CDR	Cup-to-disc ratio
SITA	Swedish Interactive Threshold Algorithms
GHT	Glaucoma Hemifield Test
UCL	University College London
ESTA	Enhanced Supra-Threshold Strategy
WEBS	Weighted Binary Search Threshold Strategy
PTD	Probability of true damage
KZN	KwaZulu-Natal
AVRI	African Vision Research Institute
UKZN	University of KwaZulu-Natal
ROC	Receiver Operating Characteristic
SPSS	Statistical Package for Social Sciences
SAPSE	South African Post-Secondary Education
DUR	Duration
DX	Disease

LIST OF FIGURES AND TABLES

Chapter 2

Figure heading **Page no.**

Chapter 2

Chapter 4

Table heading **Page no.**

Chapter 4

Abstract

Introduction

Recent statistics report a global blind population of 32.4 million and 191 million people with vision impairment, of which more than 90% of the world's visually impaired live in developing countries. Glaucoma, the third leading cause of blindness in Africa (after cataract), is responsible for approximately 15% of blindness in the continent, requiring early detection, but goes undiagnosed in developing countries because of lack of awareness of the disease and its effects. Screening methods are not always affordable and relatively inaccessible in most developing countries, posing a barrier to identifying people at risk of glaucoma blindness.

The Humphrey's Visual Field Analyser (HVFA), considered as the gold standard in assessing visual fields, is not suited to mass screening due to cost, portability, test time, physical testing requirements among other issues, thereby making it inconvenient for mass screening programmes. These shortcomings motivated the development of the Moorfield's Motion Displacement Test (MMDT), a new portable visual field instrument, at the Moorfield's Eye Hospital in London.

Aim: To determine the agreement and sensitivity between the Humphrey's Visual Field Analyser (HVFA) and the Moorfield's Motion Displacement Test (MMDT).

Methods: The study followed a comparative design based on simple random sampling, comprising two hundred and seven subjects. Of the total number of subjects included in the study, the glaucoma group comprised sixty-two subjects, whilst the control group comprised one hundred and forty-five subjects. A total of 293 eyes were included in the study, of which 94 eyes were glaucomatous (case) and 199 eyes were non-glaucomatous (control), of participants who were selected via chart review from two district hospitals in KwaZulu Natal (KZN), South Africa; McCords Provincial Eye Hospital (case) and Prince Mshiyeni Memorial Hospital (control). Both eyes were tested using the HVFA and the MMDT instruments. All subjects were asked to complete a questionnaire prior to and after testing on both instruments.

Results: Non-parametric tests were used because results were not normally distributed. The diagnostic accuracy of the MMDT was high in terms of test sensitivity (100%), but performed less well in terms of specificity (63.3% and 65.3%) for case and control participants respectively. Despite the low specificity, there was a high level of similarity and a faster testing time (for both groups) in detecting glaucomatous visual field defects on the MMDT compared with the HVFA. A significant number of participants (83.5 %) across the different race groups, preferred the MMDT over the HVFA, and found the use of the mouse over a push button to be easier (74.5% across all race groups). Majority of participants (80.5%) reported focusing on a central white dot seemed more comfortable than a central amber light and found anxiety levels reduced whilst using the MMDT.

Conclusion: The high sensitivity and design advantages of the MMDT for population screening may help improve glaucoma case finding in the community, and thereby facilitate earlier treatment and better health outcomes for those affected. The specificity issue should be addressed, however, to avoid service delivery problems associated with unnecessary false positive referrals.

Key words: *glaucoma, Humphrey's Visual Field Analyser, Moorfields Motion Displacement Test, screening*

CHAPTER 1: Introduction

1.1 Background

In 2015, it was estimated that of the global population, 36 million people were blind, 216.6 million had moderate to severe visual impairment and 188.5 million had mild visual impairment (Bourne *et al.*, 2017) with more than 90% of the visually impaired living in developing countries (Resnikoff *et al.*, 2008). Most of the burden of vision loss lies amongst those individuals 50 years and older, and although the prevalence decreased worldwide since the past 20 years, the number of blind and vision impaired people did not decrease, due to the rapid increase in the older adult population (Stevens *et al.*, 2013). Along with the increasing life expectancy, age-related co-morbid conditions increased as well which included irreversible ophthalmic diseases, affecting the overall quality of life (Loughman *et al.*, 2013).

The most common causes of blindness and vision impairment worldwide, according to studies done over the past 20 years, are reported to be: cataract, glaucoma, macular degeneration, diabetic retinopathy, trachoma and uncorrected refractive error, and are classified as avoidable vision loss (Stevens *et al.*, 2013). Naidoo *et al* (2013) in a study in the Lower Tugela Health District in KwaZulu Natal, South Africa, reported that the main causes of vision impairment (considered to be potentially blinding diseases) were: refractive error (44.5%); cataract (31.2%); glaucoma (6.0%); hypertensive retinopathy (4.1%) and diabetic retinopathy (4.1%). Those conditions linked to the cause of bilateral blindness were: cataract (54.8%); refractive error (12.9%); glaucoma and hypertensive retinopathy (6.4%), with diabetic retinopathy and other ocular conditions such as corneal scarring and retinal coloboma accounting for 3.2% of bilateral blindness (Naidoo *et al.*, 2013). It was also found that 9.7% of bilateral blindness were caused by Albinism, coloboma and age-related macula degeneration (Naidoo *et al.*, 2013).

In a study in Cape Town, South Africa, posterior segment diseases (including glaucoma) were found to be the leading cause of blindness, accounting for 65% of blindness (Cockburn *et al.*, 2012). Age related macular degeneration (ARMD), optic atrophy, trauma and macula hole made up the remaining posterior segment diseases (Cockburn *et al.*, 2012). Glaucoma is the third leading cause of blindness in Africa, after cataract, and is responsible for approximately 15% of blindness in the continent (Lawrence and Budenz, 2013). A significant challenge to blindness prevention programmes is the management of glaucoma, among other ocular diseases, since it requires significantly more resources than, for example, cataract (Cockburn *et al.*, 2012).

In developing countries, the challenge is exacerbated as there are no primary care screening strategies in place and the lack of equipment and other resources renders eye health care services inaccessible to the majority (Loughman *et al.*, 2013). The costs of standard methods for screening, including

computerised perimetry, are not affordable and are relatively inaccessible in most developing countries (Ong *et al.*, 2014). Therefore, there is a great need for more affordable and faster methods (Govender *et al.*, 2015). Compliance with medical treatment is related to many factors, some of which include the asymptomatic nature of the disease and the level of education and socio-economic status of the patient (Leite *et al*. 2011).

Africa has 15% of the world's visually impaired and just over half (50.9%) of the world's poor. It is believed that poverty and eye health are interrelated (Jaggernath *et al.*, 2014). In addition to the economic impact, educational opportunities and quality of life are also affected (Stevens *et al.*, 2013). Although treatment for glaucoma is effective, it requires early detection (community based screening), lifelong monitoring and a great level of adherence to therapy to prevent vision loss (Cockburn *et al.*, 2012). Therefore, eye care systems that address chronic eye diseases with rehabilitation and support services need to be urgently developed (Pascolini and Mariotti, 2010).

If glaucoma is left undiagnosed there are many activities of daily living that are affected, with its consequent socio-economic effects (World Health Organisation, 2006). These include difficulty in reading and writing, mobility and colour discrimination (Taylor and Keeffe, 2001; Rong-jiang *et al.*, 2011). Direct costs of blindness include treatment of eye diseases, pharmaceuticals and research and administration. Indirect costs include lost earnings of the visually impaired, state grants, cost of visual aids and caregivers, equipment, home modifications and rehabilitation (World Health Organisation, 2006).

Visual field assessment is important in the diagnosis of glaucoma and the Humphrey's Visual Field Analyser (HVFA) is one of the instruments used (Alencar and Medeiros, 2011). The HVFA is regarded as the gold standard for the assessment of visual fields (Choplin *et al*. 1998). Although recent developments have seen the advent of more sophisticated psychophysical visual function tests, visual field instruments remain expensive and relatively inaccessible in rural or underdeveloped areas (Ong *et al.*, 2014). The acknowledgement of these limitations has initiated the development of more affordable instruments for visual field testing (Broadway, 2012) which can be more easily utilised and accessed in the developing world context (Asana *et al.*, 2013)

In the 1980s, Professor Fitzke (Institute of Ophthalmology, London) developed the original Motion Displacement Test (MDT) which was found to be a detector of glaucomatous visual field loss (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). Evidence of elevated motion displacement threshold was shown in some areas of the visual field not usually affected on standard automated perimetry (SAP) assessment and the MDT proved to be resistant to the effect of media opacity (Ong *et al.*, 2014).

These properties provided the rationale for further development of the test and since 1999, new visual field testing equipment called the Moorfields Motion Displacement Test (MMDT) has been under development. The MMDT is a multi-location test, presented on a computer screen with 32 line stimuli; each scaled by estimate of retinal ganglion cell density (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). However, its accuracy in comparison to the HVFA has not yet been established. The purpose of the study was, therefore, to compare the visual field defects, if any, obtained by the MMDT to that obtained with the HVFA in diagnosed glaucoma subjects.

1.2 Research questions, aim and objectives

1.2.1 Research questions

Primary research question: Does the diagnostic accuracy of the MMDT relative to the HVFA warrant its use for mass glaucoma screenings in the community?

Secondary research questions:

1.2.1.1 Do gender, age and race affect the testing time using both the HVFA and the MMDT?

1.2.1.2 Are gender, age and race associated with the preference of fixation target (light or dot)?

1.2.1.3 Are gender, age and race associated with the preference for fixation target indicator (button or mouse) between HVFA and MMDT?

1.2.1.4 Are gender, age and race associated with the selection of visual field instrument?

1.2.1.5 Are gender, age and race associated with the level of anxiety experienced with the HVFA and MMDT?

1.2.2 Overall Aim

The aim of this study was to assess the diagnostic accuracy, acceptability, and usability of the Moorfields Motion Displacement Test (MMDT) in comparison with the gold standard Humphreys Visual Field Analyser (HVFA) as a tool for community glaucoma screening.

1.2.3 Specific Objectives

The specific objectives of the study were:

1.2.3.1 To determine the diagnostic performance of the MMDT relative to the gold standard HVFA

1.2.3.2 To determine the level of similarity in findings between the HVFA and MMDT

1.2.3.3 To explore the influence of demographic factors such as age, gender and race on the usability and acceptability of/preference for the MMDT device over HVFA, including test time, fixation, target preference, method of selection and anxiety levels.

1.2.4 Hypotheses

1.2.4.1 H_0: The distribution of test duration using the Moorfields Motion Displacement Test (MMDT) is the same across categories of race, gender and age

1.2.4.2 H_0: The distribution of test duration using the HVFA is the same across categories of race, gender and age

1.2.4.3 H_0: There is no significant correlation between the results obtained with the MMDT as compared to that found with the HVFA

1.2.4.4 H_0: The level of similarity between the MMDT and HVFA does not validate the MMDT be used as a screening or diagnostic tool for patients with visual field defects

1.2.4.5 H_0: The association between gender, age and race is the same regarding the preference for fixation target (light or dot)

1.2.4.6 H_0: The association between gender, age and race is the same regarding the preference for fixation target indicator (button or mouse) between HVFA and MMDT

1.2.4.7 H_0: The distribution of the selection of preferred visual field instrument is the same across categories of gender, age, and race

1.2.4.8 H_0: The level of anxiety experienced with the HVFA and MMDT is the same across categories of gender, age, and race

Rationale

Glaucoma is an important cause of vision impairment and blindness. Once diagnosed, however, it can be effectively managed using medical and surgical interventions. These are most effective when the condition is diagnosed early. A large number of patients with glaucoma remain undiagnosed. The condition is asymptomatic in the early stages, so detection relies on effective community-based screening. Due to a lack of affordable and accessible screening and diagnostic tools, many sufferers present to eye care facilities when the condition is advanced and irreversible vision loss has already occurred. Treatment at this stage is challenging and the risks for vision impairment and blindness are high even with treatment. The development of a user-friendly, accessible and affordable device such as the MMDT for mass population glaucoma screening offers the potential, therefore, to facilitate better community detection of glaucoma, allow earlier treatment initiation and improved health outcomes that benefits patients, families and society in general. The purpose of the current study is to explore the feasibility of the MMDT device for glaucoma screening by examining its diagnostic performance and user experience compared to the gold standard HVFA test.

Conclusion

This chapter focuses on the current global issue of glaucoma, being the third leading cause of worldwide blindness. It also addresses the urgent need for more affordable, accessible, and portable visual field

instruments, considering most of the burden of visual impairment lies in developing countries. By allowing for an earlier detection and diagnosis, the overall health and socio-economic impact of glaucoma and its role in irreversible blindness can be significantly reduced. In addition to the feasibility, the MMDT is also simple to perform, therefore technical staff can be trained on screening the community, allowing for eye health care practitioners to work optimally.

CHAPTER 2: Literature Review

The following chapter is a detailed literature review addressing glaucoma and its subtypes, the risk factors involved as well as important glaucoma prevalence and vision impairment data. It also highlights the barriers to accessing health care in South Africa, which forms part of a much larger issue in a developing world context. Also included are the current types of visual screening instruments and a discussion of the Moorfield's Motion Displacement Test (MMDT).

2.1. Glaucoma in South Africa

2.1.1 Definition of glaucoma

The evolved definition of glaucoma according to Casson *et al.* (2012) is as follows:

'Glaucoma describes a group of ocular disorders of multifactorial aetiology united by a clinically characteristic optic neuropathy with potentially progressive, clinically visible changes at the optic nerve head (ONH), comprising focal or generalized thinning of the neuroretinal rim with excavation and enlargement of the optic cup.'

In 2004, 3.9% of the total global burden of disease was caused by vision loss (Stevens *et al.*, 2013). Bourne *et al*. (2013) reported that, of the global population with vision loss, 32.4 million people are blind and 191 million people with vision impairment, with more than 90% of the visually impaired living in developing countries (Resnikoff *et al.*, 2008). In addition to this burden, increasing life expectancy and its link to age-related co-morbid conditions (including irreversible ocular diseases) have affected the overall quality of life (Loughman *et al.*, 2013).

Globally, glaucoma is the second highest cause of avoidable blindness after cataract (Bourne *et al.*, 2013) and affects around 2% of the adult population 50 years and older (Brusini *et al.*, 2005). Glaucoma is described as a characteristic optic neuropathy with retinal ganglion cell (RGC) atrophy and retinal nerve fibre layer (RNFL) damage, resulting in clinically visible changes at the optic nerve head, as well as functional changes- mainly, visual field defects (Casson *et al.*, 2012).

2.1.2 Types of glaucoma

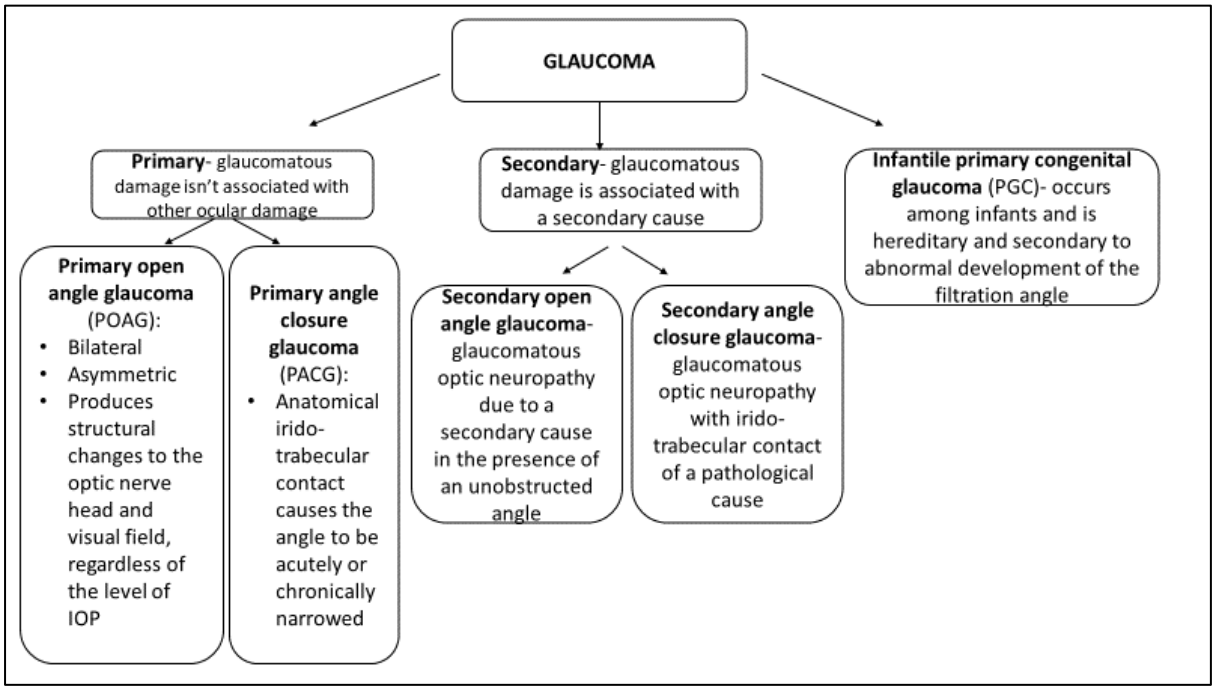

Figure 2.1 Schematic representation of types of glaucoma

Glaucoma can broadly be classified (Figure 2.1) as: primary, secondary (Rudnicka and Owen, 2007) and infantile (Schacknow and Samples, 2010), however, several different types can occur.

2.1.2.1 Primary glaucoma

In **primary glaucoma,** the glaucomatous damage isn't associated with any other ocular disorder and includes the following (Rudnicka and Owen, 2007):

2.1.2.1.(a) Primary open angle glaucoma (POAG)

Primary open angle glaucoma presents most often as an adult onset glaucoma, is generally bilateral and asymmetric and produces structural changes to the optic nerve head and visual field, regardless of the level of IOP (Rudnicka and Owen, 2007). Like the name suggests, the anterior chamber angle remains unobstructed, however the drainage of aqueous humour is compromised (Rudnicka and Owen, 2007). It is also referred to as a chronic 'simple' glaucoma (Kanski, 2007), which can further be subdivided into:

-Normal tension glaucoma which includes those with Glaucomatous Optic Neuropathy (GON) but an IOP within the normal range (between 11-21mmHg) and;

-High-tension or 'classical' glaucoma which is POAG with raised IOP (IOP being above 21mmHg)

2.1.2.1.(b)Primary angle closure glaucoma (PACG)

In this category of glaucoma, anatomical irido-trabecular contact (due to either anterior or posterior forces) causes the angle to be acutely or chronically narrowed (Casson *et al.*, 2012)

2.1.2.2 Secondary glaucoma

Increased IOP due to a secondary cause, example: cataract, uveitis, trauma and disorders affecting the drainage and structure of the anterior chamber angle, result in a **secondary glaucoma** (Rudnicka and Owen, 2007). This type of glaucoma is further subdivided into:

> 2.1.2.2.(a) Secondary open-angle glaucoma is glaucomatous optic neuropathy due to a secondary cause in the presence of an unobstructed angle (Casson *et al.*, 2012), which can occur pre-trabecular, trabecular or post-trabecular (Kanski, 2007).
>
> 2.1.2.2.(b) Secondary angle-closure glaucoma is characterised by glaucomatous optic neuropathy with irido-trabecular contact of a pathological cause (Casson *et al.*, 2012). Aqueous outflow is impaired secondary to the apposition between the peripheral iris and the trabecular meshwork (Kanski, 2007).

Examples of secondary glaucoma include, but are not limited to; uveitic, neovascular, pseudoexfoliation, pigmentary and traumatic glaucoma (Kanski, 2007).

2.1.2.3 Infantile primary congenital glaucoma (PCG)

Amongst infants and older children, the most common primary glaucoma seen is infantile primary congenital glaucoma (PCG). It is hereditary and secondary to abnormal development of the filtration angle (Schacknow and Samples, 2010).

2.1.3 The trabecular meshwork and its significance in glaucoma

The anterior chamber angle is an angular space bounded anteriorly by the posterior aspect of the cornea and posteriorly by the anterior aspect of the iris and part of the ciliary body and contains aqueous humour, produced by the ciliary body (Raluca *et al.*, 2015). At the angle of the anterior chamber is the trabecular meshwork, which is a sieve-like structure through which 90% of the aqueous humour leaves the eye (Kanski, 2007). Aqueous outflow occurs via two main channels, mainly trabecular and uveoscleral and IOP is determined by the rate of aqueous secretion and rate of outflow (Weinreb *et al*. 2014). Retinal ganglion cell death is related to the level of IOP and raised IOP secondary to reduced aqueous outflow through the filtration angle is an important risk factor for glaucoma (Kanski, 2007; Weinreb *et al*. 2014).

2.1.4 Risk factors for glaucoma

Research studies have identified possible (however, not entirely conclusive) risk factors for glaucoma which include: ocular, systemic, environmental and molecular genetic risk factors (Janssen *et al.*, 2013). The following are important risk factors for evaluation of glaucoma: older age, family history of glaucoma, being of African ethnicity, use of topical or systemic corticosteroids and high IOP (Weinreb *et al*. 2014). The above risk factors are briefly explained below:

2.1.4.1 Intraocular Pressure (IOP) and central corneal thickness (CCT)

Intraocular pressure is an important risk factor (Racette *et al.*, 2003), however, it is not a pre-requisite (Rudnicka and Owen, 2007). Some research states that patients with an elevated IOP are usually at risk for POAG (Montgomery and Yim, 2007), but whilst the accepted normal range of IOP is 10- 21mmHg, with a mean of 16mmHg, this range is debatable as some patients with elevated IOP never develop glaucoma, whilst some with normal IOP readings show glaucomatous damage (Racette *et al.*, 2003). In addition to the above, central corneal thickness (CCT) was also shown to be a risk factor, with patients having a thinner CCT being at a higher risk of ocular hypertension progressing to glaucoma (Schacknow and Samples, 2010).

2.1.4.2 Genetic predisposition

According to a study, up to 50% of POAG patients reported a positive family history for the disease (Racette *et al.*, 2003). Complex diseases, like glaucoma, collectively manifest heritability of several individual traits, therefore studies are focused on targeting the genes responsible for each individual trait (Gupta *et al.*, 2018). The characteristic optic neuropathy responsible for almost all classes of glaucoma is the reason for the growing interest in studies which identify genetic markers responsible for apoptosis of retinal ganglion cells (RGC's) at the optic nerve (Gupta *et al.*, 2018).

2.1.4.3 Systemic illnesses

Whether Diabetes Mellitus is related to the diagnosis of POAG is still being investigated, however, there has been evidence suggesting diabetes is associated with elevated IOP (Racette *et al.*, 2003). Despite no causal relationship between POAG and systemic hypertension having yet been established, studies report systemic blood pressure is closely related to IOP, which is an important risk factor in glaucoma development (Racette *et al.*, 2003)(Wong and Mitchell, 2007).

2.1.4.4 Race and gender

Among individuals of African origin, the disease onset is usually earlier and progresses more rapidly as compared to other race groups (Buhrmann *et al.*, 2000). It was also found that the prevalence of POAG among patients of African origin was independent of refractive error (Racette *et al.*, 2003). The

susceptibility of the disease was also found to be higher in males than in females (Rotchford and Johnson, 2002; Kapetanakis *et al.*, 2016).

2.1.4.5 Environmental risk factors for glaucoma

There have been a few investigations into the development of POAG through effects on IOP and/or the rate of retinal ganglion cell apoptosis (Foster *et al.*, 2002; Pasquale and Kang, 2009). The following have been reported to play a role in an increase in IOP: playing high resistant wind instruments, drinking coffee, engaging in certain yoga positions, wearing tight neck ties and weight lifting, whilst general physical exercise has shown a resultant decrease in IOP (Pasquale and Kang, 2009; Wiggs, 2012; Lin *et al.*, 2017). The predisposition to glaucoma development as a result of the related IOP increase from the above activities has not yet been studied (Pasquale and Kang, 2009).

Among those mentioned above, certain nutritional and lifestyle factors have also been identified as influencing POAG development, such as dietary fat and antioxidant intake, post-menopausal hormone use, gene- environment interaction (specifically hormone replacement therapy and Nitric Oxide Synthase 3 (NOS3) and smoking (Pasquale and Kang, 2009; Wiggs, 2012). Apart from direct influences, those residing in Northern latitudes were at a higher risk of developing exfoliation syndrome glaucoma as ambient temperature and sun exposure are triggers, although other features of Northern latitude exposures, such as vitamin D metabolism could contribute as well (Wiggs, 2012). By identifying the primary preventive measures incurred by POAG, the burden of visual disability (including the economic consequences of glaucoma) can be reduced (Pasquale and Kang, 2009).

2.1.4.6 Epigenetics role in glaucoma

Epigenetics has been described as gene expression regulation without changing the primary DNA sequence (Wiggs, 2012; He *et al.*, 2013). It was found that the application of Trichostatin A (TSA) and valproic acid (histone deacetylase inhibitors) can reduce the loss of retinal ganglion cells and enhance axonal regeneration after optic nerve damage, suggesting abnormal histone acetylation/deacetylation could possibly be related to retinal ganglion cell loss in glaucoma (He *et al.*, 2013). Recently, the CDKN2BAS locus was found to be associated with POAG and optic nerve cup-disc ratio (CDR), which is a genomic region that appears to be regulated by epigenetic mechanisms, however, although investigations in this area are at fairly recent stages, they could have a significant impact on future therapeutic approaches (Wiggs, 2012).

2.1.5 Prevalence and statistics of glaucoma

The leading cause of irreversible blindness globally, is glaucoma, with a prevalence of 3.54%, of which POAG and PACG, among those aged 40-80 years old, accounted for 3.05% and 0.50% respectively (Tham *et al.*, 2014). In 2010, 60.5 million people were affected by POAG and PACG globally, with Africa having the highest prevalence of POAG (Gilmour-White *et al.*, 2015) and Asia having the highest

prevalence of PACG (Tham *et al.*, 2014). The most prevalent of the several types of glaucoma was found to be POAG (Rudnicka and Owen, 2007) having approximately 53 million sufferers worldwide (Kapetanakis *et al.*, 2016) - about three quarters of all glaucoma cases (Kapetanakis *et al.*, 2016). However, secondary glaucoma does not have much research in its category, which is believed to represent approximately 20% of all types of glaucoma, and includes those caused by the following processes: neovascularisation, uveitic, lens related and trauma (Foster *et al.*, 2002). Buhrmann *et al*. (2000) found a prevalence of 0.06% and 0.09% of secondary OAG and secondary ACG respectively in East Africa. In 2013, Africa had the second highest number of glaucoma cases, with 8.3 million of the world's total 64.3 million cases (Tham *et al.*, 2014). The Temba glaucoma study, a population-based cross-sectional survey in urban South Africa, reported a prevalence of 5.3% of all types of glaucoma in South Africa, of which, the most common being POAG which accounted for 2.9% in South Africa (Rotchford *et al.*, 2003). These findings were similar to the findings of Kyari *et al.* (2015), who found a prevalence of 5.02% of all types of glaucoma in Nigeria.

In the Rapid assessment of avoidable blindness in the Northern eThekwini district of KwaZulu-Natal Province, South Africa (RAAB Study), Govender *et al.* (2015) found of the 1.9% of bilaterally blind individuals, 24.1% was due to glaucoma. The adjusted prevalence of all glaucoma types in individuals in KwaZulu-Natal of Zulu ethnic origin was 4.5%, occurring most in individuals 80 years and older (Rotchford and Johnson, 2002). Of all subjects with glaucoma, 58% had become blind in at least one eye and, 87% of those subjects with POAG had not been previously diagnosed (Rotchford *et al.*, 2003). The main concern is that there is a high prevalence of glaucoma sufferers. Almost half are undiagnosed in the developed world and 90% in a developing world context (Quigley and Broman, 2006).

2.1.6 Clinical presentation of glaucoma

One of the greatest challenges of the disease, apart from being a potentially blinding condition (Kanski, 2007), is its asymptomatic nature (Leite *et al*. 2011). The diagnosis of glaucoma is made by highly trained professionals performing a multitude of necessary tests, however, when resources are limited, the difficulty of this task is exacerbated (Leite *et al*. 2011). Retinal ganglion cell death and optic nerve fibre loss in glaucoma result in the characteristic "cupping" appearance occurring at the optic nerve head and retinal nerve fibre layer (Weinreb *et al*. 2014). In addition, the lamina cribrosa and its adjacent tissues, in particular, are strained by increased levels of IOP, although it is known that individuals with normal levels of IOP can also present with GON (Weinreb *et al*. 2014). According to the Journal of American Medical Association (JAMA) Rational Clinical Examination systematic review of POAG diagnosis, an increased cup-to-disc ratio (CDR), CDR asymmetry, disc haemorrhage, or elevated IOP, were high risk factors for glaucoma (Weinreb *et al*. 2014).

Whilst most patients with the disease have nearly "good" visual acuity, patients with glaucoma often complain of having "poor vision", however, Snellen visual acuity usually only deteriorates when the glaucoma has advanced (Hawkins *et al.*, 2003). Apart from light sensitivity, (probably the greatest symptom) there are other aspects which are involved when a patient has this condition- poor motion perception, decreased discrimination of high spatial frequencies and abnormal colour vision (Crabb *et al.*, 2013). In 1912, Kollner described colour vision loss due to ocular disease- Kollner's rule- which states that those patients with retinal disease will develop blue-yellow colour vision loss, whilst those with optic nerve disease will develop red-green colour vision loss, with one of the exceptions being glaucoma- presenting with predominantly tritan colour vision deficiency (Pacheco-Cutillas *et al*. 1999).

Visual field loss has been the most documented functional deficit occurring with glaucoma and has been frequently misrepresented as a black tunnel or patches obscuring parts of the patient's field of view, however Crabb *et al.* (2013) found that patients with glaucoma perceive their field of view as a combination of perceiving blur and missing areas. Scotomas in a pre-chiasmal, nerve fibre bundle-type distribution occur as a functional deficit, matching observed changes at the ONH (Casson *et al.*, 2012). Paracentral scotomas and a reduction of sensitivity in the arcuate regions are common visual field defects in early glaucomatous optic neuropathy (Pacheco-Cutillas *et al*. 1999). It was also found in patients with glaucoma, with visual acuity of 20/40 or better, there is a significant correlation between a reduction in contrast sensitivity and visual field loss- with the disease affecting contrast sensitivity more than Snellen acuity (Hawkins *et al.*, 2003).

2.2 Glaucoma in developing countries

In developing countries, vision impairment remains a serious global eye health issue, with Africa accounting for 16.6% of the current global distribution of blindness (Jaggernath *et al.*, 2014). The majority of preventable ocular problems (cataracts, trachoma, conjunctivitis, etc.) which can cause vision impairment and lead to blindness in developing countries are linked closely with poverty, mainly through lack of sanitation, poor or inadequate water supply, malnutrition and the lack of education (Jaggernath *et al.*, 2014).

Glaucoma generally goes undiagnosed in developing countries (Quigley, 1996) because of lack of awareness of the disease and its effects (Rait, 1996) and has been included as a third major cause of blindness (Jaggernath *et al.*, 2014). In developed countries, less than 50% of those affected with glaucoma are aware of their condition (VeSathyamangalam *et al.*, 2009), however, the diagnosis of glaucoma occurs at a much earlier stage than in developing countries due to the increased awareness of the condition (Attebo and Mitchell, 2007). The costs of standard methods for screening, including computerised perimetry, are not affordable, lengthy (Govender *et al.*, 2015) and are relatively inaccessible in most developing countries (Ong *et al.*, 2014).

In addition, the lack of financial and human resources required for basic eye-care services are not available, with the number of ophthalmologists available in developing countries estimated to be at one per 500 000 in Africa and one per 200 000 in Asia (Thomas, 2012). In South Africa, the ratio of optometrists to the population is approximately 1:17600 (Naidoo, 2007), however most are confined to the cities and serve only those with medical insurance. Reliance on opportunistic case finding by practitioners rather than comprehensive community based screening will, therefore, result in patients developing substantial visual field loss before glaucoma is actually diagnosed (Thylefors *et al.*, 1995).

2.2.1 Barriers to accessing eye care services in South Africa

The total population of South Africa is approximately 54 million, with males making up 51.3%, and females 48.7% (Statistics South Africa, 2014). Majority of this population is made up of individuals of African origin- 79.2%, followed by 9.6% Caucasians; 8.9% Mixed race; 2.5% Indians/Asians and 0.5% of other race groups (Statistics South Africa, 2014). Figure 2.2 below graphically depicts the distribution of eye health care in South Africa. Eighty percent of the population rely on the services of the public sector, whilst the remaining 20% are served by the private sector – see Figure 2.2 (Keeton, 2010).

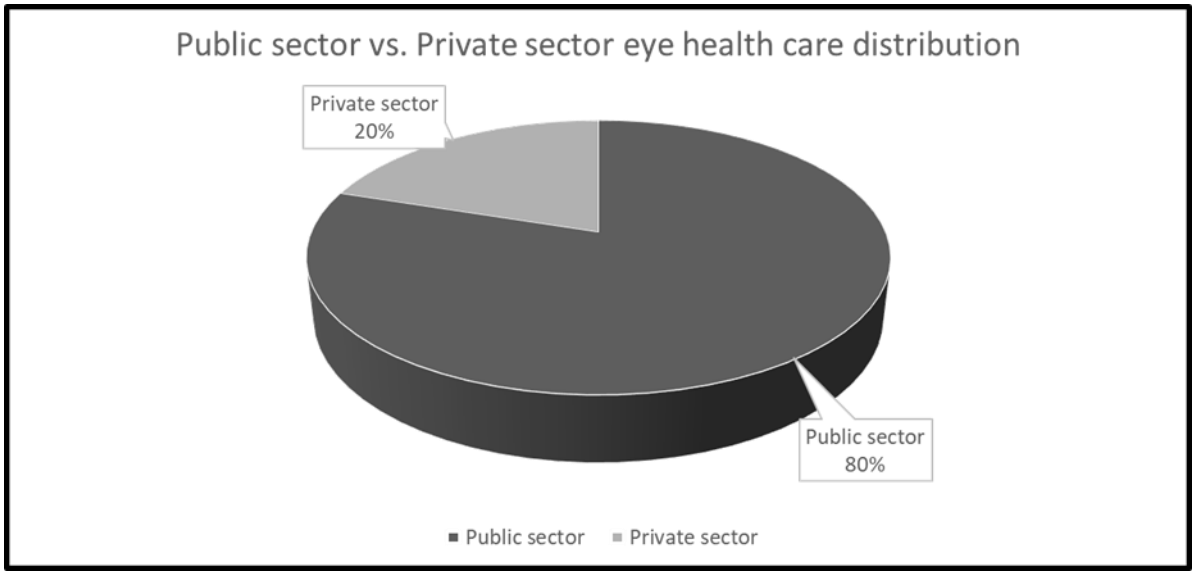

Figure 2.2. Distribution of eye health care services between the public and private sector

One of the nine provinces of South Africa, KwaZulu Natal (KZN), has the second-largest population in the country, estimated at just over 9.5million (Statistics South Africa, 2014). Making up the population are people of African, Indian, Caucasian and Mixed race origin. Individuals of African origin make up 8.1 million (83.5%) and those of Indian origin (804 839) 8.2% of the total population in KZN, with Mixed race and Caucasians making up 2.5% and 5.7% respectively (Jacobs *et al*. 2009).

Despite suggestions that around 80% of vision impairment is reversible and treatable, it still remains a serious global health issue with over 285 million people having vision impairment, and glaucoma being

the third major cause of blindness, after cataract and uncorrected refractive error (Jaggernath *et al.*, 2014). It has also been suggested that poverty and eye health often have a direct and indirect link, with poverty being closely related to education levels (Jaggernath *et al.*, 2014). Just over half (50.9%) of the world's poor are located in Africa (Jaggernath *et al.*, 2014) and Statistics South Africa reported the poverty level in KZN was recorded at 69.1% (Statistics South Africa, 2011).

In 2006 it was noted that 76.7% of households in KZN, South Africa, headed by those without formal education, were living in poverty (Statistics South Africa, 2011). In the public sector of the province, there are 38 optometrists currently employed (Naidoo *et al*. 2013) and only about 25% of ophthalmologists in the province serve the public sector (Dhlomo, 2013).

In 2003, WHO reported more than 60% of South African health care institutions found it difficult to fill existing posts and this critical shortage of trained personnel plays a fundamental role in the implementation of health services at district level (Kautzky and Tollman, 2008). Further, the public sector provides to an estimated 35 million people, and receives only about 38% of the national health expenditure, in comparison to the 62% provided to approximately 7 million people of the private sector (Kautzky and Tollman, 2008).
Research has shown that timely intervention can prevent blindness (Kayange *et al.*, 2014) and therefore screening must be efficient and effective enough to detect patients with glaucomatous changes.

2.2.2 Challenges faced in accessing health care in South Africa

In a developing country, such as South Africa, the accessibility and availability of health care to the population should not be an unaffordable burden on individuals. Factors such as: race, socio-economic status, insurance status and urban-rural location, influence the access to care. These factors should motivate broadening health-care coverage in countries with low to middle income (Harris *et al.*, 2011).

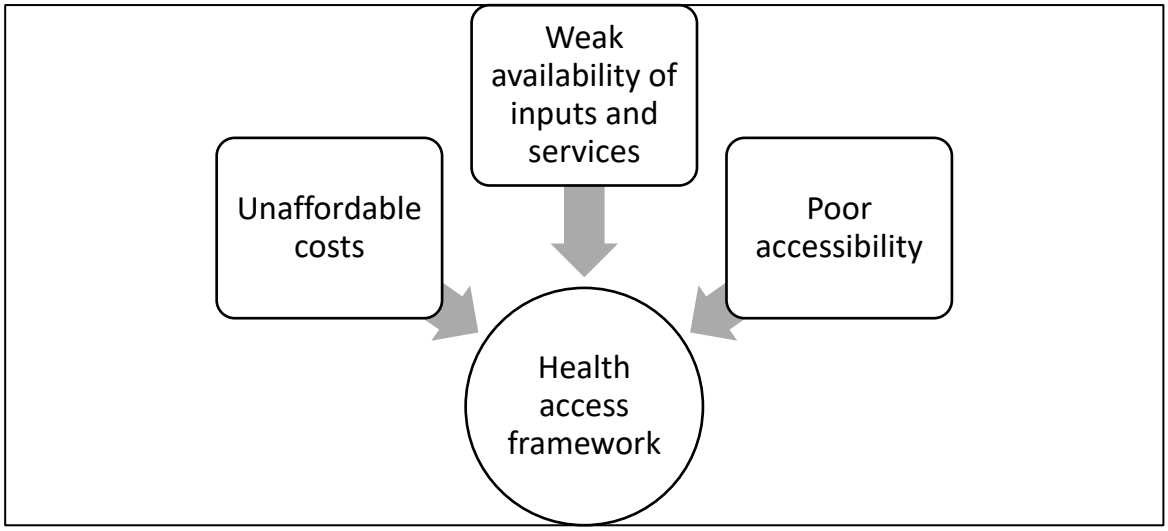

Figure 2.3 Health access framework

2.2.2.1 Accessibility, availability, and affordability of eye care services

The challenge amongst individuals residing in rural and remote areas, is the lower socio-economic status which contributes significantly to poverty. These individuals are faced with an inadequate supply of eye care services due to the limited or non- availability, accessibility, and affordability of these services, as depicted in Figure 2.3 above. These three key factors which majorly influence access to health care is collectively termed the "Health access framework''. In addition to these, cultural beliefs can also influence the utilisation of eye care services, where they are available (Ntsoane *et al*., 2012).

In comparison to other countries in Africa, South Africa has more eye care practitioners available, however, the distribution of these personnel is poor and has impacted on the inaccessibility and unaffordability of services (Naidoo *et al.*, 2003). Despite South Africa's peaceful transition into a democracy since 20 years ago, there still remains a considerable burden with regards to the health of all its citizens, which include persistent social disparities and limited human resources (Mayosi and Benatar, 2014). In addition, the reduction of the overall burden of visual impairment and blindness, globally, can be closely associated with the education and awareness of the utilisation of eye care services (Ntsoane *et al*., 2012).

2.2.2.2. Age influence

Whilst research reports that older individuals are more susceptible to ocular diseases and are more likely to seek eye care services. Ntsoane et al., (2012), however, found older individuals of Limpopo, South Africa, did not follow this trend.

2.2.2.3 Gender

It has been reported that in Africa, and globally, women are 1.4 times more likely than men to be blind (Mganga *et al*., 2011). Approximately two-thirds of the global burden of blindness is bore by women, the bulk of which is attributed to cataract (Lewallen and Courtright, 2002). It was noted that females do not receive the same rate of cataract surgery as males. According to a study, of the thirteen South African males blind by cataract, all thirteen had undergone cataract surgery intervention, whilst only less than half (20) of the 44 cataract blind South African females underwent cataract surgery (Lewallen and Courtright, 2002). In Africa, the prevalence of cataract blindness could be reduced as much as 12% if women received the same frequency of cataract surgery as men (Mganga *et al*., 2011). Socioeconomic factors such as socioeconomic status, marital status, literacy and gender-defined roles have been thought to influence the gender-based gap in seeking eye care and other health care services (Lewallen and Courtright, 2002). Another suggested factor is the increased longevity in females as compared to males, making age-related ocular conditions (such as age-related macular degeneration and glaucoma) more rife amongst females (Abou-Gareeb *et al.*, 2001).

2.3 Glaucoma screening

Screening tests are used when the gross impact of disease on the visual field is required as compared to a detailed one (Elliott, 2013). The present methods for glaucoma screening are expensive and are a barrier to identifying people at high risk for glaucomatous disease compared to other ocular diseases (Quigley, 1996). Apart from the cost, most of the current methods of screening require a significant amount of testing time (Johnson and Samuels, 1997) or sufficient expertise (e.g. for optic nerve examination). If glaucoma is left undiagnosed, treatment cannot be initiated and therefore many activities of daily living are affected as the disease progresses, including reading and writing, mobility and discrimination of colours (Taylor & Keeffe 2001); (Rong-jiang *et al.*, 2011). In addition, lack of treatment can lead to blindness with its consequent health and socio-economic effects (World Health Organisation, 2006).

2.3.1. Visual field perimetry and developments in glaucoma detection tests

Visual field perimetry is vital in detecting the functional loss that accompanies glaucoma (Nouri-Mahdavi, 2014) as well as measuring the severity and progression of disease (Peters *et al.* 2015). These tests are subjective in nature and require the patient to understand the testing instruction, fully cooperate, and complete the entire test in order to provide accurate and reliable results (Alencar and Medeiros, 2011). Visual field tests can be static, kinetic, and manual or automated (Dersu *et al.*, 2006). An essential component for accurate diagnosis and implementation of appropriate management regimens is the reliability and repeatability of the visual field test (Newkirk *et al.*, 2006). Factors influencing the

accuracy of visual field testing include refractive error, pupil size, ocular structural abnormalities and intraocular stray light. Patient profile and co-operation, defective instruments, the operator's technical skill, as well as the testing environment were also found to be contributing factors (Nussdorf and Alastair, 2003).

2.3.1.1 Non-Automated visual field tests

2.3.1.1 (a) Confrontation

This is a screening method of visual field testing that has the potential to detect gross visual field defects in eye diseases, and is useful in picking up visual field loss in advanced glaucoma (Broadway, 2012). There are many variants of confrontation testing, which involves the comparison of the examiner's visual field with that of the patient's (Elliott, 2013). Confrontation testing is used to screen many abnormalities therefore one cannot definitively diagnose glaucoma based on the results (Pandit *et al*. 2001). Confrontation tests, when performed in combination, rather than individually were found to be more sensitive in detecting visual field loss (Kerr *et al.*, 2010).

2.3.1.1 (b) Tangent Screen (Campimetry or Scotometry)

The Tangent screen allows the patient's central and paracentral 30-degree visual field to be mapped out and can detect up to 90% of all visual defects in the testing area (Broadway, 2012; Bhalla *et al.*, 2016). It is a relatively simple screening method to use and is more sensitive than the confrontation technique, however, is not as sensitive as automated perimetry in detecting early defects (Bhalla *et al.*, 2016).

As the examiner, a few precautions need to be taken, such as: careful monitoring of patient fixation and maintaining a proper testing distance, adequate illumination (Broadway, 2012) and instructions to patient, proper movement of target and mapping from blind to visible area (Bhalla *et al.*, 2016).

2.3.1.2 Automated visual field tests

2.3.1.2 (a) Standard Automated Perimetry (SAP)

Standard automated perimetry (SAP) is considered to be the gold standard methodology in the assessment of visual fields (Patyal *et al.*, 2014). The Humphreys Visual Field Analyser (HVFA) is a standard automated perimeter (Alencar and Medeiros, 2011). However, SAP instruments are expensive and not portable, with longer test duration; thus, it is not the instrument of choice for screening visual fields in primary eye care settings (Bergin, 2011). Research has shown that up to 50% of retinal ganglion cells are lost before a visual field defect can be detected with SAP (Ong *et al.*, 2014).

Although recent developments have seen the advent of more sophisticated psychophysical visual function tests, visual field instruments remain expensive and relatively inaccessible in rural or underdeveloped areas (Ong *et al.*, 2014).

2.3.1.2 (b) Humphreys Visual Field Analyser (HVFA)

The HVFA is regarded as the gold standard among standard automated perimeters (Choplin *et al*. 1998). Two thresholding strategies are offered using the HVFA, namely the 24º strategy (24-2) which tests 54 points, and the 30º (30-1) strategy which tests 76 points (Kanski, 2007). HFVA results are normally represented as a grey scale image and are further presented via analysis software (Statpac) provided by the instrument (Artes, 2012). It computes maps of the total deviation, pattern deviation and global indices such as mean deviation (Kanski, 2007). The total deviation map presents decibel deviation from age-corrected normal threshold sensitivity (Artes, 2012). Even though the grey scale map seems the easiest to evaluate, it is less reliable compared with the total and pattern deviation probability plots (which prove very useful when distinguishing the effects of cataract from glaucomatous damage on the visual fields) (Alencar and Medeiros, 2011).

The HVFA uses two programmes for glaucoma screening, the SITA Standard (SS) and SITA Fast (SF) (Pierre-filho *et al.*, 2006). The Swedish Interactive Threshold Algorithms (SITA) is incorporated into the HVFA, which also includes three reliability indices: false positives, false negatives and fixation losses (Newkirk *et al.*, 2006). Those patients whose fixation losses exceed 20% or whose false positive or false negative errors exceed 33% are not considered reliable (Newkirk *et al.*, 2006). The full threshold strategy has been the most utilised practice for monitoring glaucoma, however, recent advances have proven many other test strategies, including SITA, that reduces test duration and patient fatigue (Newkirk *et al.*, 2006). Patients may need to take a break between testing each eye due to fatigue and this can result in inaccuracies in results (Reddy, 2006). The Glaucoma Hemifield Test (GHT) provides a useful summary measure of the visual field which may be classified as outside or within normal limits, borderline, or as having a general reduction in retinal sensitivity, providing statistical evidence about a visual field defect (Burr *et al.*, 2007).

2.3.1.2 (c) Frequency Doubling Perimetry (FDP)

The frequency doubling effect is a phenomenon that occurs when a low spatial-frequency (<4cyc/deg) grating that undergoes high temporal-frequency (>15Hz) counter-phase flicker appears as a shimmering grey pattern with double the original spatial frequency (Chauhan and Johnson, 2000).

Frequency doubling technology (FDT) perimetry determines the contrast sensitivity for detecting the frequency doubling stimulus (Alencar and Medeiros, 2011). Frequency Doubling Perimetry has a high sensitivity and specificity in detecting glaucomatous visual field loss, as well as a significantly shorter

test duration as compared to conventional perimetry (Chauhan and Johnson, 2000). It is also portable and considerably easier to use for the patient and the examiner, and seems to be promising in the field of early glaucoma diagnosis (Alencar and Medeiros, 2011). Images of the patient set-up and the FDT result sheet can be seen below in Figure 2.4(a) and Figure 2.4(b).

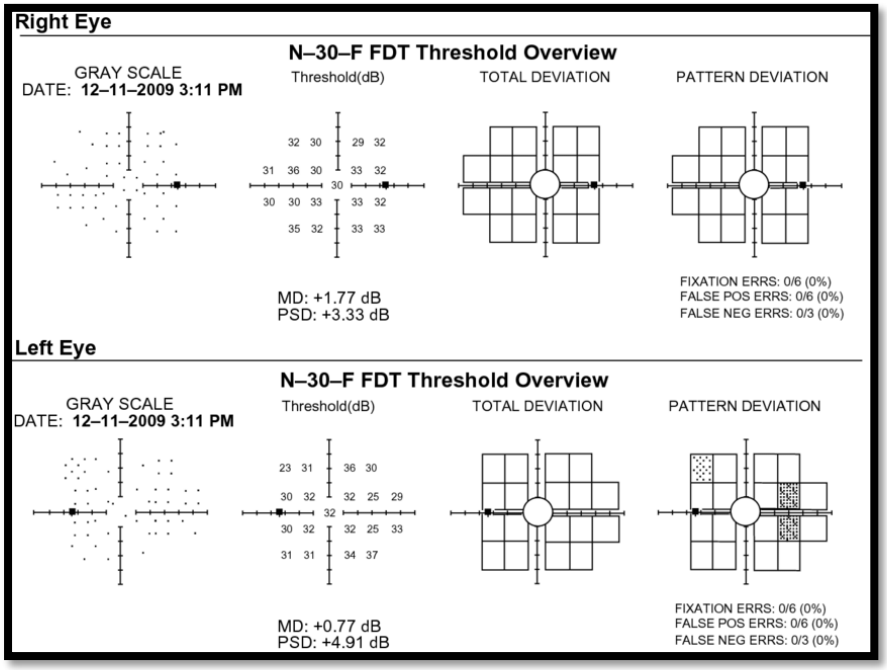

Figure 2.4(a) Frequncy Doubling Technology (FDT) result sheet **https://www.researchgate.net/figure/Frequency-Doubling-Technology-FDT-Visual-Field-Tests-showed-normal-VF-OD-and-a-few_fig7_49616993**

Figure 2.4(b) FDT patient set-up

http://oogziekenhuis.me/Frequency_Doubling_Perimetry/Frequency_Doubling_Perimetry.html

2.3.1.2 (d) Rarebit perimetry (RBP)/(Microdot perimetry)

Rarebit perimetry (RBP) is another perimetric method that comprises very small stimuli (individual dots) against a dark background, presented on a regular computer liquid crystal display (LCD) monitor

(Brusini *et al.*, 2005). Microdots are used to evaluate the density of coverage within the central 30º of the visual field, with deeper defects having a larger density of micro-holes (Alencar and Medeiros, 2011). Although the use of RBP on glaucomatous patients has yet to be reported in the literature, it has proven promising in detecting the early visual field damages in patients with neurological disorders (Brusini *et al.*, 2005).

2.3.1.2 (e) Microperimetry

Microperimetry, also known as fundus perimetry (Lima *et al.*, 2010), assesses visual field sensitivity between (0 and 34 decibels) by directly projecting a target light onto the retina, as can be seen in Figure 2.4(c) below (unlike onto a screen like with the gold standard HVFA) (Matsuura *et al.*, 2018). Tracking of the retinal location is automatic and target location is then aligned accordingly. Measurements are carried out similar to the HVFA, and the MP-3 Microperimeter uses a 4-2 full-threshold staircase strategy, assessing 68 points on the 10-2 test grid. Reliability indices of the Microperimeter is the same as compared to the HVFA and upon validating this instrument whilst evaluating glaucoma patients, the MP-3 Microperimeter was found to have a similar test-retest reproducibility relative to the HVFA, but an improved structure-function relationship with the Ganglion Cell Complex (GCC) thickness. The MP-3 Microperimeter did, however, have a longer mean test duration of 10 minutes and 29 seconds (10m29s ± 2m55s) as compared to the HVFA (mean test time of 7m06s ± 0m49s) (Matsuura *et al.*, 2018). Lima et al. (2010) concluded that Microperimetry detected a reduction in retinal sensitivity in OCT structurally damaged areas with normal SAP results, and suggests subtle paracentral functional deficits may be present in a higher number of glaucomatous eyes than what is generally believed.

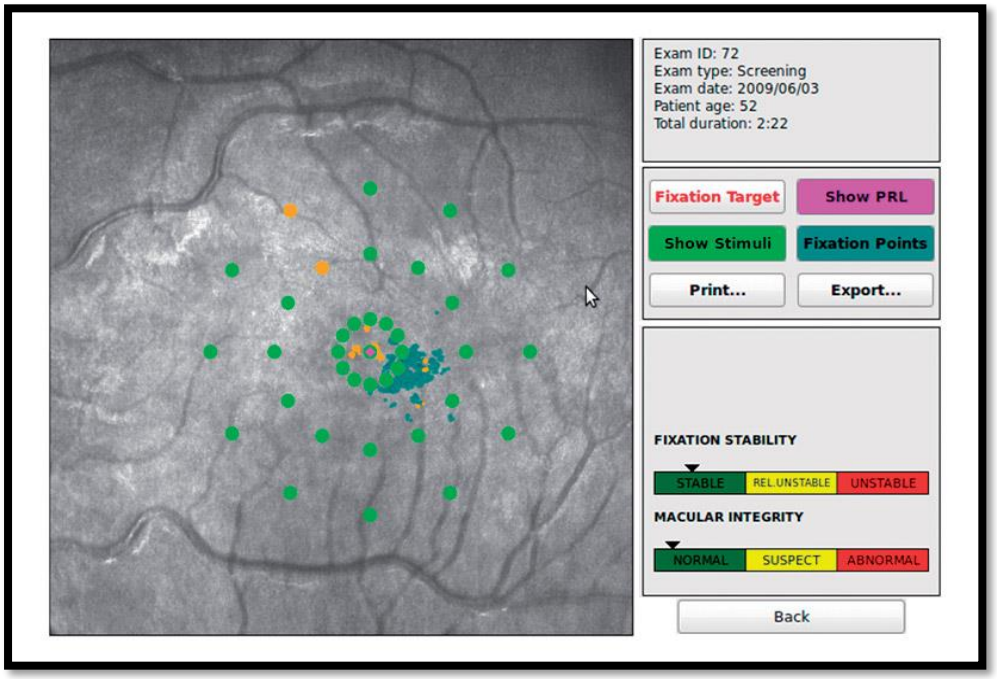

Figure 2.4(c) Microperimetry fundus view

https://www.centervue.com/products/maia/

2.3.1.2 (f) Moorfield's Motion Displacement Test (MMDT)

Professor Fitzke, from the Institute of Ophthalmology at University College London (UCL), developed the original Motion Displacement Test (MDT) in the 1980's (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). It comprised of a single line stimulus presented just above the blind spot on a computer and was found to be a detector of glaucomatous visual field loss (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). Evidence of elevated motion displacement threshold was shown in areas of the visual field not usually affected when assessed by SAP (Westcott *et al*. 1998) and the MDT proved to be resistant to the effect of media opacity (Loughman *et al.*, 2013). These properties provided the rationale for the development of the test to take on a multi-location format and in 1999 the Moorfields Motion Displacement Test (MMDT) developed by the Glaucoma Research Unit at Moorfields in combination with the Institute of Ophthalmology, UCL, was introduced (Moorfield's Eye Hospital: NHS Foundation Trust, 2008).

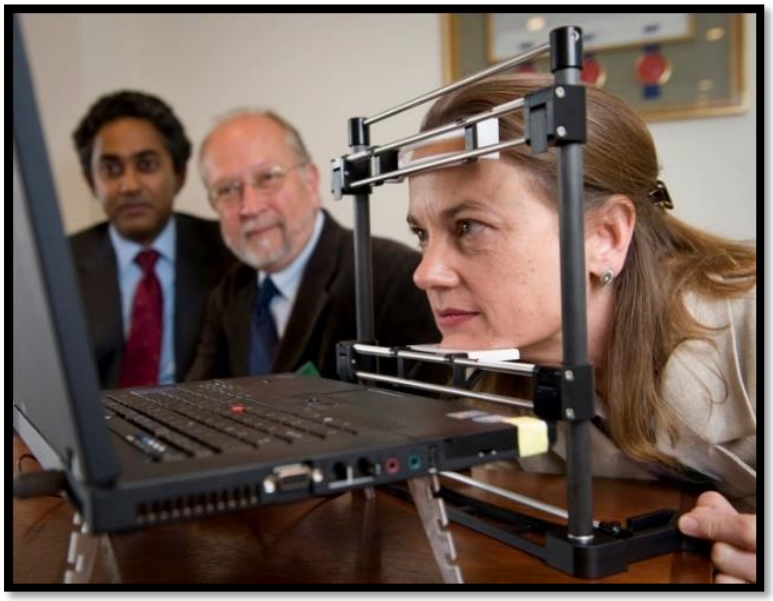

Figure 2.4(d) Moorfields Motion Displacement Test (MMDT) with patient set-up
http://www.optometry.co.uk/news-and-features/news/?article=483

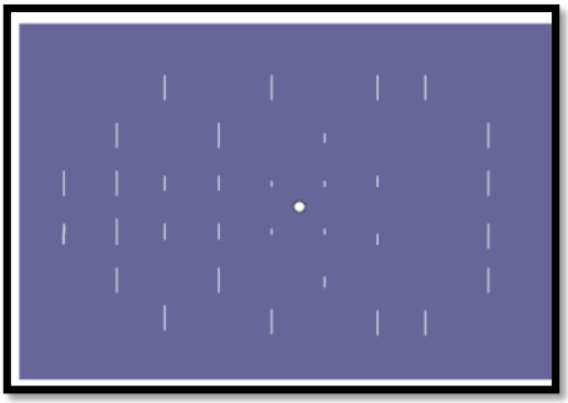

Figure 2.4(e) MMDT screen view with 32-line stimuli and fixation dot
http://www.staff.city.ac.uk/d.crabb/CB%20UKEGS%202008.pdf

The MMDT is a multi-location test, presenting vertical line stimuli in 32 test locations (Figure 2.4(e)) on a computer screen; each scaled by estimate of retinal ganglion cell density and selected using the Garway-Heath anatomical map (Loughman *et al.*, 2013). The MMDT aims to determine the smallest perceptible positional displacement, with the displacement giving rise to the sensation of movement (Verdon-Roe *et al.*, 2006). However, its accuracy in comparison to the HVFA has not yet been established. Therefore, this study set out to compare the visual field defects, if any, obtained by the Moorfields MMDT to that obtained with the HVFA in diagnosed glaucoma subjects.

Research has found that there was an indication of good topographical correspondence of the MMDT with Standard Automated Perimetry, showing 70% point-wise agreement of the 32 matched locations. Ong et al. (2014) concluded that the supra-threshold MMDT showed good diagnostic performance for diagnosing glaucoma, when glaucoma was defined by structural criteria. It was also found that this perimetric method for the detection of clinically and structurally defined glaucoma produced excellent sensitivity and specificity values of more than 85%, which are clinically significant (Ong *et al.*, 2014).

Currently, the Moorfields MMDT offers 2 strategies (Bergin, 2011):

1. The Enhanced Supra-Threshold Strategy (ESTA) which takes 90-120 seconds per eye and is designed for rapid case finding in the community (Bergin, 2011)
2. The Weighted Binary Search Threshold Strategy (WEBS) which takes approximately 9.4s per location (4.5- 5minutes per eye) and is designed for more detailed investigation in hospital settings.

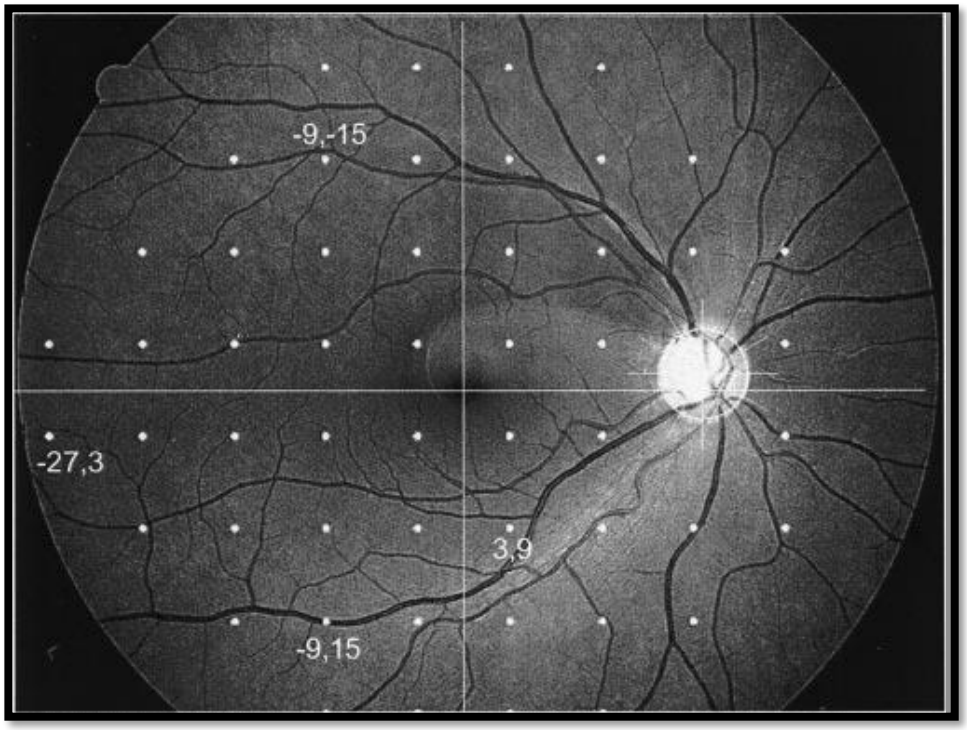

Figure 2.5 Location of MMDT locations on the retina. (Verdon-Roe *et al.*, 2006) **http://www.iovs.org/content/47/11/4847.short**

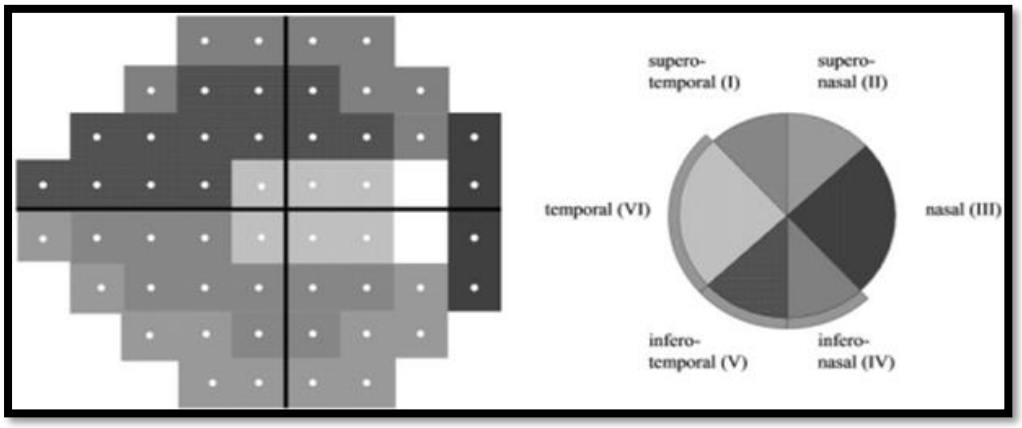

Figure 2.6 Schematic structure-function map according to (Garway-Heath *et al.*, 2000) Visual test points/sectors of the visual field can be related to sectors of the ONH. **http://openi.nlm.nih.gov/detailedresult.php?img=3585161_pone.0057663.g004&req=4**

The first plot on the MMDT result page is the 'pass/fail' plot which is determined by the displacements seen or missed at a specific location, as well as performance at anatomically related locations. The second plot is the 'probability' plot which is determined by the spatial filter of the ESTA. The values in this plot estimate the 'probability of true damage' (PTD) which is calculated according to the relationship between each field location and the number of unseen responses. A higher PTD indicates a higher

probability that the location is damaged- a value of more than 3 is regarded as a fail (Loughman *et al.*, 2013). The last plot is the 'greyscale' plot which applies the Garway-Heath anatomical map to relate the field defect to the optic nerve head. Each letter on the field corresponds to the anatomically related sector of the optic nerve head (Garway-Heath *et al.*, 2000). Global PTD represents the sum of the PTD for each location. This figure is then divided by 100, recorded to 2 decimal places. Again, the higher the value of PTD, the higher the probability of 'true damage' (Loughman *et al.*, 2013).

A challenge with making comparisons between the MMDT and Standard Automated Perimetry (SAP) is that different measurement scales are applied to different psychophysical stimuli (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). Currently, the NHIS Biomedical Research Centre for Ophthalmology at the Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology are developing a reference scale for improved comparison between the MMDT and SAP (Moorfield's Eye Hospital: NHS Foundation Trust, 2008).

2.4 Factors influencing the accuracy of visual field testing

The factors known to influence the accuracy of visual field testing include:

2.4.1 Refractive error

Refractive error has an effect on the visual field test results obtained with some instruments since it decreases stimulus clarity and therefore the determination of the subjects' refractive error and near addition is crucial when conducting the HVFA (Nussdorf and Alastair, 2003). Research has found that if the patient's prescription is incorrect, increased variability of visual fields and refractive scotomas can result (Johnson, 1996; Rowe and Meigen, 2007). A significant decrease in central sensitivity is seen in uncorrected subjects (Corallo *et al.* 1997). Myopes with normal tension glaucoma and primary open angle glaucoma were found to have a decrease in sensitivity in the lower centro-cecal area of the visual field (Johnson, 1996). Corallo *et al.* (1997) found defects in high myopes (>7.00 DS). The standard procedure is that most perimetry is performed with a stimulus at approximately reading distance, so a near correction should be used for presbyopic patients (Bergin, 2011). When using the MMDT, testing patients with uncorrected refractive error has little impact on the ability of the MMDT to discriminate between healthy and glaucomatous eyes (Bergin, 2011). This is important as the MMDT is envisaged to be beneficial as a screening test in the community, where there may be a lack of time to assess the need for refractive correction (Loughman *et al.*, 2013).

2.4.2 Pupil size

It is important to maintain a constant pupil size by maintaining standardised illumination conditions during and between tests as it influences test results (Nussdorf and Alastair, 2003). Miosis decreases sensitivity in the peripheral field and increases variability in the central field in both normal and glaucomatous eyes (Mendivil, 1997).

2.4.3 Ocular structural abnormalities

Structural abnormalities of the eyelids or orbits can bring about variations in visual field test results and abnormalities such as ptosis, dermatochalasis, prominent eyelashes, and deeply set eyes can cause a decrease in the superior visual field (Alastair and Denniston, 2009). The development of media opacities, such as cataract, can also affect the results (Chauhan and Garway-Heath, 2008), however, the Moorfields MMDT is robust to optical blur and cataract (Moorfield's Eye Hospital: NHS Foundation Trust, 2008; Bergin, 2011).

2.4.4 Intraocular stray light

Research has indicated that moderate to large increases in intraocular stray light (IOS) has significantly affected perimetry thresholds in tests like the Standard Automated Perimetry (SAP), Frequency-doubling technology (FDT) perimetry and Flicker-defined Form (FDF) perimetric tests (Bergin *et al.*, 2011). However, the Moorfields MMDT has remained largely unaffected by the same range of stray light levels (Bergin *et al.*, 2011). Furthermore, it was found that luminance reduction and light scattering have marked effects on frequency doubling and conventional white-on-white perimetry, but little effect on motion displacement perimetry (Membrey *et al*. 1998).

2.4.5 Other factors

A variety of other factors including the patient profile and co-operation, defective instruments, the operator's technical skill, as well as the testing environment can also influence the accuracy of visual field testing (Nussdorf and Alastair, 2003). Additional factors which can influence test outcomes include cognition, attention, higher order functions, practice, learning and fatigue, especially after 5-7 minutes of testing (Infeld, 1998). Since the original MMDT was found to be too long for screening purposes i.e. 5-7 minutes per eye, the development team collaborated with City University since 2006 to develop methods with the aim of reducing the test duration (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). Other factors include the stimulus size, diabetes, alcohol (Wild and Betts, 1990) and drug abuse which causes depression of the central nervous system (Nussdorf and Alastair, 2003).

2.4.5.1 Importance of improving test duration during visual field assessment

It is essential that the patient's responses are monitored during testing as these impact on the reliability of test results. Therefore, by reducing test duration, more reliable and repeatable results should be obtained due to a less fatigued patient (Newkirk *et al.*, 2006). Despite advances in automated perimetry, visual field testing (although non-invasive) still remains subjective in nature as it depends largely on the patient's responses (Rudnicka and Owen, 2007). Bergin et al.(2011) reported of three screening perimetric devices, the Frequency Doubling Technology C-20 (FDT C-20) was the fastest (63 sec), followed by the MMDT ESTA (102 sec) and lastly Standard Automated Perimetry (SAP) (171 sec), when testing glaucomatous subjects. Part of this difference in test duration could be attributed to the smaller number of test locations included in the FDT (17 test points) and MMDT (32 test points) as compared to the HVFA (54 test points) (Bergin, 2011). This is potentially highly advantageous for screening purposes as a means to optimise use in community-based settings, allowing for improved productivity in glaucoma detection (Rudnicka and Owen, 2007).

2.4.5.2 Anxiety levels and glaucoma

The patient's response with regard to their motivation and anxiety also contribute to the testing results and is one of the most important factors which often gets ignored by the practitioner (Infeld, 1998). It has been reported that up to 63% of referrals are false positives, therefore screening is essential as over-referrals generally cause an unnecessary anxiety and inconvenience to the patient, as well as excess burden on health care resources (Burr *et al.*, 2007). A study conducted by Chan *et al*. assessing psychosocial functioning with use of the Glau-QoL-36 questionnaire, found an adverse effect of early stage glaucoma on anxiety, self-image and confidence in health care. A further increase in anxiety levels as visual acuity and self-image deteriorates was also noted (2015). The study concluded that those patients with glaucoma had 63% higher anxiety, 71 % lower self-image, 38% lower psychological well-being and 32% lowered confidence in health care as compared to the control group (Chan *et al.*, 2015).

2.4.5.3 Familiarity with use of a mouse

It was reported, during a study on the impact of computer knowledge on the reliability of results obtained from the MMDT, that the majority of subjects were excluded because of their inability to effectively use a computer mouse during extended testing periods. This consequently resulted in a high false positive rate (Loughman *et al.*, 2013). In another form of screening visual fields, RareBit Perimetry (RBP) was found to be a faster and easier form of screening as compared to SAP, however, the only challenge occurred in the elderly age group who were unfamiliar with the use of a computer mouse (Brusini *et al.*, 2005). Besides the unfamiliarity with the use of a computer mouse, it is also vital to acknowledge the onset of glaucoma which predominantly occurs in the elderly, many of whom have dexterity issues, amongst various other ageing processes. Generally, reflexes slowdown in the elderly, along with hearing loss- all of which contribute to the understanding and performance of the test (Voelcker-Rehage, 2008). The above reasons indicate the need for customised buttons as a method of selection when using a computer-based visual field test (Loughman *et al.*, 2013). Due to the above-mentioned factors, it was decided that the subjects' experience using a mouse versus button be evaluated.

2.5 Advancements in visual field testing

2.5.1 Head mounted perimeter "*imo*"

The head mounted perimeter *'imo'* (CREWT Medical Systems, Inc., Tokyo, Japan) was released in 2015 and consists of a main perimeter unit, user control tablet and patient response button, with the left and right optical system completely separated and can be performed without a dark room- allowing for mass screening (Matsumoto *et al.*, 2016; Yamao *et al.*, 2017). This device can display the same test target as the HVFA using full High Definition transmissive LCD and high intensity LED backlights

(Matsumoto *et al.*, 2016; Yamao *et al.*, 2017). The examiner controls the user tablet via Wi-Fi and the patient's response button is connected via Bluetooth which receives all patient responses (Matsumoto *et al.*, 2016). The wide-angle lens system measures the visual field within 35 degrees from the fovea (Goseki *et al*. 2016). It is performed at a viewing distance set at 1m and can be performed on patients with an uncorrected refractive error of -9.00DS to +3.00DS (Matsumoto *et al.*, 2016). An additional special feature is the binocular random single eye test (Matsumoto *et al.*, 2016; Yamao *et al.*, 2017). Importantly, the *imo* test patterns are compatible with those for the HFA 30–2, 24–2, 10–2 and 24+ test programs with additional test points in the central 10°VF of the 24–2 program (Matsumoto *et al.*, 2016). It is light and compact, thereby allowing for the test to be performed in almost any location (Yamao *et al.*, 2017).

2.5.2 Melbourne Rapid Field (MRF)

The Melbourne Rapid Field (MRF), a novel visual field test, is an iPad based tangent perimeter, able to perform fast thresholding at several locations within 30 degrees of fixation (Kong *et al.*, 2016; Nesaratnam *et al.*, 2017). Its portability and shorter test duration (approximately 4.5 minutes per eye) is an advantage over conventional standard automated perimetry as it allows for the test to be performed on patients who are bed-bound or in situations where visual field testing equipment is inaccessible, such as in developing countries and rural areas (Vingrys *et al.*, 2016; Nesaratnam *et al.*, 2017). The test is performed under monocular conditions and the patient is asked to fixate a target on the iPad tablet at a distance of 33cm and is required to tap on the screen with their finger every time a stimulus is seen (Kong *et al.*, 2016; Vingrys *et al.*, 2016). As with conventional perimetry, reliability indices include fixation losses, false positive and false negative errors (Nesaratnam *et al.*, 2017).

From the literature, it is evident that medical technology has advanced to optimise patient diagnosis and management. Over the decades, there have been many improvements on visual field instruments in detecting various ocular diseases, most specifically, glaucoma. Whilst vision impairment remains a serious issue in developing countries, there are still many barriers in accessing eye health care. Some of the reasons include limited affordable and adaptable solutions enabling remote access, lack of resources, socio-economic status and level of education. It is therefore essential that the improvements in technology consider the portability, affordability and accessibility of the instruments to allow for mass community-based screening.

CHAPTER 3: Research methodology and design

The following chapter highlights and justifies the scientific basis of the study and will explain in detail the processes involved to conduct the study.

3.1 Introduction

This chapter explores the research methodology and design of the study, the processes and methods used to achieve the study objectives.

3.2 Study design: This was an observational, analytical study (involving comparative and quantitative methods).

3.3 Setting: The study was conducted at McCord's Provincial Eye Hospital and Prince Mshiyeni Memorial Hospital, district hospitals in KwaZulu Natal, South Africa. McCord Hospital was established in 1909 by Dr James McCord, who was sent to South Africa by the American Board Missions. The iconic hospital was one of the first institutions in the country to implement training programmes in 1914 for black nurses. During the apartheid days, unsuccessful attempts were made to shut the doors to McCord Hospital. After its closure in 2012, McCord Hospital was taken over in February 2014 and the doors were once again opened to serve members of the community. It now functions primarily as a provincial eye hospital (2017).

3.4 Participants: Participants with glaucomatous (case) and non-glaucomatous (control) eyes were invited to participate in the study. Permission to access patient files was obtained from hospital management to extract demographic and clinical data for potential participants (Appendix 8 and 9). A chart review revealed participants diagnosed with glaucoma who were scheduled to attendthe eye clinic to form the case group. Those participants booked for refraction at Prince Mshiyeni Memorial Hospital (PMMH) were recruited as controls.

3.5 Sampling: A purposive sampling strategy was used to select the test subjects sample from the population of participants diagnosed with glaucoma, at McCord Provincial Eye Hospital, a district hospital in KwaZulu Natal, South Africa. All those subjects booked for refraction at PMMH without ocular pathology were selected for the control group, after careful review of their chart to ensure inclusion criteria were met. Data was collected from Monday to Friday between 08h00 and 14h00.

3.5.1 Sample size: A qualified statistician from the African Vision Research Institute (AVRI) was consulted to determine the sample size. When assessing the diagnostic accuracy of a new instrument

relative to the gold standard, it is important to assess the sensitivity and specificity of the instrument, as well as the positive and negative likelihood ratios in order to further validate the performance of the new instrument. After estimating the confidence intervals, the margin of error was found to be 12.2% for sensitivity (73%) and 8.2% for specificity (90%) (Baez *et al.*, 1995). Two samples were established separately since sensitivity and specificity are calculated from the true-positive and the true-negative, respectively. These values are usually different since there is a trade-off between sensitivity and specificity. Power analysis was used to establish narrower confidence intervals for the sensitivity and specificity estimates.

Calculation:

A three-step method was used to approximate the sample size *n** with 90 % power to estimate *p* with a margin of error no more than *M*. **Step 1** calculates a preliminary estimate *n* based on *p*●, the estimated sensitivity or specificity and *M*. **Step 2** gives 'power' to the sample size estimate by calculating *p**, or the 90 % lower bound around *p*● given *n*. **Step 3** calculates *n** using the same equation as Step 1, but substituting *p** for *p*●

Step 1:

$$n = \left(\frac{1.96}{M}\right)^2 . \hat{p}\,(1 - \hat{p})$$

	M	**P**	
INPUT	5	73	←Values in %
	0.05	0.73	←Values in decimal

Step 2:

$$\dot{\boldsymbol{p}}^* = \hat{\boldsymbol{p}} - 1.282 \sqrt{\frac{\hat{\boldsymbol{p}}\,(\mathbf{1} - \hat{\boldsymbol{p}})}{\boldsymbol{n}}}$$

Step 3:

$$\boldsymbol{n}^* = \left(\frac{\mathbf{1.96}}{\boldsymbol{M}}\right)^2 . \boldsymbol{p}^*\,(\mathbf{1} - \boldsymbol{p}^*)$$

n	**51**	
	Decimal	**Percentage (%)**
P-	**0.608153153**	**60.8153153**
P+	**0.851846847**	**85.1846847**
ME=	**12.184684751**	

Where *n*= sample size; *M*= margin of error; *p*●= estimate of sensitivity or specificity; *p**= lower bound of 90% Confidence Interval (CI); *n**= approximate number of samples needed for 90% power

Using the estimates above and the desired margin of error of less than or equal to 5%, the minimum sample size for the true-positive was calculated to be 177 and the minimum sample size for the true negative calculated to be 324 (Hess *et al*., 2012).

3.5.2 Sampling technique

Inclusion criteria:

The following subjects were eligible for inclusion in the study:

- Subjects diagnosed with glaucoma
- Subjects of all race groups
- Subjects of both genders
- Adult subjects (aged 40 years and older)
- "control" subjects included all those participants without any history of ocular pathology (including glaucoma) nor visual field defects.

Exclusion criteria:

The following subjects were excluded from the study:

- Subjects diagnosed with ocular pathology other than glaucoma
- Subjects with corrected visual acuity worse than 6/12 (to rule out other pathology or sources of variability
- Subjects with refractive error greater than +4.50DS and -6.00DS (due to the custom-specific sizing of the four central stimuli, which is resistant to optical defocus within the range of +4.50DS to -6.00DS) (Loughman *et al.*, 2013)

3.6 Data collection methods:

3.6.1 Preliminary testing:

For the case group, McCord Provincial Eye Hospital was visited on the days allocated to glaucoma participants, whilst for the control group, participants booked for refraction at Prince Mshiyeni Memorial Hospital were approached regarding participation. Access to patient files was obtained from the hospital in order to extract demographic and clinical data. Each participant was provided with an information document (Appendices 1 and 2) and consent form (Appendices 3 and 4) (in their home language, which was then signed and attached to their questionnaire. The questionnaire (see appendix 5- data collection form) was provided to each participant which had to be answered prior to testing as well as after. The questionnaire was divided into two sections- the first pertaining to ocular, medical and family history, whilst the latter dealt with the factors associated with visual field testing. Prior to visual field testing, participants had undergone visual acuity testing, autorefraction, tonometry and ONH assessment. Optic nerve head assessment and tonometry were performed by a qualified ophthalmologist on the day of testing.

3.6.2 Testing procedure:

All subjects were tested in an isolated dark room, with minimal distractions from the surrounding hospital setting. Testing procedure commenced at 08h00am each day and concluded by 15:30. Most subjects were accompanied by a relative or friend, and were seated outside the testing room. The process started off by accessing patient files for the day and selecting the subjects based on the inclusion and exclusion criteria. The subjects were then approached by myself and the 3rd and 4th year optometry students to participate in the study. All those subjects who volunteered provided consent prior to visual field testing. Each subject was required to undergo a demonstration run for approximately one minute on both the HVFA and the MMDT in order to familiarise themselves with the testing procedure. Both eyes of the subjects were tested on each instrument and included in the data analysis. Subjects were required to answer a questionnaire, prior to and after visual field testing on both instruments to gain additional pertinent demographical, family, ocular and medical history, as well as subjective responses pertaining to the use and preference of the visual field instruments.

The order of testing between subjects was randomised such that approximately half started with the MMDT and half with the HVFA. The sample size required for the study were 177 case subjects and 324 control subjects. Due to the population at the two district hospitals selected, the total number of case subjects tested were 181, whilst the total number of control subjects tested were 328. Among the control subjects, 42 participants were monocular, whilst for the case group, only 12 participants were monocular. The total number of eyes tested for case and control subjects were 352 and 618, respectively. Reliable results obtained on the HVFA included: false positive rate of ≥20%, and a fixation loss value of ≤20%, whilst for the MMDT, the inclusion criteria for reliable data were: false positive value of ≤5% and a Global PTD of ≤3. Of the 352 eyes tested in the case group, reliable results were obtained for 94 eyes, whilst of the 618 eyes tested in the control group, reliable results were obtained for 199 eyes. After considering all reliable data, the total number of participants in the study for the case group were sixty-two (62) and that of the control group were a hundred and forty-five (145). This totalled a sum of two hundred and seven subjects (or 293 eyes) which were included in the study. The results for each instrument were masked from both examiners. A portion of subjects were selected at McCord's Provincial Hospital for quality assurance to ensure reliability and validity. Once the subject had been tested using both instruments, they were then asked to answer a detailed questionnaire and were provided with a small token of appreciation for participating in the study. All subjects with glaucoma had been advised to have their immediate family members screened for glaucoma.

For the control group, subjects were informed if any areas of concern were noted and were referred to the necessary hospital personnel for appropriate management. Participants were excluded from the analysis if their results displayed a false positive value of 5% and above on the MMDT, and on the HVFA, a false positive rate and fixation losses of more than 20%.

The MMDT is used in the assessment of visual fields and the 32-location program fits on a standard 15-inch laptop screen (Loughman *et al.*, 2013; Ong *et al.*, 2014), performed at a test distance of 30cm (Ong *et al.*, 2014). The patient is required to place their head and chin on a purpose-built head and chin rest and the eye to be tested has to be directly aligned with the central white spot, with the patient maintaining fixation on this spot for the duration of testing (Ong *et al.*, 2014). While maintaining fixation on the central white spot, the patient is required to click on the mouse every time a line on the screen is seen to move (Ong *et al.*, 2014). Each of the 32 line stimuli are scaled by estimation of retinal ganglion cell density and each location corresponds to a location on the Humphrey 24-2 program (Loughman *et al.*, 2013), allowing point to point (sectoral) comparison between the 2 instruments (Moorfield's Eye Hospital: NHS Foundation Trust, 2008).

3.6.3 Testing with the Humphreys Visual Field Analyser (HVFA):

The HVFA consists of a hemispherical bowl onto which a target can be projected at any location in the visual field (Kanski, 2007). Stimulus intensity is varied by altering luminance to determine the threshold level for each point tested in the visual field (Kanski, 2007). This is done by flashing random lights of different light intensities into the peripheral visual field while the patient is fixating at a source straight ahead. The patient is asked to then press the buzzer each time a light is perceived (Artes, 2012).

3.6.4 Testing with the Moorfields Motion Displacement Test (MMDT)

In contrast to the HVFA, the MMDT is a laptop-based test with 32 vertical line stimuli, each scaled by estimate of retinal ganglion cell density and selected using the Garway-Heath anatomical map (Loughman *et al.*, 2013). Whilst fixating at a central white dot monocularly, the patient is required to click on the mouse every time a movement of the vertical line is seen. Subjects who were unfamiliar with the concept of a mouse were given a short demonstration on the appropriate use of a left click. A test distance of 30cm was maintained and a near addition, appropriate to the patient's age, was only put up during testing conducted with the HVFA (as the MMDT is resistant to optical blur and refractive error of up to +5.00D). One examiner performed testing on the HVFA and one performed the Moorfields MDT, under the same environmental conditions in separate rooms, in order to minimise inter-examiner variability. Only those subjects who yielded acceptable results (where reliability indices were within norms) were included in the data analysis. The two sets of values were then compared to determine the accuracy of the Moorfields MDT in detecting visual field defects in glaucoma subjects compared to the HVFA.

3.7 Data collection process:

3.7.1 Data Analysis: The data was stored and computed using the Stata statistical software package version 14.1 software. Threshold results from the two tests were compared. The central zone (4 locations within 3 degrees of fixation) was compared to the periphery (9-27 degrees from fixation) (Verdon-Roe *et al.*, 2008). MMDT requires a global probability of true damage (PTD) of 3 or less and a false positive rate of 5% or less to ensure reliability (Loughman *et al.*, 2013). The HVFA requires a false positive rate of 33% or less and a fixation loss value of 20% or less (Newkirk *et al.*, 2006). However, Newkirk *et al*. (2006) report a false positive rate of 20% or more on the HVFA should be considered unreliable; therefore, this criterion was used in the analysis process (as opposed to 33%).

The MMDT uses cluster analysis and tests 32 points while the HFVA tests 52 points. Correlating points (32) on the HVFA plot were selected while the rest of the points were disregarded. The sensitivity was investigated by doing a point-to-point comparison between the visual field defect points of the pass/fail plot on the MMDT and the probability plot on the HVFA. Since the HVFA is regarded as the gold standard all the failed squares were counted, that is defects reflected by points (black squares on HVFA) with a probability index of $p<0.5\%$ on the HVFA and corresponding failed points on the MMDT plot were evaluated for agreement. All those points that were agreeable with HVFA on the MMDT plot were counted. Those points that were failed on the MMDT but not on the HVFA were regarded as false positives, whilst all those points failed on the HVFA but not on the MMDT were regarded as false negatives.

Given the MMDT ESTA version 99.5 corresponds to points on the HVFA central 24-2 program, the plots were compared by sector. To allow for improved comparison between the two instruments, the developers of the MMDT software are currently researching the relative dynamic range of each stimulus. (NHS trust: Moorfields eye hospital). The Shapiro-Wilk and Kolmogorov-Smirnova tests were used to test normality. As results were not normally distributed, the median test time was calculated for the case and control group for both the HVFA and MMDT. When assessing the diagnostic accuracy of a new test compared to the gold standard, the key areas of assessment include the sensitivity and specificity, as well as the positive and negative likelihood ratios (Florkowski, 2008). Sensitivity yields positive test results and refers to those participants who have the case condition. Specificity yields negative results and represents the portion of patients who do not have the case condition. Likelihood ratios (LR) are believed to be more intelligible to clinicians and allow for a more relevant interpretation of the test results. They can be separated into positive and negative likelihood ratios (+LR and -LR).

Calculations to validate the MMDT included:

- sensitivity and specificity of both case and control group
- positive and negative likelihood ratios for both case and control group
- positive and negative predictive values for both case and control group

The Mann-Whitney U Test was used to determine the distribution of average test duration amongst the two groups, gender and race, whilst the Kruskal-Wallis Test was used to determine duration of focus for the two instruments. Chi-square analysis and cross-tabs were used for the qualitative aspect of the study. These included subjects' preference of fixation target and method of selection, preference of visual field instrument and level of anxiety using both instruments.

3.7.2 Data management: All collected data was captured in a Microsoft Excel Spreadsheet daily. An optometrist independent to the study had validated 10% of the data entries to ensure minimal errors were made during capturing. The primary researcher, supervisors and statistician(s) had access to the data.

3.8 Ethical considerations:

Ethical approval was sought from the Biomedical Research and Ethics Committee (BREC) at UKZN (BE421/16) (Appendix 6) as well as KZN Department of Health (Reference: HRK289/16; KZ_2016RP47_13) (Appendix 7). Gatekeeper permissions were also obtained from management at both McCord Provincial Eye Hospital (Appendix 8) and Prince Mshiyeni Memorial Hospital (Appendix 9). Each patient was provided with an information document in their preferred language (Appendix 1 and 2), and once read and accepted, were requested to sign a consent form (Appendix 3 and 4) before participating in the study. All participants were ensured of their anonymity in their participation in the study and were given the option to withdraw from the study at any point if they needed to.

Raw data was captured into a Microsoft Excel spreadsheet which is retained by the principal researcher. Raw data was stored safely in a locked cupboard and will remain there for five years at which point they will be destroyed and disposed of securely. The principal researcher and supervisors are the only people with access to the data. The data will be stored for a period of 5 years and thereafter ethically disposed of.

This chapter discusses the procedures and protocols undertaken to conduct the study. It also highlights the measures taken to ensure reliable data collection. Unfortunately, due to time constraints of the hospital staff and participants, quality assurance could not be done daily and this is listed as one of the limitations in chapter 5.

CHAPTER 4: Manuscript 1

This chapter addresses the background of glaucoma in South Africa and the functional vision impairment that comes with the disease. Here we look at a new development in visual field testing, the Moorfields Motion Displacement Test (MMDT), and compare its level of agreement to that of the gold standard, Humphreys Visual Field Analyser, specifically in detecting glaucomatous visual field changes.

This chapter may have a considerable amount of overlap with the content covered in Chapters 2 (Literature Review) and 3 (Methodology).

Topic: Validating the MMDT in a South African context

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Abstract

Introduction Glaucoma, the third leading cause of blindness in Africa (after cataract), is responsible for approximately 15% of blindness in the continent. Generally, glaucoma goes undiagnosed in developing countries because of lack of awareness of the disease and its effects. The cost of standard methods for screening, including computerised perimetry (such as the gold standard Humphreys Visual Field Analyser), is not affordable and relatively inaccessible in most developing countries, posing a barrier to identifying people at risk for glaucoma blindness. The above factors initiated the development of more efficient, cost effective and portable visual field screening instruments, such as the Moorfields Motion Displacement Test (MMDT).

Purpose The aim of this study was to assess the diagnostic accuracy, acceptability, and usability of the Moorfields Motion Displacement Test (MMDT) in comparison with the gold standard Humphreys Visual Field Analyser (HVFA) as a tool for community glaucoma screening.

Method This was an observational, analytical study (involving comparative and quantitative methods). Ethical clearance was obtained from the Biomedical Research and Ethics commission at UKZN (BE421/16) as well as KZN Department of Health (Reference: HRK289/16; KZ_2016RP47_13). The case group (glaucoma participants) were selected via chart review of those booked for visual fields at McCord's Provincial Eye Hospital in KwaZulu-Natal (KZN), whilst the control group was selected via a chart review of participants booked for refraction at Prince Mshiyeni Memorial Hospital in KZN. Both eyes of the participant were tested, using both the HVFA and the MMDT. Threshold results from the two tests were analysed. Point-to-point comparison using the Wilcoxon signed rank test was used to compare thresholds location-wise.

Results A total of two hundred and seven subjects were tested of which, 94 eyes were diseased (glaucomatous) and 199 eyes non-diseased (control). Sensitivity to detect glaucomatous visual fields amongst case and control subjects was 100% in both groups. Specificity of the test to detect glaucomatous visual fields amongst case participants was 65.3% and was similar to that of the control group (63.3%). The average time taken on the HVFA among case subjects was 394 seconds (±80sec) and that of the MMDT was 128 seconds (±29 sec), whilst the average times among control subjects were 387 seconds (±73 sec) and 131 seconds (±29 sec) for the HVFA and MMDT respectively.

Discussion The sensitivity of the test to detect glaucomatous visual fields amongst case and control subjects was high and reflects the high ability of the MMDT in detecting glaucomatous visual field changes. Specificity of the MMDT was 63.0% for cases and 65.3% for the control group and, although lower than expected, indicates the ability of the MMDT to avoid overburdening the health care system

by reducing over-referrals. Test duration between the two instruments showed a superiority of the MMDT relative to the HVFA and this is highly beneficial to avoid inaccuracies due to patient fatigue. In addition, the faster test time allows for mass community glaucoma screenings, especially so in developing countries where access to health care is relatively limited.

Conclusion The MMDT has yielded high sensitivity for both case and control subjects in detecting glaucomatous visual field changes (>75%), however, specificity was low (<85%). There is therefore a need to modify the current methods to yield higher specificity while maintaining sensitivity. The MMDT also proved to be approximately three times faster as compared to the HVFA making mass screenings easier, ultimately delivering high volume testing where it is accessible.

Keywords: glaucoma, visual field, MMDT, HVFA

Introduction

Visual field screening tests are used when only the gross impact of disease on the visual field needs to be evaluated to rule out the presence of significant pathology. The purpose is not to perform a detailed evaluation of the visual field status (Elliott, 2013). The present methods for glaucoma screening are expensive and are a barrier to identifying people at high risk for glaucomatous disease compared to other ocular diseases (Quigley, 1996). Apart from the cost, most of the current methods of screening require a significant amount of testing time (Lawrence and Budenz, 2013) . If glaucomatous visual fields are left undiagnosed, treatment cannot be initiated and therefore many activities of daily living are increasingly affected as the disease progresses, including reading and writing, mobility and discrimination of colours (Taylor and Keeffe, 2001; Rong-jiang *et al.*, 2011). In addition, lack of management can lead to blindness with its consequent socio-economic effects (World Health Organisation, 2006).

Visual field perimetry and developments in glaucoma detection tests

Visual field perimetry is vital in detecting the functional loss that accompanies glaucoma (Nouri-Mahdavi, 2014) as well as measuring the severity and progression of disease (Peters *et al.* 2015). These tests are subjective in nature and require the patient to understand the testing instruction, fully cooperate with the test requirements, and complete the entire test in order to provide accurate and reliable results (Alencar and Medeiros, 2011). An essential component for accurate diagnosis and implementation of appropriate management regimens is the reliability and repeatability of the visual field test (Newkirk *et al.*, 2006). Factors influencing the accuracy of visual field testing include refractive error, pupil size (Nussdorf and Alastair, 2003), ocular structural abnormalities (Alastair and Denniston, 2009) and intraocular stray light (Bergin *et al.*, 2011). Patient profile and co-operation, defective instruments, the operator's technical skill, as well as the testing environment, also contribute to the overall accuracy of test results obtained (Nussdorf and Alastair, 2003).

The above factors initiated the development of more efficient, cost effective and portable visual field screening instruments, one of them being the Moorfields Motion Displacement Test (MMDT) (Moorfield's Eye Hospital: NHS Foundation Trust, 2008). The MMDT is a multi-location test, presenting vertical line stimuli in 32 test locations on a computer screen; each scaled by estimate of retinal ganglion cell density and selected using the Garway-Heath anatomical map (Loughman *et al.*, 2013). It aims to determine the smallest perceptible positional displacement, with the displacement giving rise to the sensation of movement (Verdon-Roe *et al.*, 2006). However, the accuracy of the MMDT in comparison to the HVFA has not yet been established. Therefore, this study set out to compare the visual field defects, if any, obtained by the Moorfields MDT to that obtained with the HVFA in diagnosed glaucoma subjects, as well as to assess its acceptability, usability and patients' level of anxiety during testing.

Rationale of the validating the MMDT

The purpose of this study was to determine the similarity in findings, between both the MMDT and the HVFA in detecting visual field defects, its testing time, demographic influence on participant experience (including preferred method of selection and fixation target), preferred instrument as well as the participants levels of anxiety during testing on each instrument

Methods

Ethical clearance was obtained from the Biomedical Research and Ethics commission at UKZN **(BE421/16)** as well as KZN Department of Health (**Reference: HRK289/16; KZ_2016RP47_13**). The study was conducted at McCord Provincial Eye Hospital (Durban) and Prince Mshiyeni Memorial Hospital (uMlazi) areas of KwaZulu Natal province in South Africa. Outcome measures included: sensitivity and specificity of the Moorfield's MDT results in comparison to the HVFA. After estimating the confidence intervals, the margin of error was found to be 12.2% for sensitivity (73.0%) and 8.2% for specificity (90.0%) (Baez *et al.*, 1995).

The data collection was carried out by myself for the first three weeks, whilst I trained two fourth year optometry students, two third year optometry students and one technical assistant over a period of six months from 8am to 12pm. The clinical procedures were carried out in two separate rooms to ensure that results were obtained independently of each other. For the case group, the HVFA test was carried out by a final year optometry student in room 1 and MMDT was conducted by a final year optometry student in room two (Figure 4.1), whilst for the control group, the HVFA test was carried out by a third-year optometry student in room one and MMDT was conducted by a third-year optometry student in room two.

Data was collected from 12 December 2016 to 22 August 2017. Access to daily patient files was used to recruit subjects diagnosed with glaucoma at MPH and PMMH. The total number of eyes tested for case and control participants were 352 and 618, respectively. Reliable data was obtained for a total of two hundred and seven participants, of which sixty-two were diagnosed with glaucoma and one hundred and forty-five without glaucoma. The total number of eyes included in the case group was ninety-four (94) and that of the control group was one hundred and ninety-nine (199), giving a total of two hundred and ninety-three (293) eyes being included in the study. Each participant had undergone ocular health assessment with an ophthalmologist prior to their visual field test. To assess the specificity of the MMDT, the age-matched control group was selected by accessing files of those patients at PMMH booked for refraction. Each participant was provided with an information document and consent form in their preferred language, following which a questionnaire was administered before and after testing on both instruments. Participants were randomised to which visual field test was conducted first. The results were captured daily in an excel spreadsheet and 10% of the data entry was verified by a third

party to ensure quality of the data entry process. Data was exported into the Stata statistical software package version 14.1. Non-parametric analysis was conducted as results were not normally distributed. Significance was set at an alpha of 0.05.

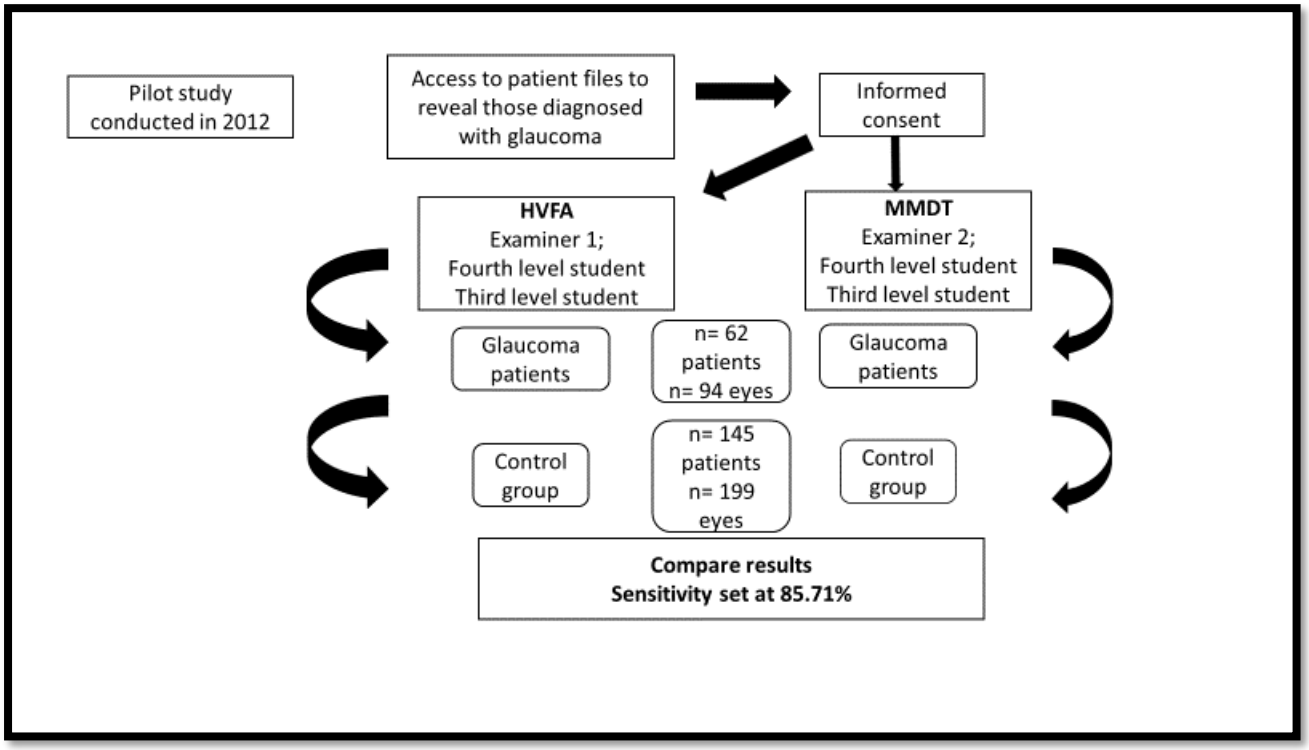

Figure 4.1. Flowchart of data collection procedure

Results

4.1 Demographic distribution

The data obtained in this study were not normally distributed and verified by the Shapiro-Wilks test (Table 1) for gender, duration, and race P< 0.05, therefore non-parametric tests were used during analysis. The case group comprised of 62 participants (ninety-four eyes) (Figure 4.1), of which, 66.1% (n= 41), were females (Figure 4.2) with the most prevalent age group distribution ranging between 60-69 years (Figure 4.3) with more than half (56.5%) being of Indian origin. The control group comprised of 145 participants (199 eyes) (Figure 4.1), of which, 64.8% (n= 94) were females (Figure 4.2), with the most prevalent age group distribution ranging between 40-49 years (31.7%) (Figure 4.3) and among the African population. The median age of case and control participants were 63.5 and 55.0 years, respectively.

Table 4.1. Table of tests of normality using Shapiro-Wilk test and Kolmogorov-Smirnova

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	df	Sig.
Dur*_MMDT	.100	199	.000	.937	199	.000
Dur*_HVFA	.119	199	.000	.932	199	.000
Age	.069	199	.022	.988	199	.079

a. Lilliefors Significance Correction (applied when the Kolmogorov-Smirnova test is used to evaluate a sample size of under two thousand).

* 'Dur' refers to test duration

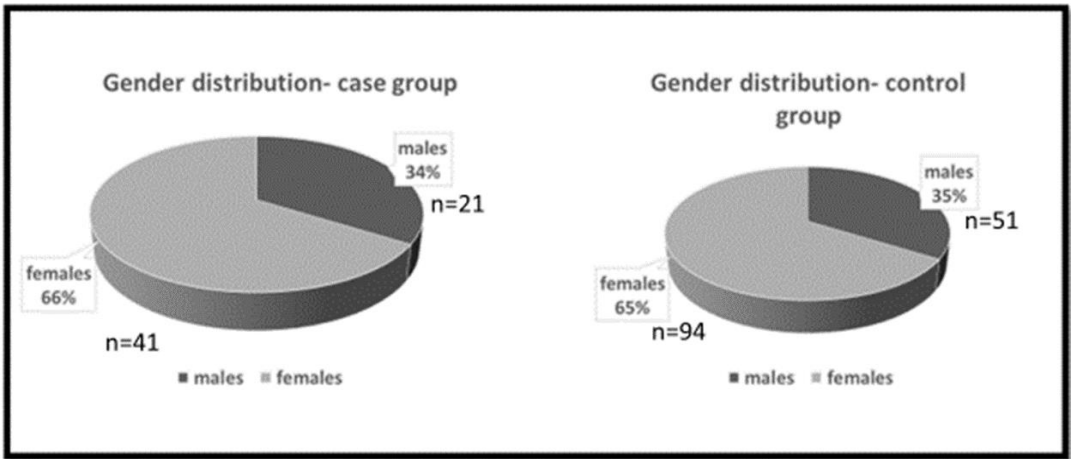

Figure 4.2. Gender distribution comparison among case and control groups

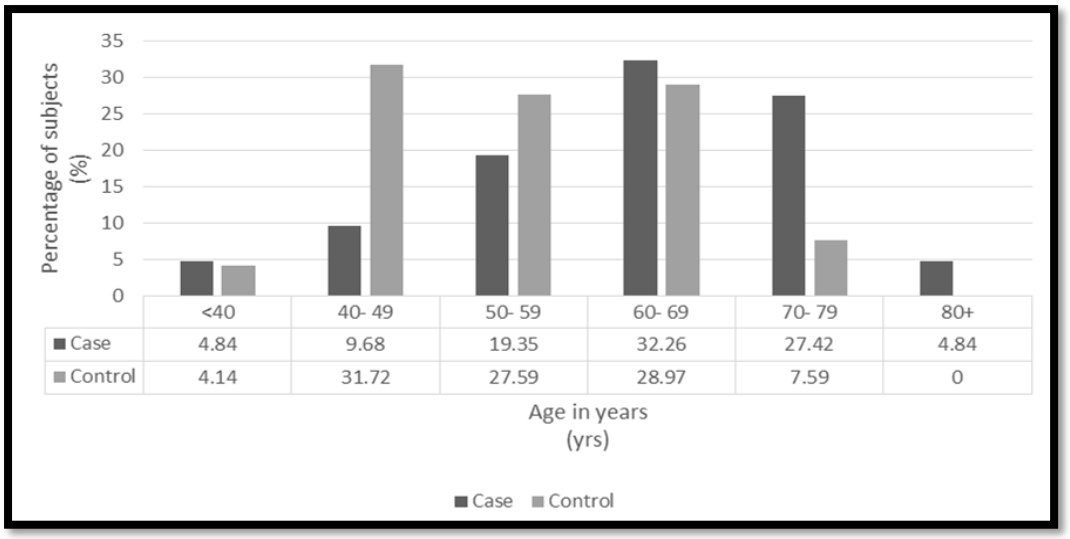

Figure 4.3. Distribution of age categories amongst case and control participants

4.2 Comparison of time taken using both HVFA and MMDT across different age groups

Results reveal there is significant positive correlation between the age of participants and duration of HVFA ($r = 0.270$), and duration of MMDT ($r = 0.347$) at 1% ($p<0.01$) level. This implies, test duration appears to increase with age using the HVFA machine, with a direct relationship existing between test duration of the participants using the two machines.

4.3 Median test time of case and control group

As results were not normally distributed, the median test time taken for the case group with the MMDT was 128 seconds (±29 sec), approximately three times faster than that of the HVFA. The HVFA had a median test time of 394 seconds (±80 sec). The median test time taken for the control group with the MMDT among females was remarkably similar to that of males which was 131 seconds and 130 seconds, respectively. Table 4.2 below shows the median test time across different age groups on both instruments, whilst Table 4.3 depicts the median test time across both the case and control groups. The median test time with the MMDT among the case group was similar with females taking an average of 130 seconds and males 128 seconds. Among the age groups, the highest average test duration of 154 seconds (±17 sec) occurred in the >80-year-olds category when using the MMDT, whilst the highest average time of 427 seconds (±90 sec), using the HVFA occurred in the 70-79-year-olds category. Those in the 40- 49-year age group performed the fastest overall on both instruments. For the case group, the shortest average test time of 123 seconds occurred among the 40-year-olds and under category. Those 80 years and older of the case group took an average test time of 154 seconds which was higher than that of the control group (149 seconds).

Table 4.2. Table of median test times of the HVFA and MMDT amongst the different age groups

Age		Dur*_MMDT	Dur*_HVFA
<40 yrs	N	9	9
	Median	0:02:00	0:05:34
	Std. Deviation	0:00:31	0:00:56
	Minimum	0:01:40	0:04:25
	Maximum	0:03:02	0:07:19
40 - 49 yrs	N	51	51
	Median	0:02:00	0:06:01
	Std. Deviation	0:00:29	0:01:05
	Minimum	0:01:31	0:04:26
	Maximum	0:03:23	0:09:13
50 - 59 yrs	N	50	50
	Median	0:02:08	0:06:25
	Std. Deviation	0:00:27	0:01:08

	Minimum	0:01:33	0:04:54
	Maximum	0:03:31	0:10:13
	N	59	59
60 - 69 yrs	Median	0:02:06	0:06:19
	Std. Deviation	0:00:29	0:01:16
	Minimum	0:01:31	0:04:40
	Maximum	0:03:16	0:09:47
	N	27	27
70 - 79 yrs	Median	0:02:13	0:06:43
	Std. Deviation	0:00:32	0:01:30
	Minimum	0:01:31	0:04:51
	Maximum	0:03:34	0:10:23
	N	3	3
>= 80 yrs	Median	0:02:40	0:07:19
	Std. Deviation	0:00:17	0:01:27
	Minimum	0:02:15	0:05:26
	Maximum	0:02:48	0:08:18
	N	199	199
Total	Median	0:02:04	0:06:18
	Std. Deviation	0:00:29	0:01:15
	Minimum	0:01:31	0:04:25
	Maximum	0:03:34	0:10:23

* ‘Dur’ refers to test duration

Table 4.3. Table of median test times of the HVFA and MMDT for the case and control group

Group		Dur*_MMDT	Dur*_HVFA
Glaucoma	N	58	58
	Median	0:02:03	0:06:25
	Std. Deviation	0:00:29	0:01:20
	Minimum	0:01:31	0:04:25
	Maximum	0:03:09	0:10:23
Control	N	142	142
	Median	0:02:05	0:06:10
	Std. Deviation	0:00:29	0:01:13
	Minimum	0:01:31	0:04:37
	Maximum	0:03:34	0:10:19
Total	N	200	200
	Median	0:02:04	0:06:18
	Std. Deviation	0:00:29	0:01:15
	Minimum	0:01:31	0:04:25
	Maximum	0:03:34	0:10:23

* 'Dur' refers to duration

4.4 Median test time between males and females using HVFA and MMDT

Females of the control and case groups using the HVFA had a higher total average test duration of 405 seconds (±78 sec) and 406 seconds respectively, as compared to males who had a total average test duration of 362 seconds (±60 sec) and 370 seconds respectively. Males using the MMDT performed marginally faster than females on both instruments; 130 seconds (±27 sec) on MMDT, whereas females took a total average of 131 seconds (±30 sec). Similar to the MMDT, the highest average test duration (437 seconds) of the control group, occurred amongst the 70- 79-year-olds. The 80 year and above category of the case group took an average test time of 420 seconds.

4.5 Validity of the MMDT

4.5.1 Sensitivity and specificity

The sensitivity of the MMDT to detect glaucomatous visual fields among the case and control group was high (>75%) 100.0%, with a low specificity (< 85%) of 63.3% and 65.3% for the case and control group respectively, as depicted in Table 4.4(a) and (b) below.

Table 4.4a. Calculation of sensitivity and specificity amongst case subjects

		HVFA CASES					
		DX* (1)		**NO DX* (0)**		**TOTAL**	$Sensitivity = \frac{true\ positive}{true\ positive\ + false\ negative}$ $= \frac{15}{15+0}$ $= \mathbf{100\%}$
MMDT	**DX***	15	1/1	29	0/1	44	
	NO DX*	0	1/0	50	0/0	50	
	TOTAL	15		79		94	$Specificity = \frac{true\ negative}{true\ negative + false\ positive}$ $= \frac{50}{29+50}$ $= \mathbf{63.3\%}$

*DX stands for disease and is represented by values of one and above.

1 represents diseased eyes; 0 represents non-diseased eyes

Table 4.4b. Calculation of sensitivity and specificity amongst control subjects

		HVFA CONTROLS					
		DX* (1)		**NO DX* (0)**		**TOTAL**	$Sensitivity = \frac{true\ positive}{true\ positive\ + false\ negative}$ $= \frac{16}{16+0}$ $= \mathbf{100.0\%}$
MMDT	**DX***	16	1/1	29	0/1	69	
	NO DX*	0	1/0	50	0/0	130	
	TOTAL	16		79		199	$Specificity = \frac{true\ negative}{true\ negative\ + false\ positive}$ $= \frac{130}{69+130}$ $= \mathbf{65.3\%}$

***DX stands for disease and is represented by values of one and above**

Table 4.4(c) below shows the positive likelihood ratio was 2.7 and 2.9 for the case and control group respectively, whilst the negative likelihood ratio was 0 for both the case and control groups.

Table 4.4c. Calculation of positive and negative likelihood ratio amongst case and control subjects

Cases	*Controls*
$LR+= \frac{Sensitivity}{1-Specificity}$ $= \frac{1}{1-0.63}$ $= \mathbf{2.7}$	$LR+= \frac{Sensitivity}{1-Specificity}$ $= \frac{1}{1-0.65}$ $= \mathbf{2.9}$
$LR- = \frac{1-sensitivity}{specificity}$ $= \frac{1-1}{0.63}$ $= \mathbf{0.0}$	$LR- = \frac{1-sensitivity}{specificity}$ $= \frac{1-1}{0.65}$ $= \mathbf{0.0}$

Table 4.4(d) below shows the positive predictive value (PPV) of the test was 34.0% whilst the negative predictive value (NPV) was 100.0% amongst the case group. Whereas amongst the control group, the PPV of the test was 19.0% whilst the NPV was 100.0%.

Table 4.4d. **Calculation of positive and negative predictive value amongst case and control subjects**

	Cases	**Controls**
PPV	$PPV = \frac{true\ positive}{true\ positive + false\ positive}$ $= \frac{15}{15+29}$ = 0.34 = 34.0%	$PPV = \frac{true\ positive}{true\ positive + false\ positive}$ $= \frac{16}{16+69}$ = 0.19 = 19.0%
NPV	$NPV = \frac{true\ negative}{false\ negative + true\ negative}$ $= \frac{50}{0+50}$ = 1.00 **=100.0%**	$NPV = \frac{true\ negative}{false\ negative + true\ negative}$ $= \frac{130}{0+130}$ = 1.00 **=100.0%**

4.6 Average test duration comparison across the different age groups, race and gender:

The Mann-Whitney U Test was used to determine the distribution of average test duration amongst the two groups, gender and race. The results show that the test duration for both the MMDT and HVFA machines did not differ significantly between the two groups of participants at 5% ($p>0.05$) level. The test duration also did not differ significantly between male and female participants using the MMDT at 5% ($p>0.05$) level. However, the duration of focus was significantly different at 5% ($p<0.05$) level between male and female under the HVFA machine.

Table 4.5a. Kruskal-Wallis Test to determine the distribution of average test duration amongst the 2 groups and race.

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Dur_MMDT is the same across categories of race	Independent-Samples Kruskal-Wallis Test	0.501	Retain the null hypothesis
2	The distribution of Dur_HVFA is the same across categories of race	Independent-Samples Kruskal-Wallis Test	0.510	Retain the null hypothesis

Asymptotic differences are displayed. The significance level is 0.05.

The Kruskal-Wallis Test reveals that the test duration for the two instruments was not significantly different among the three races at 5% ($p>0.05$) level.

4.7 Chi-square analysis and cross-tabs for qualitative components of study:

4.7a) Preferred method of selection among different race groups

Participants were questioned as to which method of selection was preferred. The results revealed in Table 4.5b below indicate 84.8% of participants of Indian origin preferred mouse to button, 72.0% of participants of African origin preferred mouse to button, 66.7% of Caucasians preferred mouse to button whilst only the mixed race group preferred button to mouse, noting however, that there was only one participant of mixed race. Overall, 74.5% of the participants preferred mouse to button. However, the result of Chi-square analysis reveals that there was no significant variation at 5% ($p>0.05$) level in the distribution of the different races based on their preference for either mouse or button.

Table 4.5b. Table of comparison of method of selection between mouse (MMDT) and button (HVFA) among the different race groups using Chi-square analysis

		Mouse_Button		Total	Chi-Square Value	Df	p-value
		Mouse	Button				
Race	Indian/Asian	39 (84.8%)	7 (15.2%)	46 (100.0%)	6.072	3	0.108
	African	108 (72.0%)	42 (28.0%)	150 (100.0%)			
	Caucasian	2 (66.7%)	1 (33.3%)	3 (100.0%)			
	Mixed race	0 (0.0%)	1 (100.0%)	1 (100.0%)			
Total		149 (74.5%)	51 (25.5%)	200 (100.0%)			

4.7b) Preferred method of selection between gender groups

Table 5c below shows the result for gender and Mouse_Button cross-tabulation. The result reveals that 73.2% of the males preferred the mouse to the button selector while 75.0% of the females preferred the mouse to the button. However, result of Chi-square analysis revealed that there was no significant variation at 5% ($p>0.05$) level in gender distribution based on their preference for either mouse or button.

Table 4.5c. Table of comparison between male and female participants of preferred method of selection between mouse (MMDT) and button (HVFA) using Chi-square analysis

		Mouse_Button		Total	Chi-Square Value	df	p-value
		Mouse	Button				
Gender	Male	52 (73.2%)	19 (26.8%)	71 (100.0%)	.092	1	0.762
	Female	97 (75.2%)	32 (24.8%)	129 (100.0%)			
Total		149 (74.5%)	51 (25.5%)	200 (100.0%)			

4.7c) Preferred visual field instrument among different race groups

It can be deduced from Table 4.5d below that among the different race groups, 95.7% of participants of Indian origin preferred MMDT to HVFA, 80.7% of participants of African origin preferred MMDT to HVFA, 66.7% of Caucasians preferred MMDT to HVFA while only the mixed-race group preferred HVFA to MMDT, noting however, the mixed race group consisted of one participant whilst the Caucasian group consisted of three participants. Overall, 83.5% of the participants preferred MMDT to HVFA. Chi-square analysis reveals that the distribution of the different races based on their preference for either MMDT or HVFA varied significantly at 5% ($p<0.05$) level.

Table 4.5d. Table of fixation stimulus comparison: Light (HVFA) and Dot (MMDT) using Chi-square analysis

		Light_Dot		Total	Chi-Square Value	df	p-value
		Dot	Light				
Race	Indian/Asian	39 (84.8%)	7 (15.2%)	46 (100.0%)	5.055	3	0.168
	African	120 (80.0%)	30 (20.0%)	150 (100.0%)			
	Caucasian	2 (66.7%)	1 (33.3%)	3 (100.0%)			
	Mixed race	0 (0.0%)	1 (10.0%)	1 (100.0%)			
Total		161 (80.5%)	39 (19.5%)	200 (100.0%)			

4.7d) Preferred fixation target among different race groups

Participants were also questioned as to which target of focus was preferred, and as can be deduced from Table 4.5d, 84.8% of participants of Indian origin preferred the dot to light, 80.0% of participants of African origin preferred the dot to light, 66.7% of Caucasians preferred the dot to light while the only mixed race group among the participants preferred the light to the dot, noting however that this group consisted of only one participant. Overall, 80.5% of the participants preferred dots to light. Chi-square analysis however revealed again that there was no significant variation at 5% ($p>0.05$) level in the distribution of the different races based on their preference for either the light or dot.

4.7e) Preferred fixation target across gender groups

Table 4.5e below shows the result for gender and Light_Dot cross-tabulation. The result revealed that 74.6% of the males preferred the dot to light while 83.7% of the females preferred the dot to light. However, result of Chi-square analysis reveals that there was no significant variation at 5% ($p>0.05$) level in gender distribution based on their preference for either the light or dot.

Table 4.5e. Table of comparison between male and female participants of preferred fixation target between dot (MMDT) and light (HVFA) using Chi-square analysis

		Light_Dot		Total	Chi-Square Value	df	p-value
		Dot	Light				
Gender	Male	53 (74.6%)	18 (25.4%)	71 (100.0%)	2.402	1	0.121
	Female	108 (83.7%)	21 (16.3%)	129 (100.0%)			
Total		161 (80.5%)	39 (19.5%)	200 (100.0%)			

4.7f) Preferred visual field instrument among gender groups

Crosstab (Table 4.5e above) also revealed 78.9% of the males preferred MMDT to HVFA while 86.0% of the females preferred MMDT to HVFA. Chi-square analysis however reveals that there was no significant variation at 5% ($p>0.05$) level in gender distribution based on their preference for either MMDT or HVFA.

4.7g) Preferred visual field instrument among age groups

The result reveals that 55.6% of participants whose ages are less than 40 years preferred MMDT to HVFA, 84.3% of those who fall within age group 40 – 49 years preferred MMDT to HVFA, 92.0% of those within age group 50 – 59 years preferred MMDT to HVFA, 79.7% of those within age group 60 – 69 years preferred MMDT to HVFA, 85.2% of those within age bracket 70 – 79 years preferred MMDT to HVFA while 100.0% of those whose ages are 80 years and above preferred MMDT to

HVFA. Result of Chi-square analysis, however, reveals that the distribution of the participants' preference for either MMDT or HVFA across different age groups did not vary significantly at 5% ($p>0.05$) level.

4.7h) Preferred method of selection among age groups

The results below (Table 4.5f) depict cross-tabulation for age group and Mouse_Button. The result reveals that 77.8% of participants whose ages are less than 40 years preferred mouse to button, 72.5% of those within age group 40 – 49 years preferred mouse to button, 82.0% of those within age group 50 – 59 years preferred mouse to button, 67.8% of those within age group 60 – 69 years preferred mouse to button, 77.8% of those within age bracket 70 – 79 years preferred mouse to button while 100.0% of those whose ages are 80 years and above preferred mouse to button. Result of Chi-square analysis however reveals that the distribution of the participants' preference for either mouse or button across different age groups did not vary significantly at 5% ($p>0.05$) level.

Table 4.5f. Table of comparison of preferred method of selection between mouse (MMDT) and button (HVFA) among the different age groups

		Mouse_Button		Total	Chi-Square Value	df	p-value
		Mouse	Button				
Age	<40 yrs	7 (77.8%)	2 (22.2%)	9 (100.0%)	4.235	5	0.516
	40 - 49 yrs	37 (72.5%)	14 (27.5%)	51 (100.0%)			
	50 - 59 yrs	41 (82.0%)	9 (18.0%)	50 (100.0%)			
	60 - 69 yrs	40 (67.8%)	19 (32.2%)	59 (100.0%)			
	70 - 79 yrs	21 (77.8%)	6 (22.2%)	27 (100.0%)			
	>= 80 yrs	3 (100.0%)	0 (0.0%)	3 (100.0%)			
Total		149 (74.9%)	50 (25.1%)	199 (100.0%)			

Discussion

This study stemmed from an unpublished pilot study which was conducted in 2012 by undergraduate students at the University of KwaZulu Natal, Westville Campus, in which, the accuracy of the Moorfield's Motion Displacement tester (MMDT) was evaluated. The study followed a quantitative cross-sectional design, comprising participants from the St Aidan's Hospital eye clinic booked for visual field testing. A total number of 260 eyes were assessed using both the Humphrey's Visual Field Analyser and the MMDT. The SITA central 24-2 threshold test was used on the HVFA and the ESTA 99.5 suprathreshold test was used on the MMDT. These two tests allow point to point comparison of the results. To be included, all participants had to meet the pass/fail criteria on both the HVFA and the MMDT.

Using ROC analysis, the sensitivity was found to be 83.18% with a standard deviation of ±7.6% (95%CI 75.6%-90.76%), slightly below acceptable sensitivity of 85.7%. (These results however, showed higher sensitivity compared to the findings of Baez *et al*. (1995) who found a sensitivity of 73.0% with the MMDT compared to the HVFA). Due to a small sample size, specificity was not found.
The level of agreement showed correspondence between the actual field defect points on the MMDT with the HVFA. A high level of agreement in about 50% of the sample was indicated, however, was not significant enough to show that the instrument can be used as a diagnostic tool. It was also found that the mean testing time with the MMDT is 4.3 times faster than with the C24-2 on the HVFA (t-test for unequal variances, p=0.000). The study concluded that the MMDT's cost and portability, and its measured sensitivity and short testing time, indicate that it is a viable vision screening tool in the context of a developing world, however, its accuracy to be used as a diagnostic tool has not yet been established. Furthermore, the lack of a control group and small sample size, did not allow all relevant objectives to be measured.

The case group in our study comprised 66.1% females (n= 41), with the most prevalent age group distribution ranging between 60-69 years and the highest prevalence occurring in the Indian population (56.5%). This is a consequence of non-random sampling influenced by the patient demographic of MPH. It therefore goes against the literature which states that glaucoma is most prevalent among those of African origin (Loughman *et al.*, 2013; Weinreb *et al*. 2014), however, is consistent with research that states the onset of disease mostly presents in those 50 years and older (Brusini *et al.*, 2005). The control group comprised 64.8% females (n= 94), with the most prevalent age group and racial distribution ranging between 40- 49 years among the African population. Again, this racial distribution could be attributed to the majority of people being of African origin and attending the eye clinic at PMMH. According to a study investigating health care utilization in South Africa, this result might also be attributed to the health-seeking behaviour of females, who are approximately twice as likely to seek health care as compared to males (Abaerei *et al.* 2017).

The average test time taken for the case group with the MMDT was 128 seconds (±29), approximately 3 times faster than that of the HVFA, which was an average of 394 (±80) seconds and is consistent with the literature which states the MMDT Enhanced Supra-Threshold Strategy (ESTA) takes an average test time of 90-120 seconds per eye (Bergin, 2011). This is an important finding given that this device has been designed for fast and reliable community based screening (Shekhar and Xiong, 2008). Given the general lack of access to eye care service in most developing countries, the efficiency of the MMDT provides a commendable platform for prospective glaucoma screening programmes (Loughman *et al.*, 2013). From a clinical perspective, the advantage of reduced test time directly impacts on reducing patient fatigue, thereby increasing the reliability of results (Dersu *et al.*, 2006; Patyal *et al.*, 2014). The advantages of faster test time will also include the ability to create bridging mechanisms between

communities and eye care facilities (Melese *et al.*, 2004), as well as a greater screening success for those who would require follow up testing (McManus and Netland, 2013). For the MMDT, the highest average test duration of 149 seconds occurred in the 70- 79-year-old category of the control group and those 80 years and older of the case group took an a slightly higher average test time of 154 seconds. The reasoning behind this result could be attributed to the general decline in gross and fine motor skills, as well as dexterity in older individuals (Voelcker-Rehage, 2008). As people age, performance of complex tasks occurs more slowly and, in some cases, less accurately than they once did, however, although motor performance tends to decline in old age, learning capabilities remain intact (Voelcker-Rehage, 2008).

Sensitivity of the MMDT in detecting visual field changes in both the case and control group was excellent, yielding 100% in both groups. The sensitivity was much higher than that found in the Tajimi study, where Frequency Doubling Technology (FDT) perimetry was found to have a low sensitivity (55.6%) when diagnosing glaucoma (and/or retinal disease) thereby limiting its ability in screening the general population (Boland *et al.*, 2016). Specificity of the test to detect glaucomatous visual fields amongst case subjects was 63.3% and was similar to that of the control group (65.3%).

The positive predictive value (PPV) for the case and control group were 34% and 19% respectively. These values are most likely as a result of a large number of false positives, therefore a positive result on the MMDT alone is poor in indicating the presence of glaucoma, which warrants further testing to confirm a diagnosis. Despite a test displaying a good sensitivity and specificity, the occurrence of a low PPV is still possible if the test has been conducted in a population where the disease likelihood is low (Ranganathan and Aggarwal, 2018). The MMDT did however yield a high sensitivity of 100% in both the case and control groups and is highly beneficial in a developing world context as this instrument proves to be successful in detecting glaucomatous visual field changes and will aid in mass screenings in the community. This study is not primarily a screening evaluation, however, it enabled us to evaluate the performance of the MMDT in screening for glaucomatous changes. The negative predictive value (NPV) for both case and control subjects was 100%. This is highly useful as it scientifically proves the MMDT will avoid the case of false negatives, thereby reducing the risk of under referrals and misdiagnosing those patients who actually have glaucoma, requiring appropriate medical attention (Saunders *et al.*, 2015).The above results show that the MMDT correctly identified 65.3% (specificity) of those who did not have glaucomatous visual field changes.

When assessing the usefulness of a diagnostic instrument, the calculation of positive and negative likelihood ratios is of more clinical significance (Akobeng, 2007). These ratios determine by how much more (or less) likely participants with a disease will present with a particular result than participants without a disease and is a combination of the sensitivity and specificity (Akobeng, 2007). In this study,

the positive likelihood ratio (+LR) for the case and control groups were similar, yielding 2.72 and 2.86 respectively, with a negative likelihood ratio (-LR) of 0 for both groups. The +LR of 2.72 indicates an approximate increase in probability of just over 15% that the MMDT detects positive results of glaucomatous visual field change. In contrast, the -LR of 0, shows a large decrease (approximately 45%) in probability of the presence of glaucomatous visual field changes. These results differ when compared to the findings of Ong et al., (2014) who found the +LR to be 12.1 at a sensitivity of 87.2%, whilst the -LR was 0.14 at a specificity of 92.8%. Although research states that a feasible diagnostic test offers a high +LR and a low -LR (Ong *et al.*, 2014), the most significant ratios are those <0.1 or >10 as they have the largest effect on post-test probability (Shah et al., 2006).

According to Shah et al., (2006), likelihood ratios between 0.5 and 2 have an insignificant effect on the post-test probability of disease, whilst those between 0.2 and 0.5 have a small effect on post-test probability and those between 0.1 and 0.2 (or between 5 and 10) having a moderate effect..

Conclusions and recommendations

The results from this study indicate there is a high level of agreement between the MMDT and the HVFA, both in detecting visual field changes in diseased (glaucomatous) eyes, as well as non-diseased (control) eyes. Scientifically proven to be faster than the HVFA (approximately three times), the MMDT has the added advantage of being more portable and cost-efficient. This is extremely useful in a developing world context since access to basic health care facilities is relatively limited. By introducing such instruments, mass screenings become readily approachable, thereby allowing for earlier detection, diagnosis and management of glaucoma. Mass screenings of ocular diseases, such as glaucoma, can in turn aid in the reduction of patients affected by avoidable blindness. The MMDT has now proven to be scientifically more likely than FDT perimetry in screening for glaucoma in the population-based setting and our results are consistent with the findings of (Ong *et al.*, 2014) who also concluded the MMDT can be used as a diagnostic tool.

Due to the irreversible effects of glaucoma, many patients affected by this disease often end up with the resultant socio-economic effects and overall quality of life being reduced. As it is a disease which presents mostly in older individuals (40 years and older), these patients often have to deal with much more than just ocular difficulties. These include mobility and dexterity issues, hearing loss, memory loss, coupled with driving inability and visual search issues. As patients experience an increase in the loss of vital senses, they become more dependent on family, friends and/or caregivers which eventually has a resultant effect on their self-esteem. These difficulties are quite evident in those patients who struggle with the impending challenges of low vision.

Another challenge in developing countries is the availability of optometrists and ophthalmologists, more especially in the public sector. There is a large ratio of patients to a single ophthalmologist and to perform further investigations on patients becomes difficult and is exacerbated when these tests are time consuming (such as the HVFA). In South Africa, the ratio of optometrists to the population is approximately 1:17600 (Naidoo, 2007). It is recommended for future studies and developments, that the above factors are considered in order to improve on current technology and systems in the field of eye health care, specifically to that which is required for visual field testing. It is also recommended that similar research is conducted on a larger sample size as well as on conditions other than glaucoma to determine if the instrument can be applicable to all kinds of visual field changes. In order to improve on the specificity from this study, age-matched controls as well as repeat tests on abnormal results are recommended. In addition, our study had not specified predefined levels of glaucoma severity which could be an essential criterion when assessing the efficacy of the MMDT to monitor the progression of glaucoma and other visual field defect-causing abnormalities. The stringency of the screening test could be altered to adjust the PPV and NPV to a desirable level. This could be done by raising the cutpoints

of the reliability indices on both visual field instruments or by performing the screening on those with moderate to advanced glaucoma only (Ranganathan and Aggarwal, 2018).

Unfortunately, there is currently no global indices such as mean deviation (MD) or pattern standard deviation (PD) available to accurately analyse the visual field defects as the MMDT is a suprathreshold test, however, the MMDT is certainly scientifically proven to be sensitive enough in screening glaucoma and possibly expanded upon in future studies.

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CHAPTER 5. General synthesis, conclusions and recommendations

5.1 General synthesis

This chapter may have a considerable amount of overlap with information from chapter 2 (literature review), chapter 3 (methodology) and chapter 4 (manuscript 1).

The overall aim of the study was to determine the similarity of visual field findings between the HVFA and Moorfields MDT. The findings of this study suggest that the MMDT is a viable alternative for use in screening visual field changes in glaucoma patients. This is reflected by the specificity of 63.3% and sensitivity of 100%. The findings are in accordance with Ong *et al*. (2014) who also suggests that the instrument provides good diagnostic performance in identifying glaucomatous eyes and shows potential as a new diagnostic tool. The MMDT is portable, faster, accessible and relatively cost effective thereby validating its use in a developing world context (Ong *et al.*, 2014).

The sensitivity found in this study (100% for both the case and control groups) was much higher than that found in the Tajimi study, where Frequency Doubling Technology (FDT) perimetry was found to have a low sensitivity (55.6%) when diagnosing glaucoma (and/or retinal disease) thereby limiting its ability in screening the general population (Boland *et al*., 2016). Specificity of the test to detect glaucomatous visual fields amongst case subjects was 63.3% and was similar to that of the control group (63%). There is therefore a need to modify the current methods to yield higher specificity while maintaining sensitivity. One particular study by Heeg et al. (2005) investigated strategies to improve the specificity of the FDT. It was found that the most effective strategy included confirming an abnormal test result with a repeat test, yielding an increase in specificity with some loss in sensitivity in the early to moderate glaucoma patients (Heeg *et al*., 2005). In 2003, Horn et al. also suggested that combined use of techniques proved to be more superior as opposed to just one method (Heeg et al. (2005). Heeg *et al*. (2005) suggested this strategy was not very useful and also deviates from the common clinical setting as it requires a second piece of equipment to be purchased.

The NPV calculated at 100% also emphasises the value of the instrument in being able to produce less false positive findings. This can have significant implications for resource limited settings where there is a significant paucity of human resources to address eye care needs. Less false positive findings during screening of glaucomatous change will mean that less time is wasted on having to provide conclusive 'gold standard' testing using the HVFA. Furthermore, in settings where financial resources and infrastructure are limited, conclusive findings could be impossible if there is no HVFA. In some cases, patients may incur hefty costs in travelling to sites with the appropriate equipment to make conclusive diagnoses of potentially blinding glaucomatous change.

The negative predictive value (NPV) for both case and control subjects was 100%. This is highly useful as it scientifically proves the MMDT will avoid the case of false positives and thereby reducing over referrals- which essentially overburdens the health care system (Kaur *et al.*, 2016). The above results show that the MMDT correctly identified 65.3% (specificity) of those who did not have glaucomatous visual field changes.

5.2 General conclusions and recommendations

5.2.1 Conclusions

The study concluded that the Moorfields Motion Displacement Test (MMDT) is sensitive enough (100%) in detecting visual field changes of diseased (glaucomatous) and non-diseased (control) eyes, when compared to the gold standard Humphreys Visual Field Analyser (HVFA). In a developing world context where resources are limited, the MMDT has the added advantage of being portable, inexpensive and faster (approximately 3 times), which is necessary for rapid case-finding in a community. The MMDT has now proven to be scientifically more likely sensitive than Frequency Doubling Technology (FDT) perimetry in screening for glaucoma in the population-based setting and our results are consistent with the findings of Ong et al. (2014), however, our study shows the instrument to be sensitive enough to be used as a screening tool due to its low specificity (63.3%).

The results from this study showed no significant association between gender, age and race with regards to the test duration on both the MMDT and HVFA. Whilst there was no significant variation amongst the different gender and age groups when choosing a preferred visual instrument, 83.5% of participants across the different race groups, preferred the MMDT. There also seemed to be no significant variation among the different race, gender and age groups in selecting the preferred fixation target between the light (HVFA) or dot (MMDT) nor the method of selection using the button (HVFA) and mouse (MMDT). Overall the results did not indicate any significant anxiety between the associated groups using both instruments.

5.2.2 Recommendations

Glaucoma generally affects older individuals, who often have to deal with more than just ocular challenges, such as mobility and dexterity issues, hearing loss, memory loss, coupled with driving

inability and visual search issues. The availability of optometrists and ophthalmologists in the public sector is another challenge in developing countries with a large ratio of patients to a single practitioner, thereby making it even more difficult for follow up testing, more especially when tests are of longer duration and expensive to purchase and maintain (such as the HVFA). It is therefore recommended for future studies and developments, that the above factors are considered in order to improve on current technology and systems in the field of eye health care, specifically to that which is required for visual field testing. The findings of the study suggest that the MMDT can be successfully used as a screening tool for visual field changes accompanying glaucoma. It is recommended that similar research is conducted on a larger sample size as well as on conditions other than glaucoma to determine if the instrument can be applicable to all kinds of visual field changes. An adjustment to the referral criterion may remove the need for repeat testing. To optimise the reliability of test results, the study investigators would recommend that a custom designed and simple push button response system, that would require less manual dexterity and coordination, should replace the mouse in future versions of the test.

5.2.3 Limitations of the study

During the conduct of the study there were a few challenges which arose. At initial stages of data collection, recruitment of the desired number of participants per day were difficult to obtain, purely due to administrative processes at the location. This essentially meant fewer participants were tested per day, lowering the weekly target required. Another challenge encountered during the data collection process was the recruitment of control participants, as majority of the participants attending McCords Provincial Hospital had already presented with pathology. The location was then changed to Prince Mshiyeni Memorial Hospital to obtain the control participants.

Due to time constraints, the recommended sample size was not obtained for both the case and control groups, and therefore, should be considered for future studies.

The Moorfield's Motion Displacement Test is relatively new when compared to the gold standard, Humphreys Visual Field Analyser and therefore no algorithm had yet been developed (at the time of this study) to directly compare the results from these two instruments. As a result, cluster analysis was done to ensure a clinically and statistically acceptable comparison. The format of choice was manuscript format, and including one article to summarise the best findings of the study also proved challenging. The structure could have been reconsidered to allow for more of the findings to be included in the dissertation, perhaps even in an additional article.

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APPENDICES

Appendix 1. Information document- English version

INFORMATION DOCUMENT

Study title: An evaluation of the accuracy of the Moorfield's Motion Displacement Test

Greeting: Dear Participant

Introduction: I, Keshia Chetty, am conducting a research study on a recently developed visual field tester known as the Moorfields Motion Displacement Test (MMDT). The aim of the study is to compare the results from the Moorfields MDT to the tried and tested method which is the Humphreys Visual Field Analyser (HVFA). These devices are used to detect whether any changes occurring inside the eye, as a result of glaucoma, are affecting your awareness of your surroundings. The HVFA has been thought to be the best at detecting subtle changes in one's visual field. However, the Moorfields MDT is more affordable and if found to be as accurate as the HVFA, can be used as an alternative, especially in developing countries. For this reason, this study is of particular importance to us as it could provide our public health care system with a cost effective method of diagnosing glaucoma.

Invitation to participate: We are inviting you to participate in this research study which has the potential to help millions of other people with glaucoma.

What is involved in the study: By being part of this study you are agreeing that both eyes be tested, using both instruments.

Risks: There are no potential risks of being involved in the study. You will not be identified.

Benefits: The benefits involved are a comprehensive, free analysis of your visual field and knowledge of the quality of sight.

Treatment: No treatment is required, however, if we do pick up any additional eye problems, we will advise you on possible steps to take.

Reimbursements: There is no cost to be a participant in this study.

Confidentiality: Efforts will be put in place to keep personal information completely confidential. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committee and the Medicines Control Council. All information will be kept confidential and kept in a locked cupboard for 5 years, after which they will be destroyed. Your participation in this study is completely voluntary and a refusal to participate will involve no penalty. You may discontinue your participation from this study at any time.

For further information, please contact:

Miss Keshia Chetty: 074 303 5532 kbchetty.za@gmail.com

Miss P Govender: 031 202 3811 p.govender@brienholdenvision.org.za

Appendix 2. Information document- isiZulu version

INFORMATION DOCUMENT (ZULU VERSION)

UMBHALOOQUKETHEULWAZI

Ukucwaningango kuthiumshini i-Moorfields motion displacement tester usebenza ngokunembayona ngobuchuleyini

Kuwe ozobayinxenye yocwaningo:

Isingeniso:

Mina, ngiKeshia Chetty, senza ucwaningo ngomshini wokuhlola amehlo omusha i-Moorfields MDT,siwuqhathanisa ukusebenza kahle kwawonalo omdala owaziwange-Humphrey's visual field analyzer (HVFA). Lemishini isetshenziselwa ukuhlola ukuthi ushintsho olwenzeka phakathi ehlweni ngenxa yezifo ezinjenge-Glaucoma luyayiphazamisa yini indlelaobonangayo, isibonelo: ukukwazi nokuqaphela indawo ukuyo. Lo omdala i-HVFA, ubusucwaningwe isikhathi esidewathwalwa ngeqoma njengo sebenza kahlengo kwedlulele. Kulolucwaningo sizo qhathanisa ukuthi i-Moorfields MDT isebenza kancono yinikune-HVFA. Umshini i-Moorfields MDT ushibhilekune-HVFA ngakho-ke ungasiza emazweni asathuthuka ashodayo ngezinsiza. Ukuhlola ubuchule be-Moorfields MDT sizohlola abane-Glaucoma.

Isisimemo sokubayingxenye yocwaningo:

Siyakumema ukuba uzibanda kanye nalolucwaningo.

Yini engizoyenza ocaningweni:

Uma uzibanda kanye kusho ukuthi uyavuma ukuhlolwa amehlo womabili kusetshenziswa imishini yomibili.

Ubungozi:

Abukho ubungozi ubuyobakhona, noma ubuyo bangumthelela wokubamba iqhaza noma ingxenye yogcwaningo. Umbono wababambe iqhaza uyogcinwa uyimfihlo, kodwa umphumela wamaqembu uyosakazwa, waziwe izwelonke. Lokhu kuhlolwa ngeke kuwalimaze amehlo noma indlela obona ngayo ngakho-ke ucwaningo alukubeki engcupheni.

Uzosizakala ngokuhlolwa amehlo mahhala nokwazi ukuthi ukubona kwakho kusezingeni elihle yini.

Isimo sezokukhokha:

Akukho mali ozoyikhokha.

Imfihlakalo:

Lonke ulwaziluzo gcinwa luyimfihlo ngaphandle uma lufunwa yingalo yomthetho. Ukuzibanda kanyak uzoba ukuthanda kwakho kanti ungayeka noma nini uma uthanda futhi ngeke uhlawuliswe ngokwenzenjalo.

Thola imininingwane egcwele ngokuthintana no:

Miss Keshia Chetty: 074 303 5532 kbchetty.za@gmail.com

Miss P Govender: 031 202 3811 p.govender@brienholdenvision.org.za

Appendix 3. Consent form- English version
CONSENT FORM (ENGLISH VERSION)

Research Study: An evaluation of the Moorfields Motion Displacement Tester

Dear Sir/Madam

Glaucoma is a condition in which a patient is very often diagnosed with an increase in the pressure inside the eye. This causes damage to the optic nerve found at the back of the eye, resulting in decreased awareness of one's surroundings. This affects many activities of daily living such as, difficulty reading and writing, moving around and difficulty seeing colours. If left untreated, glaucoma can lead to blindness. Since glaucoma is a condition which causes subtle changes in the visual field of the effected individual, we thought it pertinent to assess how accurate the new instrument, used for assessing visual fields, is in detecting these subtle changes.

The Moorfields Motion Displacement Test (MMDT) and the Humphrey's Visual Field Analyser (HVFA) are used to test how aware one is of their surroundings. The aim of this study is to investigate how accurate the Moorfield's MDT is in comparison to the tried and tested Humphrey's Visual Field Analyser (HVFA).

You will be required to sit through both visual field tests, i.e. MMDT and HVFA. During the eye examination, each of your eyes will be tested using both visual field tests. The approximate test duration for the HVFA is 15 minutes for each eye, and for the Moorfields MDT, 5-7 minutes per eye. The results will then be compared. During the process, should we find any additional problems related to your eyes, we will advise you of possible steps you can take to address them. The equipment used will not cause any pain or harm to your eyes or your vision in any way. Your personal details will be kept confidential although results from the test will be analysed. You have the right to withdraw from the study at any point during the examination should you wish to do so.

If the above is understood and you agree to participate in this study, please sign in the space provided below. By signing this document, you are agreeing to grant us permission to analyse and compare the results obtained from each test.

The research will be conducted by myself, Keshia Chetty, with permission from the Medical Research Office at the Nelson R Mandela School of Medicine. This study is being supervised by Ms. P. Govender (Brien Holden Vision Institute), Prof. Kovin Naidoo (Department of Optometry at the University of KwaZulu Natal), and Prof. James Loughman from The Dublin Institute of Technology.

_____ _____

Patient Date

_____ _____

Clinician Witness

Appendix 4. Consent form- isiZulu version

CONSENT FORM (ISIZULU VERSION)

IFOMU LOKUVUMA UKUBA YINXENYE YOCWANINGO

Mnumzane/Nkosikazi/Nkosazana:

Isifo esaziwa ngokuthi yi-glaucoma yisifo lapho kuba nengcindezi phakathi ehlweni bese kulimala umthambo omkhulu obizwa ngokuthi yi-optic nerve engemuva kwehlo. Lokhu kukhinyabeza ukusebenza kwehlo, kunciphe amathuba okubona okwenzeka endaweni okuyo. Lokhu kuphazamisa okuningi empilweni yomuntu yansuku zonke njengobunzima bokufunda nokubhala, ukuhamba okujwayelekile kanye nokuhluleka ukubona imibala. Ngakho-ke, uma ingalashiwe i-glaucoma ingenza umuntu agcine eyimpumputhe.

Inhloso yalolu cwaningo ukuphenya ukuthi umshini omusha owaziwa nge-Moorefield's MDT unobuchule nobuchwepheshe kangakanani uma uqhathaniswa nenhlobo endala eyaziwa ngokuthi yi-Humphrey's Visual Field Analyzer.

Ngesikhathi kuhlolwa amehlo, ihlo lakho ngalinye lizohlolwa kusetshenziswa imishini yomibili ukuze kuqhathaniswe ukuthi imiphumela etholakalayo iyefana yini. Ukusetshenziswa kwale mishini ngeke kuwalimaze amehlo akho nokusebenza kwawo. Igama lakho nemininingwane yonke yakho izogcinwa iyimfihlo kodwa. Uma ufisa ukunyomuka ungabe usaba yinxenye yocwaningo unelungelo lokwenzenjalo noma nini.

Uma uluqondisisa lolu lwazi olunikwe ngenhla futhi uzivumela ngokwakho ukuba yinxenye yocwaningo uzosayina esikhaleni esinikwe ngezansi. Lolu cwaningo luzobe lwenziwa uKeshia Chetty ngemvume yophiko lokucwaninga ngezempilo enyuvezi olwaziwa nge-Faculty of Health Sciences Research and Ethics committee.

_____ _____

Igama nesibongo Usuku

_____ _____

Owezempilo Ufakazi

UKZN Eye Clinic (E5-525): 031 260 7352

Medical Research Office @ Nelson R Mandela School of Medicine:

Tel: 031 260 4604

Appendix 5. Data collection form

Surname:		Date:	Y Y Y Y M M D D
First Name:		Patient number:	
Age:		Gender:	M F
Postal address:		Type of glaucoma:	

POAG	PACG	SOAG	SACG
INFANTILE PCG	OTHER		

Number of years diagnosed with glaucoma:

Please tick the correct choice with **black** ink only.

*Question 12-16 to be answered at the end of the examination.

Ocular history:

1. When was your last eye examination?

≤ 1 month ago		≤ 1 year ago		≥ 2 years ago		≥ 5- 10 years ago	

2. Did your last eye examination include a visual field assessment?

Y	N

3.(a) Have you previously been diagnosed with any eye disease other than glaucoma?

Y	N

(b) If you have answered “yes” to the above question, please specify.

(c) If you have answered yes to the previous question, please specify what treatment you are on, if any.

4. Have you sustained any injury or had surgery to your eye(s)?

Y	N

5. Which of the following systemic illnesses, if any, do you have?

Diabetes	
Hypertension	
Thyroid disease	
Autoimmune disease	
Other	
None	

6. Are you on any chronic medication for any illnesses? If yes, please list them below.

Y	N

Name of medication	Dosage

7. Is there a family history of glaucoma?

Y	N

Question 8 and 9 are multiple response questions i.e. more than one choice can be ticked.

8. Which activities of your daily living would you say have been affected since your glaucoma diagnosis?

Mobility	
Driving	
Visual search	

9. How do you feel when going in for visual field testing?

Anxious	
Intimidated	
Frustrated	
Scared	
Depressed	
Neutral	

10. What do you like least about visual field testing?

_____

_____

_____

11. On a scale of 0 to 5, (0= no anxiety; 5= extreme anxiety), please rate your anxiety levels during visual field testing on the Humphreys Visual Field Analyser (HVFA):

0	
1	
2	
3	
4	

5	

*12. To be answered at the end of the examination

On a scale of 0 to 5, (0= no anxiety; 5= extreme anxiety), please rate your anxiety levels during visual field testing on the Moorfield's Motion Displacement Test (MMDT):

0	
1	
2	
3	
4	
5	

*13. To be answered at the end of the examination

How would you rate the ease of use of the MMDT, as compared to the HVFA? (0= extremely difficult; 5= extremely easy)

0	
1	
2	
3	
4	
5	

*14. To be answered at the end of the examination

Please select which method of response indication was easier to use between the HVFA and the MMDT (please tick appropriate choice):

Push button on HVFA		Mouse on MMDT	

*15. To be answered at the end of the examination

Between the two methods of visual field testing (which you were exposed to) which <u>fixation target</u> did you prefer?

The central white dot of the MMDT	
The center of the 4 sets of lights on the HVFA	

*16. To be answered at the end of the examination

Between the two methods of visual field testing (which you were exposed to) which method (HVFA or MMDT) did you prefer? Please provide reasons for your choice.

END

Thank you for answering all of the above questions

Appendix 6. Ethical clearance letter of approval- BREC

UNIVERSITY OF
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI

RESEARCH OFFICE
BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 260-4609
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

12 April 2017

Ms K Chetty (209500227)
Department of Optomerty
School of Health Sciences
kbchetty.za@gmail.com

Dear Ms Chetty

Title: An evaluation of the accuracy of the Moorfield's motion displacement test.
Degree: MOptom **BREC Ref No: BE421/16**

We wish to advise you that your correspondence received on 08 April 2017 submitting an application for Amendments to add additional site - Prince Mshiyeni Memorial Hospital (PMMH) Eye Clinic -for the above study has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee.

PLEASE NOTE: PI will need to submit provincial KZN DOH permission for use of the additional site at PMMH.

This approval will be **ratified** at the next BREC meeting to be held on **09 May 2017.**

Yours sincerely

Ms Anusha Marimuthu
Senior Admin Officer: Biomedical Research Ethics Committee

cc supervisor: K.naidoo@brienholdenvision.org
cc postgraduate administrator: nenep1@ukzn.ac.za

Appendix 7. Department of Health letter of approval

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

330 Langalibalele street,
Private Bag X9051 PMB. 3200
Tel: 033 395 2805/3189/3123 Fax: 033 394 3782
Email. hrkm@kznhealth.gov.za
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management (HKRM)

Reference: HRKM289/16
KZ_2016RP47_13

20 September 2016

Dear Ms K Chetty
(University of KwaZulu-Natal)

Subject: Approval of a Research Proposal

1. The research proposal titled '**An evaluation of the accuracy of the Moorfield's Motion Displacement Test**' was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at McCord Provincial Eye Hospital.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Ms G Khumalo on 033-395 3189.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee
Date: 20/09/16

Appendix 8. Gatekeeper permission- McCord Provincial Hospital

This letter serves a provision approval to access the glaucoma patient database at the McCords Eye Hospital, contingent on DoH approval of the study.

Dr Kapil Moodley

McCord's Provincial Eye Hospital

PO Box 37587

Overport

4067

RESEARCH OFFICE

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION,

Westville Campus,

Govan Mbeki Building,

Private Bag X 54001,

Durban,

4000,

KwaZulu-Natal, SOUTH AFRICA

BREC@ukzn.ac.za BREC Ref No: BE421/16

Subject: Letter granting permission to conduct Master's study at McCord's Provincial Eye Hospital

23 August 2016

Dear Biomedical Research Ethics Committee:

On behalf of McCord's Provincial Eye Hospital, I am writing to grant permission to Ms Keshia Chetty who is conducting her Masters in Optometry at the University of KwaZulu-Natal Westville Campus. The title of her research is: *An evaluation of the accuracy of the Moorfield's Motion Displacement Test*. I understand that Ms K Chetty will recruit approximately 350 of our diagnosed glaucoma patients, as well as approximately 200 normal subjects, for visual field testing at McCord's Provincial Eye Hospital over the next year. We are happy to support the data collection for this research study.

Sincerely,

Dr Kapil Moodley

UMUNYANGO WEZEMPILO
DEPARTMENT OF HEALTH
McCORD PROVINCIAL EYE HOSPITAL
24 AUG 2016
P.O. BOX 37587
OVERPORT 4067

Appendix 9. Gatekeeper permission- Prince Mshiyeni Memorial Hospital

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE: Senior Medical Manager

Mangosuthu Highway, Private Bag X 07
MOBENI
Tel: 031 907 8317/8304 Fax: 031 906 1044 Email:myint.aung@kznhealth.gov.za
www.kznhealth.gov.za

Prince Mshiyeni Memorial Hospital

Enquiry: Dr M AUNG
Ref No: 14/RESH/2017
Date: 27/03/2017

TO: Keshia Chetty

RE: LETTER OF SUPPORT TO CONDUCT RESEARCH AT PMMH

Dear researcher;

I have pleasure to inform you that PMMH has considered your application to conduct research on **"An evaluation of the accuracy of the Moorfield's Motion Displacement test"** in our institution.

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Please ensure this office is informed before you commence your research.
4. The institution will not provide any resources for this research.
5. You will be expected to provide feedback on you finding to the institution.

Should the following requirements be fulfilled, a Permission/ Approval letter will follow.

- Full research protocol, including questionnaires and consent forms if applicable.
- Ethical approval from a recognized Ethic committee in South Africa

Thank you.

MYINT AUNG
Senior Medical Manager & specialist in Family Medicine
MBBS, DO(SA), PGDip in HIV (Natal), M.Med.Fam.Med (natal)
Tel: 031 9078317
Fax: 031 906 1044
myint.aung@kznhealth.gov.za

Appendix 10. Timeframe