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EVALUATION OF LOW VISION SERVICES ON THE QUALITY OF LIFE OF
INDIVIDUALS WITH AGE-RELATED MACULAR DEGENERATION

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THESIS SUMMARY

Aston University

Evaluation of Low Vision Services on the Quality of Life of Individuals with Age-Related Macular Degeneration

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2015

Background: Age-related macular degeneration (ARMD) is a major cause of irreversible visual loss in the elderly and a significant threat to their quality of life. Although low vision services often improve the functional outcomes of individuals with macular disease, it remains unclear whether or not they have any impact on quality of life. The principal aim of this study was to determine the effect of a hospital-based low vision clinic on the quality of life of individuals with ARMD.

Methods: Forty patients with ARMD attended the low vision clinic at Milton Keynes University Hospital. Quality of life was measured with the vision-specific Low Vision Quality of Life (LVQOL) questionnaire and the general health EuroQol (EQ-5D-5L) questionnaire. Measures were completed at baseline (time zero, T0), and at three- (T3) and six-month (T6) follow-up visits.

Results: The near visual acuity of individuals attending the low vision clinic for the first time improved significantly between visits T0 and T3 ($p=0.005$), reflecting the practiced use of their newly-dispensed low vision aids. As expected, there was no significant change in near acuity over this time period for existing patients. For both new and existing patients, a significant increase in LVQOL score was evident between visits T0 and T3, with a further significant improvement between T3 and T6. Similarly, there was a significant decrease in EQ-5D-5L questionnaire scores between visits T0 and T6.

Conclusions: The higher LVQOL scores obtained at the end of the study period (T6) provide evidence that low vision services at Milton Keynes University Hospital served to improve patient quality of life. The reduction in EQ-5D-5L scores over the same time period suggests that low vision services also provide for an improvement in general health-related quality of life.

Impact: The findings support the cause of low vision services to improve not only the vision and functional outcomes of individuals with macular disease but also their quality of life. Moreover, the findings suggest that a more efficient allocation of resources at low vision clinics may be possible through the standardisation of patient follow-up frequency.

Key words: ARMD, EQ-5D, Hospital Eye Service, LVQOL, questionnaire

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PREFACE

The results of the thesis will be presented at the Hospital Optometrists Annual Conference 2015, Glasgow.

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LIST OF ABBREVIATIONS

Acronym	Definition
ANOVA	Analysis of variance
AREDS	Age Related Eye Disease Study
ARM	Age related maculopathy
ARMD	Age related macular degeneration
BrM	Bruch's membrane
CC	Choriocapillaris
CCTV	Closed circuit television
CF	Count fingers
CNV	Choroidal neovascularisation
CO	College of Optometrists
CVI	Certificate of Vision Impairment
DR	Diabetic retinopathy
DVA	Distance visual acuity
ECLO	Eye Clinic Liaison Officer
EQ	EuroQol
EQ-5D-5L	EuroQol five-dimension, five-level (questionnaire)
FAF	Fundus autofluorescence
GA	Geographic atrophy
GP	General practitioner
HES	Hospital Eye Service
HM	Hand movements
LE	Left eye
LOCSU	Local Optical Committee Support Unit
logMAR	Logarithm (base 10) of the minimum angle of resolution.
LP	Perception of light
LV	Low vision

Acronym	Definition
LVA	Low vision aid
LVQOL	Low Vision Quality of Life (questionnaire)
LVS	Low vision service
LVSCG	Low Vision Services Consensus Group
LVSW	Low Vision Service Wales
MAI	Mass of Activity Inventory (questionnaire)
MK	Milton Keynes
MKUH	Milton Keynes University Hospital
MLVQ	Manchester Low Vision Questionnaire
MSVI	Moderate and severe visual impairment
NEI-VFQ	National Eye Institute Visual Function Questionnaire
NHS	National Health Service
NICE	National Institute for Clinical Excellence
NPL	No perception of light
NVA	Near visual acuity
NVA-LVA	Near visual acuity with a low vision aid
OD	Oculus dexter (right eye)
ONS	Office for National Statistics
OS	Oculus sinister (left eye)
PR	Photoreceptor
QoL	Quality of life
RCO	Royal College of Ophthalmologists
RE	Right eye
RMANOVA	Repeated measures analysis of variance
RNIB	Royal National Institute of Blind People
RP	Retinitis pigmentosa
RPE	Retinal pigment epithelium

Acronym	Definition
RVI	Referral of Vision Impairment
SARC	Sensory Advice Resource Centre
SD	Standard deviation
SF-36	Medical Outcomes Study 36-Item Short Form (questionnaire)
SI	Sight impaired
SPSS	Statistical Package for the Social Sciences (software)
SSI	Severely sight impaired
UK	United Kingdom of Great Britain and Northern Ireland
VA	Visual acuity
VAS	Visual analogue scale
VCM1	Vision-Quality of Life Core Measure (questionnaire)
VEGF	Vascular endothelial growth factor
VF-14	Visual Function-14 (questionnaire)
WHO	World Health Organisation

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1 INTRODUCTION

1.1 Low Vision

1.1.1 Definition and prevalence

Visual impairment is a major world health issue that is an economic burden and reduces quality of life (QoL). Monitoring prevalence data on visual impairment allows for research and planning of policies to prevent and eliminate treatable causes (Pascolini and Mariotti, 2012; Bourne *et al.* 2013; Stevens *et al.* 2013).

The global prevalence of blindness and low vision is 39 million and 246 million respectively, and which collectively form the magnitude of 'visual impairment' (Pascolini and Mariotti, 2012). These data form part of the World Health Organisation (WHO) Prevention of Blindness and Deafness Programme where the authors carried out a systematic review of data for 2010 from 39 countries across 6 WHO regions. Blindness was defined as a presenting visual acuity (VA) in the better eye of less than 3/60, and moderate and severe visual impairment (MSVI, also referred to as 'low vision') as VA in the better eye less than 6/18 but at least 3/60.

This analysis was expanded by Bourne *et al.* (2013) and Stevens *et al.* (2013) in systematic reviews of additional published and unpublished data from 1980 to 2012, from 227 studies in 84 countries, using the same definitions of blindness and MSVI. The authors estimated that in 2010, 65% of 32.4 million blind people, and 76% of 191 million people with MSVI had a preventable or treatable cause.

Their data are interesting because, as with Pascolini and Mariotti (2012), it highlights the unequal distribution of visual impairment across the world. These studies do not present UK specific data. Figures from the Royal National Institute of Blind People (RNIB; Access Economics, 2009) estimated that in 2008, the collective level of low vision comprising data for blindness (VA of <6/60 in the better-seeing eye) and partial sight (VA of <6/12 to 6/60 in the better-seeing eye), was approximately 2 million (3.25 % of the UK population).

The objective definitions based on visual acuity for low vision used by the WHO and RNIB are different from that of the Low Vision Services Consensus Group (LVSCG, 1999), who defined a person with low vision as:

‘One who has an impairment of visual function for whom full remediation is not possible by conventional spectacles, contact lenses or medical intervention and which causes restriction in that person’s everyday life.’

The above definition also includes people who do not necessarily meet the WHO / RNIB criteria, but for whom low vision impacts on their daily life. This involves a more subjective assessment of low vision that would be difficult to apply across different nations in different regions of the world due to different living standards; however this approach is useful as it includes the debilitating effect of blindness and low vision on people’s lives.

Even small levels of visual impairment could have a significant impact on QoL (Loughman *et al.* 2011). A visual acuity of ‘just below’ driving standard would result in a loss of license and potential loss of independence, whereas more substantial impairment could impact upon a person’s ability to perform everyday functional tasks such as reading, shopping, and watching television (The College of Optometrists and The Royal College of Ophthalmologists (CO-RCO), 2013).

The effects of low vision and consequential reduced functioning are well documented and include reduced social interaction (Loughman *et al.* 2011), a reduction in psychological wellbeing (McManus and Lord, 2012), and an increased prevalence of depression (Ryan, 2014), particularly in the elderly population (Evans *et al.* 2007). Tabrett and Latham (2009) reported on the levels of depression in visually impaired patients being comparable to those of patients with other chronic conditions (e.g. stroke, cancer and diabetes).

In the UK, the Department of Health aims to minimise preventable / treatable causes of blindness and low vision and provide support to manage untreatable causes through various methods including low vision services (LVS) and registration.

Registration

Visually impaired patients in the UK who meet the appropriate criteria¹ are certified as 'sight impaired' (SI), or 'severely sight impaired' (SSI), by a consultant ophthalmologist.

A Certificate of Vision Impairment (CVI) is used to register with the patient's local authority. The benefit of registration for the patient is easier access to a range of practical and financial support, although access to low vision services and social services rehabilitation can still be obtained by those who do not meet registration criteria.

Epidemiological statistics on certification are not an accurate representation of the actual number of people in the UK living with visual impairment severe enough to impact upon their daily life (Access Economics, 2009). This is estimated to be almost 2 million (about 1 person in 30), a greater number than the 360,000 obtained from SI and SSI registration figures (Access Economics, 2009).

A large number of patients will be affected by low vision, even though their acuity levels and visual field are not below the stated thresholds for registration. For these patients, provision of low vision (and rehabilitation services) can be as important to QoL as for those who are registered.

1.1.2 Minimizing the impact of low vision

The economic impact of low vision in the UK is substantial. An RNIB report estimated the combined direct and indirect health care costs in 2008 from SI and SSI in UK adults to be £22 billion, with the largest component cost from reduced QoL and premature mortality, reducing the stock of health capital by £14.53 billion (Access Economics, 2009). These costs were predicted to increase by 21.4% to 2013 (Access Economics, 2009), with the

¹ Severely sight impaired: Group 1 – VA below 3/60; Group 2 – VA of 6/60 but below 3/60 with a very contracted field of vision; Group 3 – VA of 6/60 or above with a contracted field of vision, especially in the lower part of the field. Sight impaired: VA 3/60 to 6/60 with full field; or up to 6/24 with moderate contraction of the field, opacities in media or aphakia; or, 6/18 or even better if they have a gross defect, for example hemianopia, or if there is a marked contraction of the visual field. Adapted from the Certificate of Vision Impairment, Department of Health (2013).

demands on the UK economy set to rise further with a predicted large increase in the number of people affected by sight loss in the future.

Using prevalence data for future projections, it has been estimated that there will be approximately 3.99 million people in the UK affected by low vision in the year 2050 (122% of 2008 estimations). This is partly due to an ageing UK population (Access Economics, 2009), with epidemiological studies consistently demonstrating the link between increased age, increased prevalence of eye disease and associated vision loss (Bunce and Wormald, 2008; Evans and Wormald, 1996).

Data from the Office for National Statistics (ONS) show that the number of people in the UK population is rising steadily, with an associated increase in the population median age over time (ONS, 2012). The continuing increase in the number and proportion of people over 65 years of age has led to a prediction that this group will account for 23% of the total population in 2035, an increase from 17% in 2010 (ONS, 2012). The fastest growing population group comprises those aged 85 and over (ONS, 2012). This group also has the highest levels of sight loss, with one in three people affected (RNIB, 2013).

Understanding the causes of low vision and the temporal trends for each cause are essential in both prevention and treatment. Treatment should also include the provision of low vision services to enable people to live as independently as possible (LVSCG, 1999), thus reducing the economic burden on UK resources.

1.1.3 Causes of low vision

The causes of low vision can be extensive, originating from a range of congenital, hereditary and age-related eye conditions; or as a direct result of trauma (CO-RCO, 2013). Low vision can also be associated with general health conditions such as stroke, obesity and diabetes, or related to learning disabilities (CO-RCO, 2013).

Global causes of low vision

Pascolini and Mariotti (2012) and Bourne *et al.* (2013) demonstrated that 54% of global blindness in 2010 resulted from two treatable causes, cataract and uncorrected refractive error. In both studies, uncorrected refractive error was the largest cause of overall visual impairment inclusive of blindness (42%; Pascolini and Mariotti, 2012), and MSVI (51%;

Bourne *et al.* 2013) worldwide. This highlights the significance that adequate provision of a simple refractive correction could have on the global health economy.

The differences in the magnitude and causes of blindness and (MSVI) low vision between high and low-income regions are stark (Figure 1.1), further representing the significance of treatable causes (Bourne *et al.* 2013).

In less developed (low-income) regions, blindness and MSVI are caused by a range of preventable / treatable and untreatable conditions. In more developed nations, the improved medical care means that causes are predominantly untreatable. Results over a 20 year time period from 1990 to 2010 (Bourne *et al.* 2013) are consistent with other studies in demonstrating an increased global prevalence of untreatable causes, particularly age-related macular degeneration (ARMD) in high-economy regions (Klaver *et al.* 1998; Taylor *et al.* 2005).

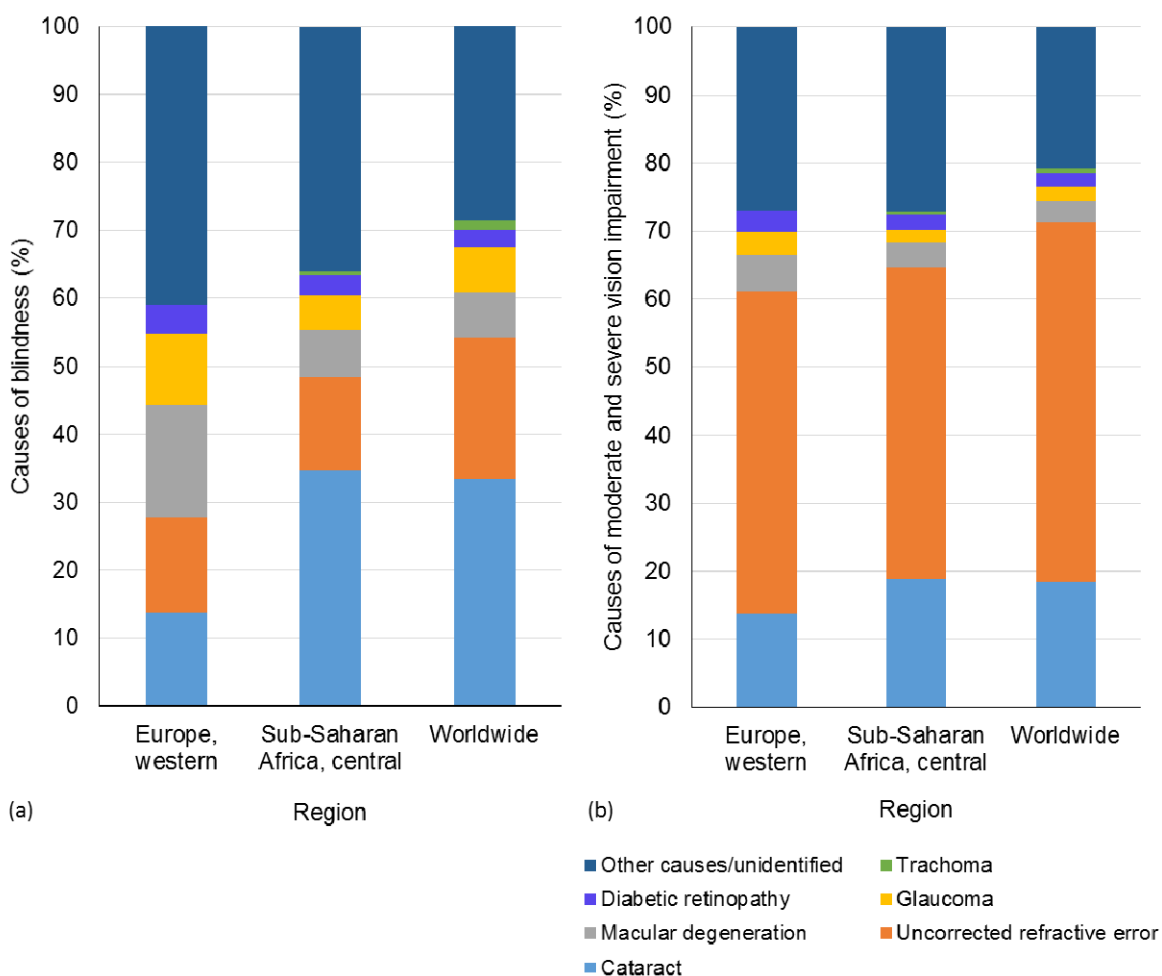


Figure 1.1 The contrast in causes of (a) blindness and (b) moderate and severe visual impairment (MSVI) / low vision in 2010 between developed Western Europe, developing central Sub-Saharan Africa and Worldwide. Adapted from Bourne *et al.* (2013).

Causes of low vision in the UK

Access Economics (2009) reported on the leading causes of sight loss in UK adults (Table 1.1), defining sight loss as SI or SSI in the better eye. These figures include data from correctable causes of sight loss. In the UK it is estimated that more than 50% of sight loss can be avoided on the basis of improvement in sight with the correct treatment, including correction of refraction error with a spectacle prescription (Access Economics, 2009). When compared with global figures of 80% (Pascolini and Mariotti, 2012), although this UK figure is lower, the burden on the UK health economy from treatable causes is still unnecessarily large.

Table 1.1 Leading causes of sight loss in UK adults, adapted from Access Economics (2009). The percentage of affected adults with sight loss from all other causes (7.4%) was calculated as the remainder after each of the five leading causes had been subtracted from total sight loss causes of 100%. SI – sight impaired, SSI – severely sight impaired (in the better eye).

Cause of sight loss	Percentage of adults in the UK affected
Sight loss equivalent to partial sight (SI) or blindness (SSI) due to refractive error	53.5%
Age-related macular degeneration	16.7%
Cataract	13.7%
Other eye diseases	7.4%
Glaucoma	5.3%
Diabetic retinopathy	3.5%

Bunce *et al.* (2010), reported on the main causes of blindness (broadly equivalent to SSI) and partial sight (broadly equivalent to SI) from certifications in 2007-2008 in England and Wales. Table 1.2 shows that the principal cause of new certifications of both SI and SSI was the same – ‘degeneration macular and posterior pole’, which mainly comprises ARMD (Bunce *et al.* 2010). This was followed to a much lesser extent by glaucoma and diabetic retinopathy / maculopathy for SSI certificates, and diabetic causes with a marginally higher percentage than glaucoma in the case of SI.

Proportional comparison with historical data confirms these trends (Bunce and Wormald, 2006 & 2008). Although the exact numbers of patients with certifiable visual loss may not be available, epidemiological data through CVI’s is important to monitor trends in the causes of low vision, and therefore predict the numbers of people requiring support from low vision

services. This is particularly relevant in the case of ARMD due to the resulting high numbers of certifications from this condition.

Table 1.2 Causes of new blindness (SSI) and partial sight (SI) certifications, April 2007 to March 2008, adapted from Bunce et al. 2010.

Cause of certification	Blindness	Partial sight
Degeneration macular and posterior pole	58.6%	57.2%
Glaucoma	8.4%	7.4%
Diabetic retinopathy / maculopathy	6.3%	7.6%
Hereditary retinal disorders	5.5%	4.2%
Optic atrophy	4.2%	2.9%
Disorders of visual cortex	2.3%	2.9%
Retinal vascular occlusion	1.8%	1.2%
Cerebrovascular disease	1.5%	4.3%
Progressive myopia	1.2%	1.3%
Keratitis / corneal opacity and other disorders of cornea	-	1.2%
No information on main cause	2.7%	2.7%
Other causes	7.5%	7.1%

1.1.4 Macular disease

The macula is responsible for central vision. Macula disease is one of the main causes of irreversible visual impairment in the UK and affects all age groups, predominantly those over 60 years in the form of ARMD.

Stargardt's disease, a form of juvenile macular degeneration, is the most common form of inherited macular dystrophy (Kanski, 2003), with presentation by the second decade. The most commonly affected daily living tasks were reported to be reading, driving and recognizing faces (Miedziak *et al.* 2000). The authors made psychological comparisons

between patients with late onset Stargardt's disease and those with ARMD. Other, rarer juvenile macular degenerations include Juvenile Best Disease and Cone Dystrophy.

1.1.5 Glaucoma

Glaucoma is a progressive, age-related optic neuropathy known to cause retinal ganglion cell death (Sehi *et al.* 2009). This leads to structural changes including loss of the neuroretinal rim of the optic nerve head and thinning of the retinal nerve fibre layer. The resultant irreversible peripheral visual field defects (Greaney *et al.* 2002) lead to reduced levels of functional vision affecting mobility and driving, eventually resulting in 'tunnel vision'.

Intraocular pressure is the only modifiable risk factor for primary open angle glaucoma (Coleman and Miglior, 2008). Reduction of intraocular pressure by medication or surgery remains the only approach known to be effective against visual loss (Steele and Spry, 2009).

Quality of life studies have reported on both the side effects of medication and the loss of visual function associated with glaucoma. Nordmann *et al.* (2003) reported that reduced vision-related QoL was attributed to side effects from topical medication. Nelson *et al.* (2003) highlighted the disability caused by bilateral loss of peripheral vision; tripping over, problems with mobility and bumping into objects. Evans *et al.* (2009) concluded that although QoL was affected to a similar level in both glaucoma and ARMD, different problem areas were highlighted. These were predominantly general and mental health for glaucoma, with physical function more restricted for those with ARMD. The authors proposed that the retention of central vision in glaucoma may explain these findings, although they could not state concisely that QoL was worse in patients with one disease or the other.

1.1.6 Diabetic retinopathy

Diabetic retinopathy (DR) is a progressive and potentially sight-threatening eye disease. It has been proposed that neurovascular changes in the retina preceding, although coexisting, with microvascular changes, are responsible for its multifactorial pathogenesis (Heng *et al.* 2013). Involvement of the foveal area by oedema and ischemia (diabetic maculopathy) is

the most common cause of visual impairment from diabetes (Bhagat *et al.* 2009) with established ischemia leading to untreatable central vision loss (Heng *et al.* 2013).

Laser treatment for sight-threatening clinically significant macular oedema is now being superseded by anti-vascular endothelial growth factor (anti-VEGF) therapies such as ranibizumab (*Lucentis*), approved for use in the UK by the National Institute for Health and Clinical Excellence (NICE) in 2013. The current treatment strategy for proliferative DR, panretinal photocoagulation, is destructive and after multiple treatments the resultant loss of visual field may preclude driving (Heng *et al.* 2013).

Vision loss from DR, principally attributed to clinically significant macular oedema, is an economic burden as one of the leading causes of visual impairment and disability in the working age population of the UK (Access Economics, 2009). The impact of diabetic related vision loss on QoL has been examined, and one study found that QoL reduction in patients with DR was similar to those with ARMD (Brown *et al.* 2002). Overall, the evidence using various patient-reported outcome measures suggests that DR has a negative effect on both health and vision-related QoL (Fenwick *et al.* 2012); although the authors concluded that further research is required in this area.

1.1.7 Hereditary retinal disorders

Hereditary retinal disorders are a wide group of inherited conditions, with diagnosis confirmed by electrodiagnostic testing.

The most common hereditary retinal disorder is retinitis pigmentosa (RP), a progressive rod-cone dystrophy characterised by nyctalopia, visual field loss and deterioration in visual acuity (Goodwin, 2008). There is no cure for RP and no proven treatment that slows its progression. Hahm *et al.* (2008) evaluated vision-related QoL and depression in patients with RP. The authors concluded that those patients with depression had poorer vision-related function scores, although these did not correlate to visual acuity levels.

In a review of the causes of visual impairment registration in England and Wales, Bunce and Wormald (2008) found that hereditary retinal disorders accounted for 2.8% of blindness, and 2.0% of partial sight certifications across all age groups. These disorders appear to have higher prevalence in areas of increased consanguinity (Liew *et al.* 2014), which may be reflected in a greater demand for low vision services in these areas. Data for individual

age groups shows that the majority of those certified blind (66%) fall into the 16-64 year age group. Liew *et al.* (2014) reported on the significance of an increase in blindness registrations for this 'working age' group in 2009-2010 compared with 1999-2000. The authors suggest that this could reflect either improvement in certification or a true increase in incidence; however improved diagnostic techniques and research in this area will assist with accurate diagnoses, and CVI data.

Research into inherited retinal diseases is progressing rapidly; with potential new gene therapy treatments being the main focus as responsible genes are isolated (McClements and MacLaren, 2013). This is in the early stages and currently, due to irreversible visual loss, management of patients is focused around registration, low vision services and rehabilitation training. These will be of particular importance for the working age group to enable patients to continue in employment where possible, reducing the burden on the UK economy.

1.1.8 Rationale for the focus on age-related macular degeneration in this thesis

Age-related macular degeneration is by far the leading cause of certifiable visual impairment in the UK accounting for 58.6% SSI and 57.2% SI new certificates from April 2007 to March 2008 (Bunce *et al.* 2010). However, these registers only give information on those newly registered within that time period (i.e. incidence of certification), not the true prevalence or incidence of the disease (Evans and Wormald, 1996).

In an attempt to estimate this more accurately, Owen *et al.* (2003) established a pooled prevalence for ARMD related vision loss and applied these to the UK population. The authors reported that in 2003 there were an estimated 214,000 people with ARMD related disease at vision levels suitable for registration, with this figure predicted to increase to 239,000 by 2011. However, they concluded that because only one of the six prevalence studies considered was in the UK, it was difficult to know exactly how many people in the UK were living with ARMD related irreversible vision loss.

Predominantly, ARMD occurs in the elderly population, with increased prevalence associated with increasing age (Lim *et al.* 2012). This has a large impact on QoL, and is associated with a higher prevalence of depression, falls and reduced independence in this age group. Due to the fact that ARMD is largely untreatable, geographically accessible LVS are important in assisting patients to maintain their social and functional independence and

QoL. At Milton Keynes University Hospital NHS Foundation Trust (MKUH), 72% of patients attending the low vision clinic have visual impairment related to ARMD. It is therefore important to gain further insight on the impact of ARMD on QoL, and to evaluate LVS with this disease in mind. Furthermore its economic burden will increase in the future because of the ageing UK population.

To manage the impact of ARMD on patients and Hospital Eye Service (HES) resources requires an understanding of the fundamentals of the disease. The following section reviews the anatomy of the macula and the physiology of ARMD and its progression.

1.2 Age-Related Macular Degeneration (ARMD)

1.2.1 Introduction

Age-related macular degeneration is a progressive, degenerative disease (Lim *et al.* 2012). The disease occurs at the macula area of the retina, damaging central vision as it progresses. Early stages are referred to as age-related maculopathy (ARM), and occur when changes to the macula are observed before the onset of loss of vision (Lim *et al.* 2012). ARM can progress to two more problematic late forms, atrophic (“dry”) and exudative (“wet”) – referred to as ARMD (Nowak, 2006).

Late ARMD results in a loss of macula function causing reduction in high-resolution visual acuity and central vision loss (Chakravarthy *et al.* 2010a). The consequence is a reduction in distance and near vision, along with a reduced ability to carry out tasks for daily living e.g. reading, driving and shopping (Loughman *et al.* 2011). This results in a reduced QoL (Mitchell *et al.* 2008).

Although the atrophic form of the disease is more prevalent, affecting more than 80% of people with intermediate and advanced ARMD (Nowak, 2006), it can also rapidly progress to exudative disease with significantly greater loss of vision. These aspects of ARMD are discussed in detail below, following a description of the relevant macula anatomy in relation to function and progression of the disease.

1.2.2 Anatomy of the macula

Introduction

The macula is a 5-6 mm diameter area located centrally within the retina (Provis *et al.* 2005), with its centre, the fovea, lying 4.5 to 5 mm away from the optic nerve head (Figure 1.2). This area, although representing less than four percent of the total retinal area, permits high-resolution visual acuity, along with optimal spatial and colour vision (Fine *et al.* 2000; Loughman *et al.* 2011). Macula health is of great importance; a small lesion in this area will have a significant impact on visual function (Provis *et al.* 2005).

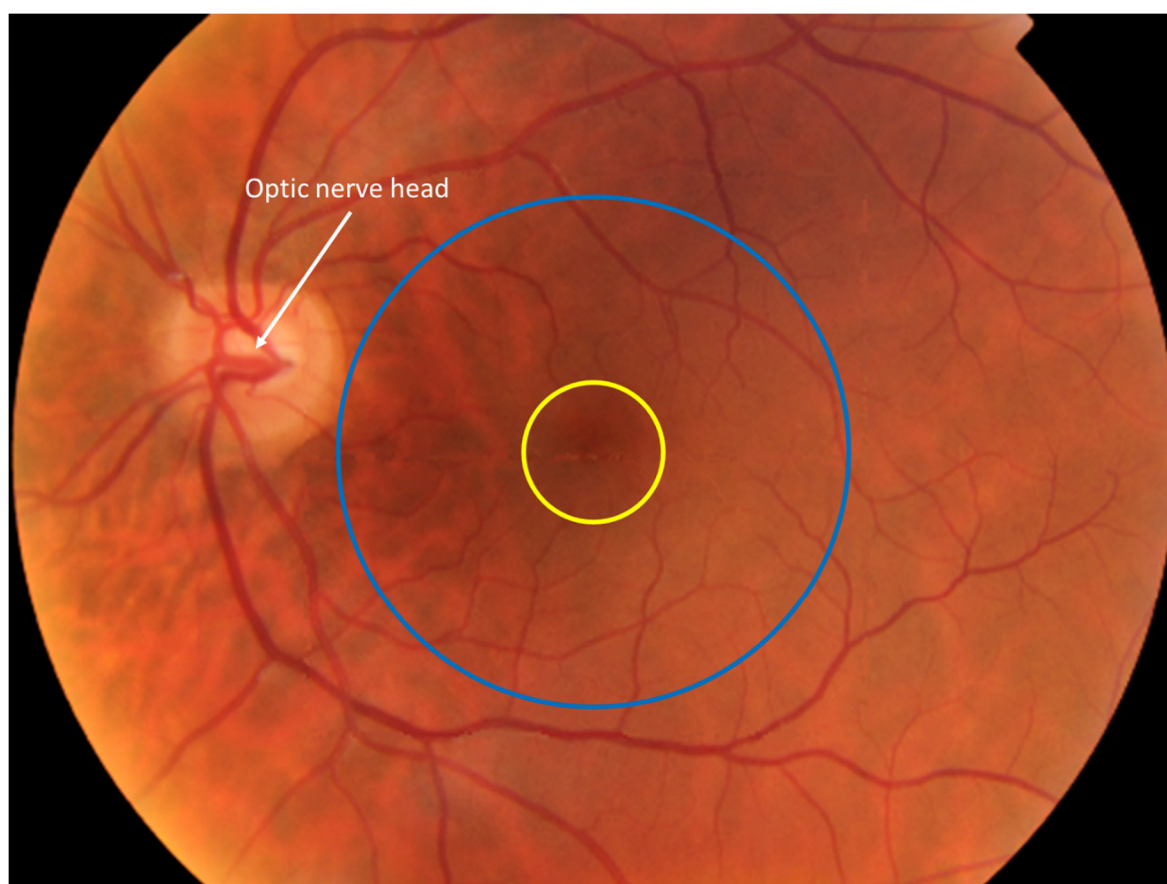


Figure 1.2 Ophthalmoscopic view of the macula (blue circle) and the fovea (yellow circle) in relation to the optic nerve head.

The structure of the retina

The human retina is an extremely complex and highly specialised structure comprising ten discrete layers of various cells (Figure 1.3), varying in thickness, density and type across the retina from its centre to periphery.

Inner limiting membrane (ILM) – inner surface of the retina composed of Müller cell end feet and basement membrane constituents.

Nerve fibre layer (RNFL) – contains 1.2 – 1.5 million ganglion cell axons which become the optic nerve fibres.

Ganglion cell layer (GCL) – facilitates the travel of ganglion cell impulses to the brain.

Inner plexiform layer (IPL) – contains axons of bipolar cells and the dendrites of the ganglion and amacrine cells. Synapses between ON (OFF) bipolar and ganglion cells facilitate the detection of light on dark backgrounds (and vice versa), whilst horizontal and amacrine cells influence and enhance ganglion cell signals.

Inner nuclear layer (INL) - contains the nuclei and the surrounding cell bodies (perikarya) of the bipolar, horizontal, amacrine and Müller cells.

Outer plexiform layer (OPL) – comprising cone and rod axons, horizontal and bipolar cell dendrites. Responsible for synapses between terminal processes of the photoreceptors (rod spherules and cone pedicles) and bipolar and horizontal cell dendrites.

Outer nuclear layer (ONL) – containing cell bodies (nuclei) of photoreceptors.

Photoreceptor (PR) layer - comprising the outer and inner segments of two types of specialised neurones (rods and cones) which convert light photons into nerve signals via phototransduction.

Retinal pigment epithelium (RPE) – a monolayer of pigmented cells forming part of the blood/retinal barrier.

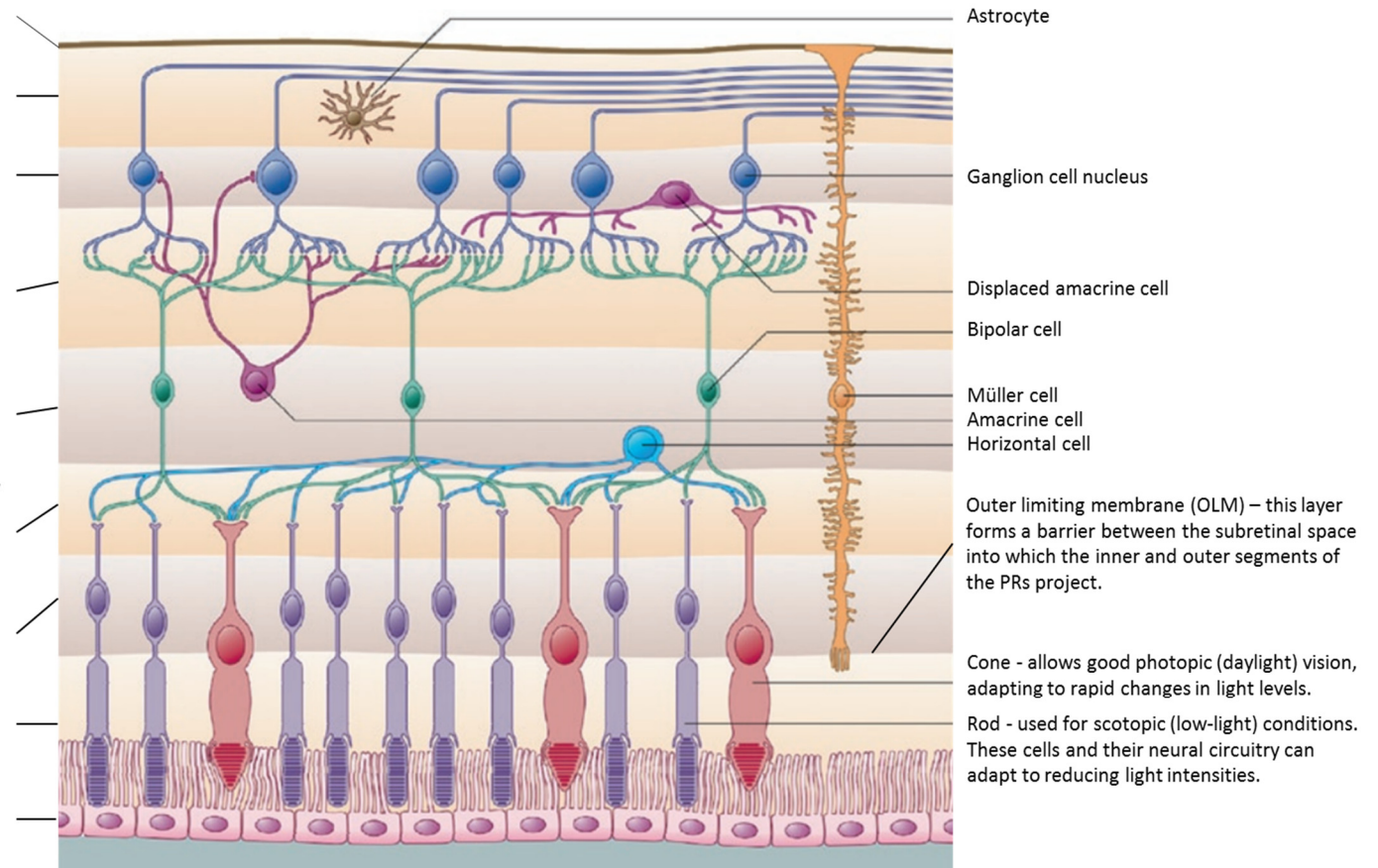


Figure 1.3 An overview of retinal neural circuitry. Adapted from Hildebrand and Fielder (2011), and Kolb (2003).

The structure of the macula

Adaptation of the macula region with its highly specialized neural circuitry results in high-resolution visual acuity (Provis *et al.* 2005). The cone-dominated cell structure of the macula within the central retina is different from the rod-dominated surrounding periphery, reflected in their different functions. Three anatomically distinct regions comprise the macula: perifovea, parafovea and fovea (comprising the foveal slope and foveola; Figure 1.4). Provis *et al.* (2005) suggested that anatomical adaptations at the macula, and the fact that its unique topography allows for high level of visual processing, may also be significant in the pathogenesis of ARMD.

Age-related changes within the retina and choroid

Although ageing does not inevitably lead to ARMD, age-related changes within the retina are thought to be significant in its pathogenesis and occur in the choriocapillaris (CC), Bruch's membrane (BrM), the retinal pigment epithelium (RPE), and the photoreceptors (PR; Ehrlich *et al.* 2008; Carneiro, 2011).

The choriocapillaris, situated within the choroid, is a vascular network supplying oxygen and nutrients to Bruch's membrane and all retinal layers within the macula region, ensuring that the outer retina (RPE and photoreceptors) can meet its high metabolic demands (Carneiro, 2011). With increasing age, there is a progressive reduction in choroidal thickness and choriocapillary density, along with decreased lumina of the choriocapillaries (Ramrattan *et al.* 1994). These changes, in combination with a reduction in choroidal blood flow, give rise to the 'vascular theory' of ARMD proposed by Friedman (1997). This theory suggests that an increased resistance in choroidal blood vessels and decreased choroidal perfusion may lead to RPE cell dysfunction (Ehrlich *et al.* 2008).

Bruch's membrane is a connective tissue separating the choriocapillaris from the RPE (Hildebrand and Fielder, 2011). It regulates ionic and metabolic transport between these two layers (Carneiro, 2011), and provides nutrition to RPE cells (Ehrlich *et al.* 2008). With age the thickness of Bruch's membrane increases (Ramrattan *et al.* 1994) and its lipid content increases (Ehrlich *et al.* 2008). These lead to a loss of fluid permeability and nutrient transport across the membrane, adversely affecting the availability of nutrients for normal outer retinal function (Ehrlich *et al.* 2008; Carneiro, 2011).

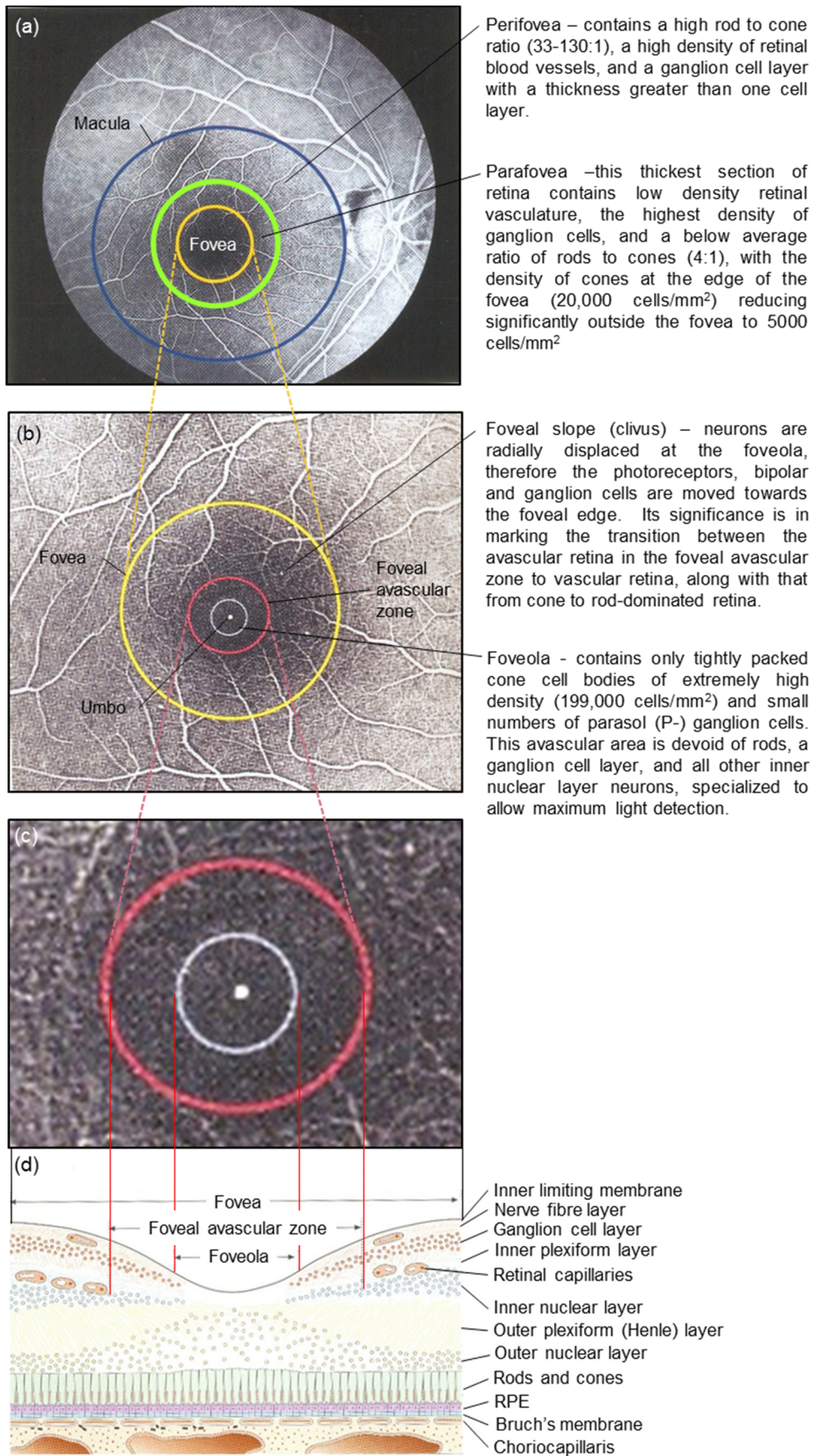


Figure 1.4 (a) the macula (blue circle), comprising the perifovea, the parafovea (green circle) and fovea (yellow circle); (b) the fovea (yellow circle), foveal avascular zone (red circle), foveola (white circle), umbo (white dot); (c) a close-up of the foveal avascular zone with (d) cross section of the fovea. Adapted from Provis et al. (2005) and Kanski (2003).

In healthy eyes, a continuous monolayer of RPE cells separates the choriocapillaris from the photoreceptors, forming the outer blood retinal barrier which is essential for maintaining photoreceptor function (Ehrlich *et al.* 2008; Hildebrand and Fielder, 2011).

The RPE also has highly specialised transport functions, essential for photoreceptor integrity and renewal (Bonilha, 2008). The reduced ability of ageing RPE cells to remove debris, along with inadequate nutrition may predispose the formation of deposits in the RPE and Bruch's membrane region (Taylor, 2012). The accumulation of basal linear deposits in particular, is thought to precede the formation of drusen (Taylor, 2012), the first clinical sign of ARMD (Nivison-Smith *et al.* 2014).

As a result of oxidative stress damaging mitochondria within RPE cells, it is hypothesised that cells undergo apoptosis and a reduction in number (Ehrlich *et al.* 2008). Along with the onset of an inflammatory response resulting in choriocapillary atrophy these form the 'nonvascular theory' of ARMD. This theory together with the aforementioned 'vascular theory' may ultimately be responsible for ARMD development (Ehrlich *et al.* 2008). There is as yet, no unified theory for the pathogenesis of ARMD in a highly active area of ongoing research.

1.2.3 Early age-related macular degeneration (age-related maculopathy)

A number of schemes exist for the classification of ARMD, both for clinical and research purposes (Lim *et al.* 2012). Whilst there is still no universally accepted system (Williams *et al.* 2009), it is generally accepted that early ARMD is characterised by the presence of drusen and / or RPE abnormalities (Nowak, 2006; Lim *et al.* 2012).

Drusen

Considered to be the hallmark of ARMD, drusen are discrete deposits of the subretinal pigment epithelium (Sivaprasad *et al.* 2005). These are located between the basal lamina of the RPE and the inner collagenous layer of Bruch's membrane (Carneiro, 2011). Clinically, they are seen as circular, yellow dots (Williams *et al.* 2009) and can be classified based on their size and shape into 'hard' and 'soft' forms (Figure 1.5).

Drusogenesis is a complex process and not fully understood (Nowak, 2006; Williams *et al.* 2009). The presence of RPE cell debris within the structure of drusen suggests that

inadequate transport between the RPE and Bruch's membrane may be responsible, although current theories now implicate oxidative damage through the accumulation of lipoproteins in Bruch's membrane (Nivison-Smith *et al.* 2014). As the formation of drusen may be influenced by genetics and environmental factors in a selective, rather than a passive process, Ehrlich *et al.* (2008) hypothesise that this explains why not all elderly patients develop ARMD. Additionally, although it is universally accepted that almost all patients with ARMD have drusen, it is not understood why only a proportion of patients with drusen go on to develop late ARMD, and therefore, whether drusen do indeed play a role in this progression (Williams *et al.* 2009).

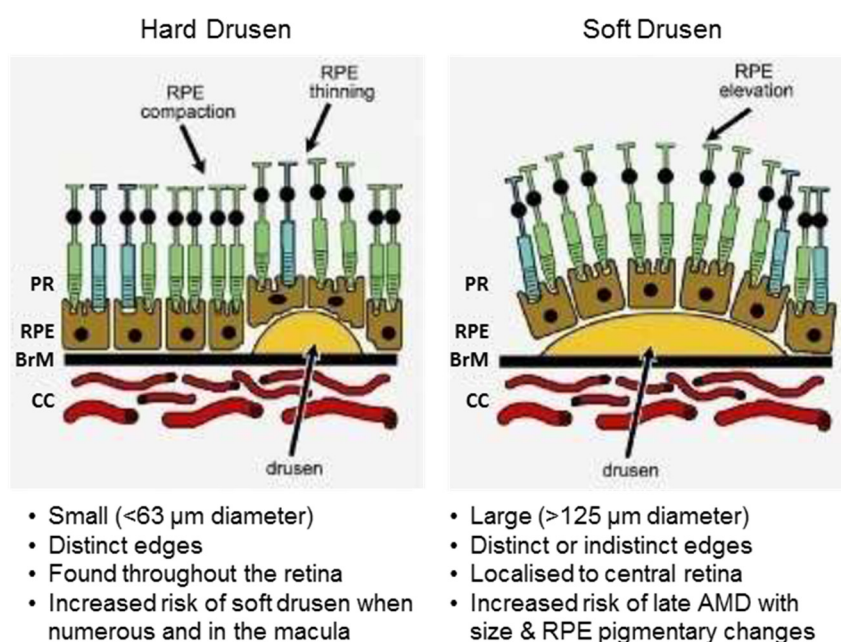


Figure 1.5 Schematic of the retinal location of hard and soft drusen, with characteristic features and implications for age-related macular degeneration risk. Adapted from Nivison-Smith *et al.* (2014). PR – photoreceptors, RPE – retinal pigment epithelium, BrM – Bruch's membrane, CC – choriocapillaris.

RPE hyperpigmentation and hypopigmentation

Morphological changes to the RPE observed in early ARMD are also characteristically seen in both late forms of the disease, with impairment of RPE cell function hypothesised to be a critical event in the development of late ARMD (Nowak, 2006; Nivison-Smith *et al.* 2014).

In early stages of the disease, non-geographic atrophy of the RPE is characterized by hyper- and hypopigmentation (Nowak, 2006), and thinning of the neurosensory retina (Carneiro, 2011; Figure 1.6). Hyperpigmentation is hypothesised to occur as a result of

RPE dysfunction (Bhutto and Lutty, 2012). This is likely to indicate proliferation, clumping or migration of RPE cells (Nivison-Smith *et al.* 2014). Hypopigmentation results from a decrease in RPE pigment (Nivison-Smith *et al.* 2014), and / or RPE atrophy (Bhutto and Lutty, 2012).

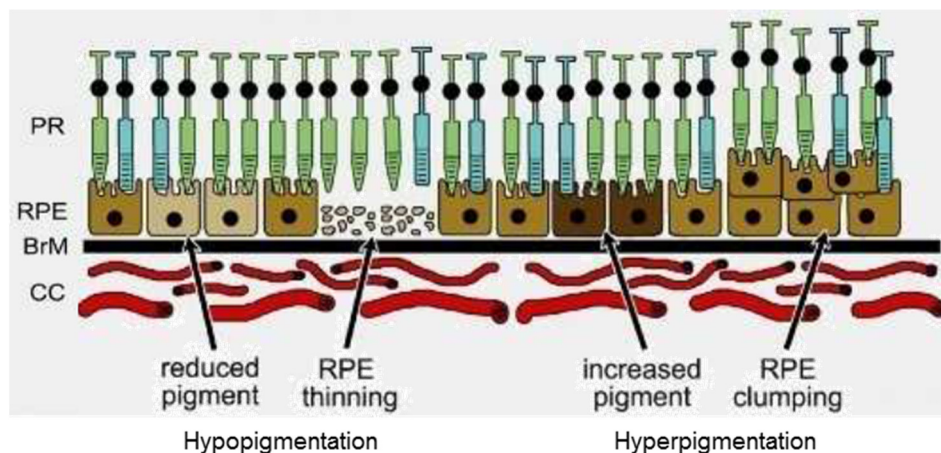


Figure 1.6 A schematic for the possible sources of pigmentary changes (hypopigmentation, hyperpigmentation) in age-related macular degeneration. PR – photoreceptors, BrM – Bruch's membrane, CC – choriocapillaris. Adapted from Nivison-Smith *et al.* (2014).

The impact of early ARMD

Early age-related macular degeneration is often diagnosed incidentally at routine eye examination because patients are generally asymptomatic (Chakravarthy *et al.* 2010a). In contrast to late stage ARMD, early changes are not associated with central vision loss (Lim *et al.* 2012; RCO, 2013) and are expected to have much less impact on visual acuity (and in turn, the patient's QoL). Lamoureux *et al.* (2011) assessed the impact of early versus late ARMD on vision-specific function and concluded that early ARMD had no impact on this measure, however they highlighted the need for education to prevent disease progression. Bennion *et al.* (2012) reviewed literature from qualitative studies on the experience of living with ARMD, and observed that many patients with good vision still reported concerns regarding future visual impairment.

Multiple studies have revealed that a proportion of patients with early changes will ultimately develop late ARMD (RCO, 2013). Although the percentages of patients converting from early to late disease differs between study groups, the longer the disease duration, the greater the risk of progression (Mitchell *et al.* 2002; Klein *et al.* 2007).

With more effective treatments for neovascular ARMD now available, the identification of clinically significant early signs as markers for a high risk of progression to late ARMD is imperative in the prevention of visual loss (Chakravathy *et al.* 2010b). Future developments in the understanding of ARMD pathogenesis and novel preventative treatments, along with additional clinical diagnostic techniques may help further quantify and reduce this risk.

1.2.4 Atrophic (late) age-related macular degeneration

In the absence of choroidal neovascularisation (CNV), geographic atrophy (GA) reflects the natural endpoint of the atrophic process of ARMD (Sunness, 1999). Atrophy of the RPE, choriocapillaris and photoreceptors is responsible for a slow, progressive reduction of central vision (Chakravarthy *et al.* 2010a; Lim *et al.* 2012) resulting in moderate to severe vision loss. At present, there is no available treatment for GA (Mata *et al.* 2013) and therefore, its prevalence will inevitably increase as the population ages.

Pathogenesis and progression

Although the precise mechanisms leading to GA development remain evasive (Mata *et al.* 2013), multiple theories have been proposed for its pathogenesis. Nowak (2006) described these as lipofuscin formation, drusogenesis and local inflammation. An additional 'vascular theory' for its pathogenesis is that of choroidal vascular resistance proposed by Friedman (1997).

Signs and symptoms

GA appears as a distinct area of RPE and photoreceptor loss greater than 175 µm in diameter and atrophy of the choriocapillaris (Nivison-Smith *et al.* 2014). This is observed clinically as a round / oval area with defined edges, paler in colour compared to the surrounding tissue, often with internal hypopigmentation (Nivison-Smith *et al.* 2014), and through which the choroid and its vessels may be seen more distinctly (Sunness, 1999; Figure 1.7).

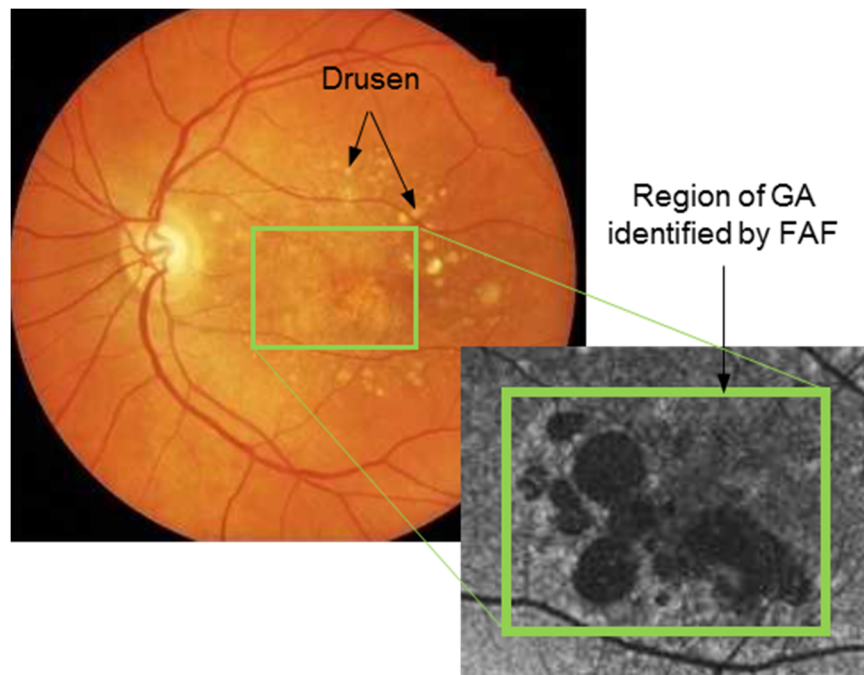


Figure 1.7 Retinal photograph of geographic atrophy (GA) highlighting retinal pigment epithelium pigment changes and drusen. The expanded view shows the region of geographic atrophy identified by fundus autofluorescence (FAF). Adapted from Nivison-Smith et al. (2014).

Primarily GA develops as small, focal areas of depigmentation (Chakravarthy *et al.* 2010a), and initial symptoms may be reported as an inability to read very small print (RCO, 2013). As the disease progresses, many small areas of atrophy may enlarge and coalesce, sometimes forming a horseshoe configuration, and then a ring, around the fovea until the onset of foveal atrophy at later stages (Sunness, 1999; Nivison-Smith *et al.* 2014). Difficulty in reading print of increasing size occurs gradually over time.

Permanent scotoma(s) will be present in areas of GA (Figure 1.8). Although the patients measured visual acuity may appear to be good, the presence of multiple scotomas near to fixation cause greater visual impairment than predicted from acuity alone (Sunness, 1999).



Figure 1.8 The impact of a scotoma on patient vision of the normal image (left) with increasing severity from centre to right. In those patients with good measured acuity, reading and recognising faces may be difficult if the word or face does not appear within the small central island of remaining vision, devoid of scotomas (Sunness, 1999). Adapted from Phillips (2008).

As GA cannot be treated it causes a slow, progressive reduction of vision resulting in severe visual impairment (Chakravarthy *et al.* 2010a). Contrast sensitivity is often reduced and impairment in dim lighting can be significant (Sunness, 1999). Although GA results in a slower deterioration and better preservation of VA than exudative ARMD (Fine *et al.* 2000), in more than half of patients it is bilateral causing significant problems with daily living tasks (Sunness, 1999).

1.2.5 Exudative (late) age-related macular degeneration

Late stage exudative ARMD occurs as a result of choroidal neovascularisation (Figure 1.9). Abnormal new blood vessels growing through to the neural retina can bleed or leak fluid causing a sudden loss of central vision (Nowak, 2006). This rapidly progressing form of ARMD accounts for two thirds of late stage disease and 90% of ARMD related blindness (Chakravarthy *et al.* 2010b).

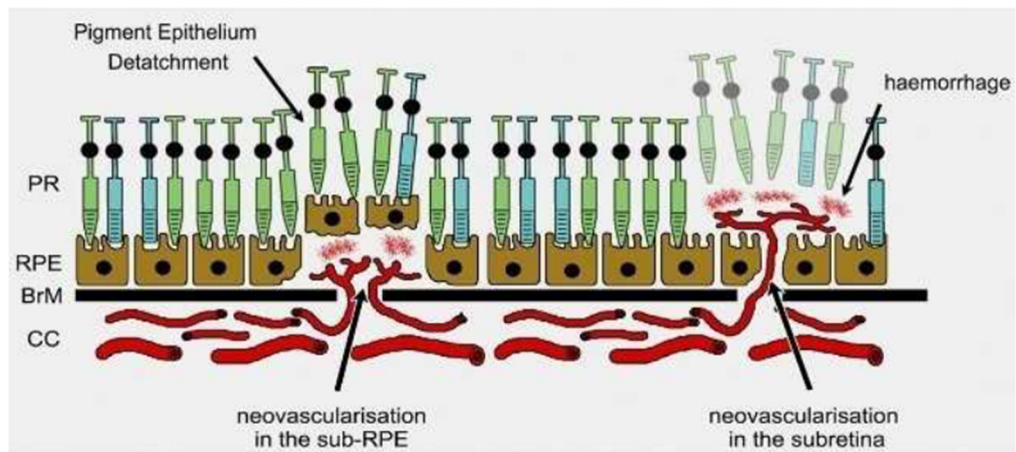


Figure 1.9 A schematic of the growth of choroidal neovascularisation (CNV) from the choriocapillaris (CC) through Bruch's membrane (BrM) into the sub-retinal pigment epithelium (RPE, left) and the subretina (right). PR is the photoreceptor layer. Also shown are some of the associated complications - pigment epithelial detachment and haemorrhage. Adapted from Nivison-Smith *et al.* (2014) and Ehrlich *et al.* (2008).

Pathogenesis

Nowak (2006) reported on the two possible mechanisms leading to CNV – hypoxia and inflammation:

1. Hypoxia – ischemia / hypoxia from reduced choroidal perfusion results in increased oxidative stress (Ehrlich *et al.* 2008), leading to the up-regulation of pro-angiogenic growth factors e.g. vascular endothelial growth factor (VEGF; Nowak, 2006).
2. Inflammation – an inflammatory response is stimulated by damaged RPE cells, resulting in a release of pro-angiogenic factors (Nowak, 2006; Ehrlich *et al.* 2008).

Signs and symptoms

Compared with GA, vision loss in patients with exudative ARMD is rapid, with a sudden onset reduction in central vision taking the form of either a blind spot (scotoma) or distortion of straight lines (metamorphopsia), or both (Lim *et al.* 2012; Figure 1.10). In cases where exudative disease is unilateral, it is possible that the diagnosis could be an incidental finding (Chakravarthy *et al.* 2010a).



Figure 1.10 Image depicting a patient's view of scotoma and metamorphopsia resulting from exudative ARMD. Source: The Macula Society www.maculasociety.org

If untreated, the prognosis for vision is poor. Wong *et al.* (2008) published the first systematic review of visual acuity loss in untreated eyes with exudative ARMD. The severity of vision loss was shown by the percentage of patients with VA less than 1.0 logMAR (base 10 logarithm of the minimum angle of resolution) which increased from 19.7% at baseline to 75.7% at 3 years. The lack of specific data on the ethnicity and countries of analysed populations makes it difficult to conclude whether this would apply to the UK population. With more effective treatments now available in the UK, diagnosis and referral for potential treatment should be made at the earliest opportunity (Chakravarthy *et al.* 2010).

Exudative ARMD is characterised by the presence at the macula of subretinal or intraretinal fluid and / or haemorrhage (Lim *et al.* 2012), with or without peri-retinal fibrosis (RCO, 2013). If untreated, the disease follows a rapid progression resulting in a fibrous scar at the macula with an associated severe central loss of vision (Chakravarthy *et al.* 2010a). Figure 1.11 demonstrates this progression over a three year period (Lim *et al.* 2012).

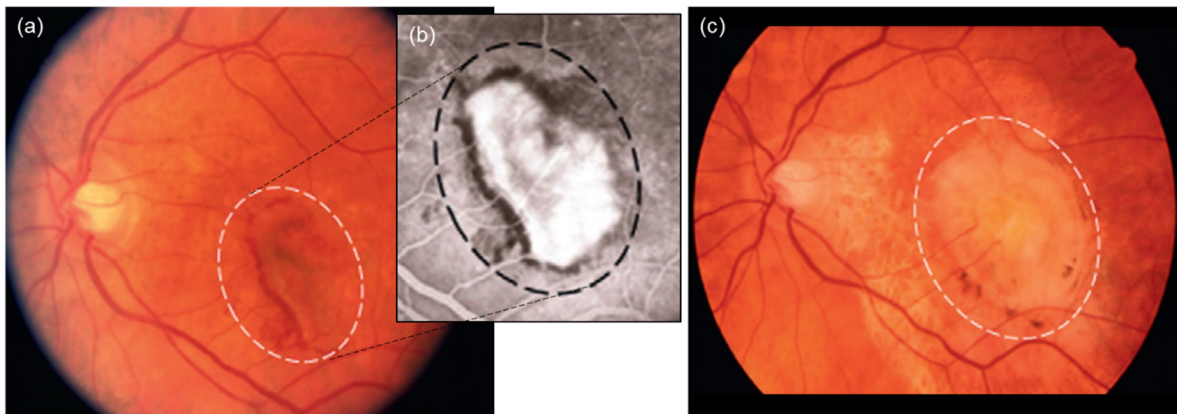


Figure 1.11 The progression of untreated exudative age-related macular degeneration over a three year period: (a) a choroidal new vessel beneath the sensory retina (within the dashed oval); (b) appearance on fluorescein angiography; (c) after three years an enlarged area of subretinal fibrosis (within the dashed oval) at the site of the previous new vessel with an area of surrounding atrophy (nasal to the macula). At this stage the scotoma will have enlarged extensively resulting in severe visual disability. Adapted from Lim *et al.* 2012.

1.2.6 Treatment strategies for atrophic age-related macular degeneration

Currently, unlike exudative ARMD, there is no available pharmacological treatment to treat or slow the progression of GA (Holz *et al.* 2014). Mata *et al.* (2013) over a two year period, investigated the efficacy of oral fenretinide (N-(4-hydroxyphenyl)retamide) as a potential treatment aimed at reducing its progression. This work was inconclusive and additional studies into fenretinide and other therapeutic agents are required before these become widely available.

RPE transplantation aimed at the protection of photoreceptors has also been attempted (Sunness, 1999). Schwartz *et al.* (2012) reported on the first transplant of human embryonic stem cells into one eye of a patient with GA. The authors observed a seven letter (from 20/500 to 20/320) improvement in VA over a three-month period.

The surgical implantation of miniature telescopes for the treatment of end stage ARMD uses magnification from the telescope to project images from the damaged central retina onto parafoveal areas, thus reducing the impact of the scotoma (Macular Society, 2015). Hudson *et al.* (2006) reported on the one-year postoperative results from a clinical trial of 217 patients with bilateral vision loss from GA and / or exudative forms of the disease who had undergone telescope implantation in one eye. The authors reported that 53% eyes gained an improvement of ≥ 3 lines in best corrected distance and near VA, compared to 10% of contralateral eyes. Relating this to an improvement in scores from the 25 item National Eye Institute Visual Function Questionnaire (NEI-VFQ), Hudson *et al.* (2006)

concluded that this procedure improved QoL as well as VA, due to a reduction in the effect of the patient's central scotoma. Unfortunately, this procedure is not suitable for all patients with late stage ARMD and is currently only available privately in the UK (Macular Society, 2015).

Ultimately, without any approved therapeutic treatment, GA will present a significant burden on UK health and social care resources in the future due its untreatable nature and the ageing population. The National Health Service (NHS) continues to rely heavily upon LVS as the only treatment option, and timely referral should be made to the service to ensure that patients can access help at an early stage of vision loss.

1.2.7 Treatment strategies for exudative age-related macular degeneration

The lack of significant clinical results with the use of laser photocoagulation and photodynamic therapy as treatments for exudative ARMD resulted in a decline in their use once significant developments in anti-VEGF therapeutics had been made (Chakravarthy *et al.* 2010a; Holz *et al.* 2014).

In two landmark trials using ranibizumab (*Lucentis*), the authors reported improvements in visual acuity, not just stabilisation as was previously the case with the first approved anti-VEGF pegantib (*Macugen*; Lim *et al.* 2012; Holz *et al.* 2014). The most recent anti-VEGF agent to be introduced at MKUH is aflibercept (*VEGF Trap-Eye*). It is hypothesised that this drug will have a greater period of action (Holz *et al.* 2014). Trials comparing monthly ranibizumab with aflibercept at longer re-treatment intervals (three initial monthly doses followed by dosing every two months) showed similar efficacy in VA improvement and safety, with the advantage of a reduced injection and monitoring regime (Heier *et al.* 2012).

Although anti-VEGF therapeutics have been demonstrated to be successful in reducing vision loss in patients with exudative ARMD, the intense (often monthly) long term treatment and monitoring regime places a burden on patients, carers, and economic resources (Chakravarthy *et al.* 2010a). As injections are often initiated after significant retinal damage has occurred (Melville *et al.* 2013), the requirement for LVS is ongoing because treatments do not cure the problem completely, just stabilise it. Treatments may result in useful parafoveal vision, but many patients report frustration at not being able to effectively use this remaining vision – this is where low vision aids (LVAs) become important.

1.2.8 Preventative strategies for age-related macular degeneration

Along with developments in novel treatment strategies for ARMD, there has been ongoing research into the prevention of disease and reduction of its progression, of which evaluation of risk factors plays a major role (Chakravarthy *et al.* 2010b). Apart from increasing age which showed a strong association with ARMD in all observed studies, Chakravarthy *et al.* (2010b) highlighted the significance of cigarette smoking, previous history of cataract surgery and a family history of ARMD with risk of disease development and progression. Other factors showing a moderate association with ARMD risk were found to be higher body mass index, a history of cardiovascular disease, and hypertension. The authors recommended that patients be advised on self-identification of early visual changes that may be amenable to treatment, along with lifestyle changes, particularly stopping smoking.

Dietary nutrient supplementation is another area of research currently undergoing close evaluation, and is particularly aimed at disease prevention and limitation of progression to advanced stages (Loughman *et al.* 2011; Holz *et al.* 2014). The Age-Related Eye Disease Study (AREDS) a multicentre double-masked clinical study reported in 2001, that daily supplementation with high doses of vitamins C and E, beta-carotene and zinc reduced the progression to late stage ARMD by 25% over a 5 year study period (AREDS, 2001). The AREDS 2 Research Group more recently reported that the addition of lutein and zeaxanthin, and / or omega-3 to the AREDS formulation was not significant (AREDS 2, 2013).

1.3 Low Vision Treatment Strategies

1.3.1 Introduction to low vision services

Low vision services aim to improve the ability to function independently in daily life for those who suffer from low vision. The LVSCG (1999) defined this service as:

‘A rehabilitative or habilitative process which provides a range of services for people with low vision to enable them to make use of their eyesight to achieve maximum potential’.

Anybody with low vision, anywhere in the UK, should be able to access LVS at any stage following diagnosis, regardless of their registration status and level of VA (CO-RCO, 2013).

Other important considerations include the patient's social situation, emotional and psychological requirements, and any relevant educational or occupational issues (LVSCG, 1999). Flexible and timely access to LVS is imperative, with timely intervention found to be an important factor in rehabilitation outcomes (CO-RCO, 2013).

The service within the UK generally involves a process of rehabilitation that aims to minimise the impact of vision loss, promoting independence and autonomy in daily living. A range of low and high-intensity intervention strategies encompassing various sectors (healthcare, social services and voluntary services) and professionals often exists (CO-RCO, 2013; Ryan, 2014), delivered in a variety of different models (Binns *et al.* 2012).

Together, professionals from multidisciplinary teams aim to provide the elements of support to address the social, financial, practical and psychological needs of the visually impaired patient via any (or all) of the following (Ryan *et al.* 2009):

- Low vision assessment – either based within the HES or, other centres that are contracted to social services providing an assessment of visual function, LVAs and other equipment.
- Rehabilitation services – local authority funded services, delivered by charities or other contracted organisations, providing information and support to enable patients to understand their eye condition and regain confidence and independence through training in essential skills.
- Education services – Special Educational Needs Co-ordinators within schools, specialist teachers for the visually impaired, educational psychologists, rehabilitation and social workers.
- Employment services – finding and remaining in work through the Access to Work scheme (providing adaptations to the place of work and / or equipment, advice on travel to and from work and support workers).
- Voluntary organisations - national and local organisations including disease specific groups, providing wide ranging emotional and practical support, information and advice to patients and their carers / families.

Integration of the above services is important, with effective communication and flexibility between providers essential to enable effective access to services. There may also be links with other broader teams e.g. falls prevention services and GPs, together with those working specifically in eye health (CO-RCO, 2013).

Low vision aid (LVA) assessment and rehabilitation will be considered here in more detail, although the effectiveness of multidisciplinary models including other aspects of LVS will be considered later.

1.3.2 Low vision assessment

A low vision assessment follows a generalised routine, but is adapted for each patient to assess vision and discuss individual needs. This is followed by the provision of practical support and bespoke advice to help achieve specific visual goals whilst working within the limitations of the disease.

A low vision aid (LVA) can be any piece of equipment, including optical (Figure 1.12), electronic, or non-optical (Figure 1.13), to enhance visual performance in those with low vision (LVSCG, 1999). Improvement of functional vision by provision of LVAs is of particular importance, and can lead to enhanced QoL and independence for visually impaired patients (Scott *et al.* 1999; Gallagher and Jackson, 2012).



Figure 1.12 Image depicting a variety of optical low vision aids regularly issued by the Low Vision Clinic, Milton Keynes University Hospital. Use of the double-ended clamp allows hands-free viewing.

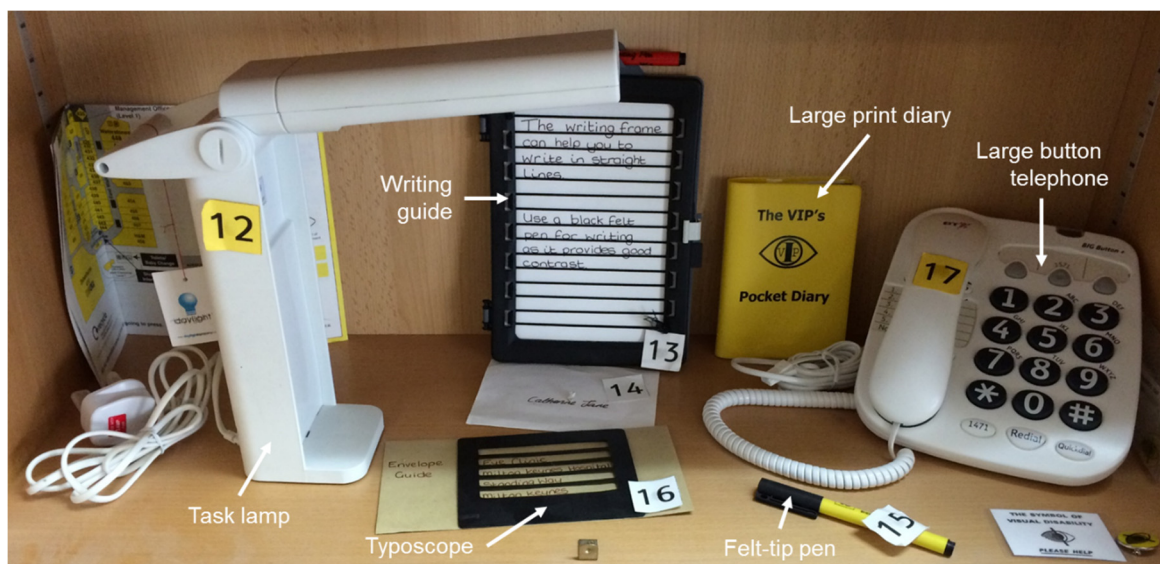


Figure 1.13 A number of non-optical low vision aids demonstrated to patient's attending the Low Vision Clinic, Milton Keynes University Hospital.

The protocol followed by optometrists working in the low vision clinic at MKUH for a new patient undergoing low vision aid assessment can be found in Appendix 1.

1.3.3 Rehabilitation services

The LVSCG (1999) made the recommendation that following diagnosis a patient should receive immediate support and information, whilst LVS provision should begin within six weeks. Eye Clinic Liaison Officers (ECLOs) based within HES clinics are often the first professionals to provide this initial support, and the patient may be able to access their services on the day of diagnosis.

The ECLO service exists to provide diagnosed patients (regardless of registration status) with the information and support that they require to understand their eye condition and the impact this will have on their lives and on those closest to them (CO-RCO, 2013). This may involve referral to employment, educational, rehabilitation and other services. It is often the ECLO who provides the link between the ophthalmologist and the local authority by ensuring that referral is made for assessment by the sensory impairment team (Johnson *et al.* 2015). In the case of newly certified patients, ECLOs assist with CVI completion.

Not all hospital eye clinics within the UK have an ECLO (Slade and Ledwidge, 2013) and to date there is a lack of unbiased independent study on their effectiveness. In their absence however, referral of a patient for rehabilitation services may be delayed (Johnson *et al.* 2015). Within community optometric practice, those patients who are not registered but for whom social services input would be beneficial can be referred using the Low Vision Leaflet.

Assessment by the sensory impairment team at social services is a legal right for those with low vision because they fall within the classification of 'disabled' under the NHS and Community Care Act (1990; Ryan *et al.* 2009). Adequate funding should exist for social services, or those contracted to them, to provide support and advice in any (or all) of the following areas:

1. Emotional support – to work with the patient (and carers) to ensure that they understand the eye condition and its impact on vision and daily living. To listen and to address emotional needs through other support networks as required.
2. Certification – assistance with completion of the CVI form and information regarding the registration process.
3. Orientation and mobility - training and the provision of aids to ensure that the patient can manage to complete local routes independently (if desired).
4. Daily living skills – advice and training in making drinks, cooking, communication (using the telephone, writing). Providing appropriate specialist equipment and training in its use.
5. Modification of the patient's environment – provision of advice and equipment for adapting the living and working environment. For example, assessment of and advice on the correct lighting and colour contrast to help navigation within the home.
6. Financial support – information on welfare benefits and other financial support that the patient may be entitled to (including help with the application process).
7. Information on relevant local and national (including voluntary) organisations, support groups and services.
8. Rehabilitative techniques – further training in the use of LVAs, eccentric viewing and steady eye strategy to enable skills to be utilised in the home and other environments.

There is considerable overlap between clinicians providing LV assessments, ECLOs and rehabilitation workers. This integration and communication with other healthcare, educational and employment teams is essential in promoting flexible access to multiple rehabilitative services for patients (CO-RCO, 2013).

1.3.4 Current model of low vision service delivery in the UK

In the UK, all patients who require LVS should have prompt access via a number of different routes (CO-RCO, 2013). These may include referral from an ophthalmologist, GP, community optometrist, ECLO, social worker, rehabilitation worker or other (CO-RCO, 2013). Ryan (2014) reviewed the evolution of LVS over the past 50 years and the changes that have occurred within services towards the multidisciplinary approach often seen today. At present, there is no standard model for the delivery of low vision services within the UK (CO-RCO, 2013).

Traditional hospital based services with LV assessments provided by optometrists or other trained professionals (orthoptists, nurses and more recently occupational therapists, Ryan, 2014), often with strong associations to social services (Binns *et al.* 2012), are still commonplace. One example of such a system can be found in Milton Keynes (Buckinghamshire) whereby LV assessments are carried out by optometrists working within the hospital LV clinic. From here, patients can be referred, on completion of a Referral of Vision Impairment (RVI), for home / telephone assessment by the Sensory Advice Resource Centre (SARC). SARC is funded by the local authority through a contract with BID Services (a charity) who provide assessments, rehabilitation advice and specialist equipment for patients aged over 18 years with visual and / or hearing impairment.

Through SARC patients can also be referred into the hospital LV clinic. The part-time ECLO at MKUH also works for SARC, therefore very close links and efficient communication between services is possible. In the neighbouring county of Bedfordshire, a different model of LVS provision exists. LV assessments are not carried out within the hospital setting but provided by Sight Concern Bedfordshire, a voluntary society working in partnership with the sensory impairment team who are hosted by the local authority.

In other areas of the UK LV assessments are provided by community optometrists, with primary care LVS increasing in prevalence since the late 1990s due to the rising numbers of people with visual impairment (Ryan, 2014). In 2011, The Local Optical Committee Support Unit (LOCSU) issued the 'Adult Community Optical Low Vision Community Service Pathway' (LOCSU, 2013). This pathway was designed to offer cost-effective LV assessment in a primary care setting. Provision is via accredited community optometrists and dispensing opticians who have access to rehabilitation workers / other locally commissioned services. Patients are able to access the scheme via a number of routes

including self-referral, with the LV assessment taking place at the community optometric practice or the patient's home (LOCSU, 2013). Currently however, not all areas in the UK employ the scheme and to date there is no published research to evaluate how effective this system is.

One example of a scheme provided by community optometrists that has demonstrated effective results in improved access to LVS is Low Vision Service Wales (LVSW; Ryan, 2014). This government-funded service was set up in 1994 and uses accredited community optometrists in the provision of LV assessment, with links to social services and other organisations. One year after its implementation, Ryan *et al.* (2010) reported a significant reduction in both waiting times for LV assessment and journey time to the service, with Court *et al.* (2011) reporting the outcomes for patients to be as effective as the traditional hospital based service. A recent audit of LVSW has highlighted the areas within Wales where accreditation of more optometrists is required to meet the demand for LVS (John, 2014). This is one example of why there is a need for periodic audit of LVS and its users to ensure cost-effective and quality service provision across the UK (CO-RCO, 2013).

Ryan *et al.* (2010) suggested that LVSW can provide an efficient model going forward for expansion of LVS into community optometric practice, thus relieving the burden on hospital based services. This reasoning is also fundamentally the basis of the instigation of the Community Optical Adult Low Vision Service pathway by LOCSU (2013). Currently it is not known whether these models are likely to be more effective than traditional methods of LVS delivery in the long term.

1.3.5 Future delivery of low vision services

Access Economics (2009) predicted a doubling of the number of people in the UK (to almost 4 million) who will suffer from sight loss that impacts upon their daily lives by 2050. Regardless of any future developments in improved treatments for the causes of low vision, there is predicted to be a consequential rise in the number of people requiring LVS in the future due to the ageing population (Ryan, 2014), particularly from age-related diseases such as ARMD (Owen *et al.* 2003).

A novel approach to the provision of eye care services in the UK will be required to meet this increasing demand (Lightstone, 2012). The UK Vision Strategy, a component of VISION 2020, was founded in 2008 to respond to this challenge (Lightstone, 2012). The

strategy is a collaboration between many different cross-sector groups, with the focus of improving eye care in the UK (UKVSAG, 2013). An updated framework for 2013 to 2018 (UKVSAG, 2013) sets out three main outcomes:

1. Everyone in the UK looks after their eyes and their sight – aims to raise awareness of eye health and an understanding of the prevention, detection and impact of sight loss amongst the public and health professionals.
2. Everyone with an eye condition receives timely treatment and, if permanent sight loss occurs, early and appropriate services and support are available and accessible to all – aims to improve integration and effectiveness of eye health treatments and sight loss support services to ensure that patients receive improved treatment outcomes, and timely emotional and rehabilitation support.
3. A society in which people with sight loss can fully participate – aims to improve awareness and acceptance of sight loss, whilst promoting independence and equality for patients.

The UK Vision Strategy (UKVSAG, 2013) compiled a framework for LVS known as the 'Adult UK sight loss pathway' which was developed around the ten most important outcomes that services should deliver for the benefit of patients. A map of the systems required to deliver the processes / outcomes, and how these are integrated is shown in Figure 1.14.

Additional guidelines for those commissioning low vision services published by The College of Optometrists and The Royal College of Ophthalmologists (CO-RCO, 2013; see also Section 1.3.1) mirror those produced by the UK Vision Strategy. Their report highlights the requirement for dedicated funding to be made available for future service provision. The continuous process of evaluation of LVS is therefore essential to ensure ongoing and improved access to quality services for future generations where there will be an even greater demand on resources (CO-RCO, 2013).

1.4 Evaluation of Low Vision Services

1.4.1 Introduction

Access Economics (2009) reported the estimated economic cost of sight loss in the UK to be £22.0 billion in 2008. This comprised £2.14 billion of direct healthcare costs (e.g. hospital recurrent expenditure, residential and community care services, etc.) and £4.34 billion of indirect costs (such as informal care costs, lower employment, and devices and modifications). The largest proportion of cost comes from the burden of disease (£15.51 billion) as a result of years lost due to morbidity and premature death.

Access Economics (2009) grouped the costs of delivering LVS within indirect costs, including costs associated with LVAs, adaptations to the home and mobility devices. These costs, estimated to be £336.5 million in 2008, take into account the average cost of devices multiplied by the prevalence of moderate and severe sight loss in the UK (Access Economics, 2009). Wolffsohn and Cochrane (2000) suggest that the cost of providing LVS may be relatively small compared to the economic consequences of visual impairment, however the authors do not state a currency value for these.

There is still a need for real evidence to evaluate the cost-effectiveness of such services (Binns *et al.* 2012; Ryan, 2014). It is not known whether the true cost of visual impairment would be greater without the input of LVS, and therefore whether the cost of provision of LVS provides benefits which in turn reduce other indirect costs such as years of life lost due to morbidity.

This is difficult to evaluate as the effects of LVS are measured in terms such as improvement in QoL, psychosocial status (Binns *et al.* 2012), and other such intangible benefits which are difficult to assess economically. Nonetheless, it is reasonable to assume that an increased QoL would result in lower cost to UK society through increased independence and reduced burden on health and social care services. Additionally, a visually impaired patient's dependence on carers / family for support could result in a loss of income for the carer (Wolffsohn and Cochrane, 2000). This results in an increased burden on UK resources through the provision of carers allowance and other benefits, along with loss of income tax payments from the carer.

Quantification and evaluation of the outcome of low vision rehabilitation is essential to enable continued funding to be provided for LVS (Raasch *et al.* 1997; Wolffsohn and Cochrane, 2000). Evaluation data will also educate clinicians working in community

optometric practice as to which patients are most likely benefit from LVS, ultimately ensuring that referrals to these services are made correctly.

1.4.2 Quality of life

Previously, the impact of a treatment in health care was assessed using mainly objective measures. With the move towards a greater emphasis on the patient's subjective perception of treatment outcomes, this is no longer the case (Parrish, 1996). It was recognised that although patients were advised that a specific intervention (e.g. medication) had improved a specific bio-indicator (e.g. cholesterol level), the real importance for the patient was how that treatment outcome had affected their well-being and ability to function independently – in effect by assessment of its impact on their QoL (Parrish, 1996). This assumption ignores the impact of cholesterol reduction on coronary heart disease and how this could increase life expectancy, something the patient would not be considering in their evaluation of quality of day-to-day life.

As a result of the increased recognition of the importance of patient reported outcomes, QoL has been increasingly used as an outcome measure in clinical trials to evaluate new treatment interventions (Mitchell *et al.* 2008). This has been applied to a wide range of systemic diseases (Parrish, 1996), and is one technique utilised and reported upon in the evaluation of LVS as a measure of the effectiveness of low vision rehabilitation (de Boer *et al.* 2006).

The WHO defined QoL as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns' (Wolffsohn and Karas, 2004). A wide ranging concept encompassing interactions between physical and mental health, independence, and social wellbeing (Parrish, 1996), QoL cannot therefore be defined simply by the absence of disease / infirmity (Ellwein *et al.* 1995). Bradley (2001), in reviewing the association between health status and QoL in patients with diabetes, expands on this with the observation that although a person who feels that they have poor health or wellbeing may also believe that they have an impaired QoL, this may not be the case. Outcomes which measure QoL therefore have the potential to be both informative and misleading (Mitchell *et al.* 2005) due to the complex nature of the concept being measured.

The importance of measuring QoL to inform decisions on treatment strategies and policy planning in healthcare was reviewed by Guyatt *et al.* (1993). The authors report on the two different approaches to achieve this – measurement of the generic health-related QoL, and / or QoL as measured in specific disease states.

1.4.3 Quantification of quality of life

Subjective QoL questionnaires utilise psychometric information to quantify the impact on the patient of the generic and / or specific disease state (Parrish, 1996). The assessment of general health-related QoL can be used to obtain measurements of the health of populations, provide information for policy making decisions, and detect informative changes as a result of treatments in clinical trials (Guyatt *et al.* 1993). Alternatively, questionnaires can be used to target specific disease states to allow evaluation of the effects of treatments in a particular area of the body (Guyatt *et al.* 1993), along with assessment of treatment programs for wider-ranging diseases such as cancer and mental health (Parrish, 1996).

Questionnaire design is a complex process and a number of factors need to be considered to ensure that the questionnaire measures what it intends to, that it does so reliably, and that it can be used effectively with the population studied. This is achieved through three psychometric properties:

- Validity – whether or not the questionnaire measures what it is supposed to (Guyatt *et al.* 1993). Included in this are the need for clinically relevant and understandable questions (content / face validity), the ability to discriminate between groups e.g. those with the disease compared to those without (construct validity), and how well the questionnaire compares with an existing well established and widely used questionnaire (criterion validity; Donovan *et al.* 1993).
- Reliability – the repeatability or consistency of the measure. Includes the relationship between items in the questionnaire (internal consistency), and the between and within observer variability (reproducibility). Demonstration that the questionnaire measures the same outcomes in the same person over time (stability) is also important (Donovan *et al.* 1993).
- Responsiveness – that the questionnaire is responsive to changes (e.g. in QoL) occurring as a result of treatment (Donovan *et al.* 1993), even if changes are minor (Guyatt *et al.* 1993).

Also of importance is the suitability of the questionnaire for application in clinical practice. It should be quick and easy to use and avoid overburdening the patient by use of the appropriate number of items. The selection of items is therefore critical to the psychometric properties of the questionnaire, as discussed by Wolffsohn and Cochrane (2000). The format of questions should also be considered as open-ended questions, although this can lead to a greater variation in scores (Wolffsohn and Cochrane, 2000). Scores should also correlate easily to interpretable differences in QoL (interpretability; Guyatt *et al.* 1993; de Boer *et al.* 2004), to accurately report any clinical significance of treatment.

Consideration must be given to the appropriate implementation method: in-person (self or interviewer-administered), by post or by telephone (de Boer *et al.* 2004; Wolffsohn and Karas, 2004). It is imperative to choose a pre-tested method so as not to bias the results and invalidate its psychometric properties (de Boer *et al.* 2004). This could be particularly relevant in the case of low vision patients who may not be able to read the questionnaire easily (Wolffsohn *et al.* 2000).

Mangione *et al.* (1992), in their development of the 'Activities of Daily Vision Scale' (ADVS) questionnaire for cataract patients, found no difference in results between in-person and telephone implementation. Similar results were observed by Wolffsohn *et al.* (2000) in their study of different implementation methods of the Low Vision Quality of Life (LVQOL) questionnaire. The authors reported that postal, telephone and in-person administration demonstrated similar validity and reliability. Although a reduced QoL score from postal implementation was reported, Wolffsohn *et al.* (2000) concluded that using this method the questionnaire was no less likely to be completed or to suffer bias from assistance with completion where patients could not self-complete.

Evaluative questionnaires measure changes in QoL over a period of time for one patient. This is in comparison to discriminative methods which assess the QoL differences between different patients at one point in time (Guyatt *et al.* 1993). Only the former is relevant in this thesis and therefore all discussion of questionnaires to follow refers to evaluative types. The ability of the questionnaire to quantify accurately QoL changes over time is also dependent upon the interval between the first (baseline) and subsequent measures. This interval will not be the same for every disease state due to variable rates of disease progression. Wolffsohn and Karas (2004) discuss this with regards to low vision patients who may initially show a reduced QoL that is then artificially increased if QoL is re-measured too soon after low vision rehabilitation.

1.4.4 Use of quality of life questionnaires to evaluate low vision services

Rationale for measuring quality of life within low vision services

Although clinical measurements such as visual acuity and visual field assessment allow an objective assessment of the visual status to be made, they do not reflect the subjective impact of this disease on the patient (Margolis *et al.* 2002). Visual impairment from an untreatable eye disease has been shown to impact negatively on health-related QoL (Loughman *et al.* 2011) and daily functioning through carrying out activities of daily living (Binns *et al.* 2012). It is important for the clinician to be able to assess this from the patient's perspective and make an onward referral to rehabilitation services at the earliest opportunity if necessary.

Many studies have analysed the outcomes of LVS through either assessment of patient's valuation of the services, the use of the prescribed LVAs, or through measurement of reading speed. It is only more recently that studies have used vision-specific QoL measurements to provide quantitative outcomes (de Boer *et al.* 2006). Those involved in the forward planning and prioritisation of LVS are better informed to make decisions when they have quantifiable evidence of the benefits of services e.g. improved QoL. Any improvement in QoL would be a positive reflection of LVS in both financial and subjective terms. Although this would be difficult to measure, it would certainly be useful in support of the continuing need for LVS (Wolffsohn and Cochrane, 2000).

The application of questionnaires to evaluate low vision services

Nilsson and Nilsson (1986) assessed the effect of a full range of rehabilitation techniques through multiple training sessions provided by a number of different professionals. Patients with ARMD were given specific training in eccentric fixation and in the optimum use of LVAs. The authors observed that the numbers of patients able to read television titles and newspaper text increased significantly from 6.7% to 57.5% and 0.8% to 92.5%, respectively, following training. A mention was made also to a 'dramatic improvement in an individual's situation of life', which could be taken to imply QoL.

Mcllwaine *et al.* (1991) investigated the cost-effectiveness of LVS by evaluating the extent of prescribed LVA use and patient satisfaction, rather than QoL. The authors suggested that a more extensive approach to LVS provision similar to that described by Nilsson and Nilsson (1986) should be considered. As their service did not routinely provide a follow-up appointment Mcllwaine *et al.* (1991) concluded that based on the 29 patients who requested

follow-up or further training via their responses to the questionnaire, additional follow-up appointments would improve the effectiveness of the service provided.

Leat *et al.* (1994) observed that variability between studies using different criteria to measure LVS outcomes made comparisons difficult. The authors designed a questionnaire that aimed to assess more widely the perceived benefits / success of LVS for the patient in performing a number of specific daily tasks (e.g. reading newspaper headlines, bank statements and letters). In their conclusions, they discussed the importance of evaluating the success of LVS by multiple outcomes and not just one definition (e.g. whether the patient can achieve the ability to read). This emphasis on comprehensive and multiple outcomes such as optimum functioning and gaining more independence could be considered as QoL outcomes, although Leat *et al.* (1994) do not specifically refer to this terminology.

One disadvantage of some of the early QoL questionnaires is that they were developed for patients who were not suffering from permanent visual impairment but from eye conditions with the potential to be treated. These included the 'Catquest' questionnaire (Lundström *et al.* 1997), which focussed specifically on the effect of cataracts on subjective QoL by administration of the questionnaire before and after cataract surgery. Wolffsohn and Cochrane (2000) observed the limitations of such instruments and others, including those from Parrish (1996), and Lowe and Drasdo (1992) that were designed to assess QoL in patients with glaucoma and retinitis pigmentosa, respectively. Questionnaires that focus on a single cause of visual impairment may have reduced validity if applied to a low vision population where multiple causes of impairment exist.

To use an appropriate questionnaire designed specifically for patients with low vision is therefore essential when an accurate evaluation of the outcome of LVS is required. To highlight this Wolffsohn and Cochrane (2000) referred to a study by Scott *et al.* (1999), which used three questionnaires to assess QoL at one week prior to and three months following low vision rehabilitation. These were: the Medical Outcomes Study 36-Item Short Form (SF-36) for assessment of general health-related QoL; the Visual Function-14 (VF-14) designed to assess vision-dependent activities known to be affected by cataract; and the 51 item Field Test Version of the NEI-VFQ.

Scott *et al.* (1999) observed that 98.7% of 156 patients in the study reported a beneficial impact upon functional status from attendance at LVS, with significant improvements in the VF-14 scores. However, the SF-36 scores did not support this trend, showing no significant change post rehabilitation and leading to the conclusion that the SF-36 was less sensitive to QoL differences than the vision-specific instruments. Also, as these three questionnaires

were not designed specifically for patients with low vision, the authors hypothesised that some of the daily activities assessed with the VF-14 in particular may not be expected to improve as a result of LVS. It could therefore be hypothesised that the use of such questionnaires could affect the validity of results, and it is justifiable to say that questionnaires that have not been well validated for use within low vision populations should not be used when trying to evaluate LVS.

Wolffsohn and Cochrane (2000) attempted to overcome this problem. Their LVQOL questionnaire was initially based on the accumulation of questions from 16 previous studies, with all duplicates removed before questions were assessed for relevance, coverage and face validity. The resulting 74 items were trialled on 150 patients suffering from a range of conditions causing visual impairment, and were ultimately reduced in number to 25 questions that were found to meet specific criteria: greatest reliability, internal consistency, not redundant and with good relevance. The final version of the 25 question LVQOL questionnaire was then posted to 515 low vision patients prior to their appointment, and an age and gender matched control group completed the questionnaire during attendance at a routine eye examination appointment. A low vision appointment included optometric assessment plus input from a wider rehabilitative team (as required). One month following the clinic visit, a post-rehabilitation LVQOL questionnaire was posted to the patients who had submitted an initial questionnaire.

Wolffsohn and Cochrane (2000) demonstrated that their questionnaire was able to discriminate between the control population with 'normal' vision and those with visual impairment, with an average LVQOL score of approximately 40 units lower in those with visual impairment. Furthermore, QoL scores increased by an average of 6.7 points (equivalent to 17%) in those with low vision following rehabilitation, in comparison to 0.8 points on the control group. This demonstrated that LVS resulted in improved QoL for patients with visual impairment, and correlated well with findings from Scott *et al.* (1999). Wolffsohn and Cochrane (2000) also highlighted the observation that those who received additional multidisciplinary rehabilitation showed a greater improvement in QoL compared with those who did not. This led to the conclusion that the multidisciplinary approach to LVS may be important in QoL improvement, and fits well with the findings of Nilsson and Nilsson (1986) and the recommendations of McIlwaine *et al.* (1991).

Quality of Life and comparisons between models of LVS provision

Vision-related QoL outcomes have also been used as a way of making comparisons between different models of LVS provision. Reeves *et al.* (2004) compared the outcome of three different models of low vision rehabilitation over a 12 month period. The authors compared standard hospital based optometric LVS (at the Manchester Royal Hospital), with enhanced services (involving standard LVS together with up to three home visits to advise on training and provide alternative LVAs as needed). The third group of patients received standard LVS plus up to three home visits from an Age Concern community care worker to discuss daily and other activities.

Questionnaires used in the study were the SF-36 and the 'Vision-Quality of Life Core Measure' (VCM1; Frost *et al.* 1998). Although designed primarily for use in patients with cataracts (Wolffsohn and Cochrane, 2000), the VCM1 questionnaire does investigate factors such as anger, depression and loneliness in more detail than other more functional based questionnaires (e.g. LVQOL). Reeves *et al.* (2004) hypothesised that those patients receiving additional home visits and LVA training would demonstrate higher QoL scores and be more able to continue with daily tasks compared to those who attended the hospital clinic only. However, results showed that this was not the case and there was no significant difference in QoL improvement between the three groups, concluding that evidence of effectiveness was required before adopting enhanced (multidisciplinary) LVS.

In a non-randomized trial, de Boer *et al.* (2006) agreed with these findings when reporting on QoL outcomes at baseline and at one year follow-up for patients with varying causes of visual impairment referred to either optometric or multidisciplinary LVS (type dependent upon the patients geographical location). The authors reported no significant difference in QoL outcomes between the two types of rehabilitation using the VCM1 and LVQOL questionnaires, except one finding showing less deterioration in mobility for those attending optometric LVS. However, 27% of patients were lost to follow-up and de Boer *et al.* (2006) discussed the use of a control group in future studies where comparison is made between patients receiving LVS and placebo. It remains an open question as to whether it is ethical to withhold LVS rehabilitation treatment from patients that require it.

Pearce *et al.* (2011) used one approach to overcome this. In a study of 96 patients within the LV clinic at Moorfields Eye Hospital London, patients randomised to an intervention group received a further review appointment whilst those in a control group did not. The authors found through Mass of Activity Inventory (MAI) questionnaire scores that although self-reported improvement in daily tasks increased significantly following the initial LV

assessment, the additional follow-up visit where additional LVA training was administered resulted in no further improvement. Although the LVSCG (1999) highlighted that it is the duty of the person supplying the LVAs to ensure that the patient receives training in their optimal use, there is mixed evidence as to whether patients benefit from further / additional LVA training beyond that provided initially (Binns *et al.* 2012; CO-RCO, 2013).

Binns *et al.* (2012) in a systematic review of LVS discussed a number of different models and concluded that what is defined as a 'multidisciplinary' approach in one area may vary widely from that provided in another. Therefore, it is difficult to make comparisons between standard (hospital or community based) and multidisciplinary models of LVS provision, particularly where studies are based in different geographical areas. What is theoretically more important for clinicians working in any area of the UK is that there is a process by which they can gain an increased understanding of a patient's needs at or prior to LV assessment, which will help decide whether referral to social services or other rehabilitation centres is required. This is where another benefit of QoL questionnaires may be recognised.

1.4.5 Evaluation of quality of life in patients with age-related macular degeneration

A review by Finger *et al.* (2008) evaluated a number of QoL questionnaires that may be used specifically with patients suffering from ARMD. They concluded that out of the six questionnaires assessed, the 25 item NEI-VFQ was found to be the most extensively used and the best validated. The authors also suggested that future studies should aim to use a standard questionnaire when measuring vision-related QoL to allow for international comparison. Although they do not define what this particular standard should be, they do state that the 25 item NEI-VFQ should be included.

However, an earlier analysis of the 25 item NEI-VFQ carried out by Langelaan *et al.* (2007) recommended deleting some items. However, their study consisted of 129 adult visually impaired patients, where only 9.4% suffered from macular disease. It may be argued that: (1) on the basis of one study the 25 item NEI-VFQ cannot be completely discounted due to its previous wide usage amongst ARMD patients (Finger *et al.* 2008); and (2) it is very difficult to review literature which concentrates specifically on QoL questionnaires for ARMD patients, when often the questionnaires themselves can be used with a wide variety of eye conditions.

One more recent development which could help overcome this latter problem is the Macular Disease-dependent Quality of Life (MacDQoL) questionnaire. Finger *et al.* (2008) observed that this may allow a more in-depth approach in the measurement of vision-related QoL specific to macular disease patients. Mitchell *et al.* (2008) concluded that this 22 item questionnaire demonstrated good psychometric properties and allows for an individualised assessment of the impact of macular disease on QoL that goes beyond that of 'visual function' questionnaires. Although this is potentially of great benefit, Finger *et al.* (2008) stated that this particular questionnaire needs evaluation on a larger scale and therefore it could be argued that for the current study a questionnaire that is already well validated for use with ARMD patients (such as the LVQOL) would be better. Indeed, van Nispen *et al.* (2009a) questioned the exclusion of the LVQOL from the review by Finger *et al.* (2008) and highlighted its qualities as a measure of QoL.

1.4.6 Rationale for using the Low Vision Quality of Life Questionnaire in the current study

The 25 item, four dimension (distance vision; mobility and lighting; adjustment, reading and fine work; and activities of daily living) LVQOL questionnaire was chosen for this study as it has shown to be a reliable, fast method to measure vision-specific QoL (Wolffsohn and Cochrane, 2000). Moreover, it is free to use, which is of importance when considering its use in NHS LV Clinics. Covering the functional, psychological and social dimensions of QoL, the questionnaire has seven response categories ranging from '5' (having no vision-related difficulty with the specific item) to '1' (having a great difficulty). The options '0' (item could no longer be carried out due to the level of vision) and 'N/A' (the item was not relevant in that patient's daily life) were also included, with 'N/A' given an average score to prevent the bias towards a lower QoL overall (Wolffsohn and Cochrane, 2000).

Wolffsohn and Cochrane (2000) reported the LVQOL questionnaire to be a consistent, reliable and sensitive measure of the QoL in patients with irreversible visual impairment. This was also the conclusion of de Boer *et al.* (2004), who at that time rated the LVQOL amongst the two best questionnaires (out of 31 evaluated) to use with visually impaired patients. However, de Boer *et al.* (2004) did make reference to the lack of evidence for the construct validity and responsiveness of the LVQOL questionnaire. Further work to re-evaluate the questionnaire using an item response theory model (van Nispen *et al.* 2007) concluded that some questionnaire items should be removed - this will be considered in more detail in Section 4.2.2.

De Boer *et al.* (2006) concluded that there was no significant difference in LVQOL scores between patients attending either optometric or multidisciplinary LVS at one year follow-up. The current study will include patients attending optometric and / or multidisciplinary low-vision services, as these are often run in parallel in the UK. To offer optometric low vision without other multidisciplinary (rehabilitation) services to a particular cohort may be considered unethical.

1.4.7 Rationale for using the EuroQol five-dimension five-level questionnaire in the current study

There should be consideration of a patient's co-morbidities during LV assessment. The higher prevalence of multiple chronic health-related conditions in the elderly (e.g. stroke, diabetes and cancer) was reported by van Nispen *et al.* (2009b) to lead to reduced QoL through deterioration of physical, social and psychological functioning. Due to the increased prevalence of visual impairment with age, it is also more likely that a significant percentage of elderly patients with low vision will suffer from co-morbidity (Brody *et al.* 2001; van Nispen *et al.* 2009b). Less clear is the relationship between visual impairment and the number (and type) of co-morbidities on QoL.

The inclusion of a generic health status questionnaire in QoL studies of elderly visually impaired patients is hypothesised to reveal important non-vision-specific information. The EQ-5D was developed for use in clinical studies to provide a supplementary assessment of general health status and functional ability of patients (Rabin and de Charro, 2001). The development of the five level EQ-5D questionnaire in 2005 arose after studies published by the EuroQol group found that the additional two levels significantly increased the questionnaires sensitivity and reliability (Janssen *et al.* 2013). Its use has been extensively validated within populations of general and disease-specific states, and in a large number of geographical locations and languages (Janssen *et al.* 2013). The EQ-5D is widely used in the UK, as recommended by NICE.

The questionnaire consists of five items, representing five different health domains; three relate to function (mobility, self-care and usual activities) whilst two relate to feelings (pain / discomfort and anxiety / depression). Each domain has three (EQ-5D-3L) or five (EQ-5L-5D) levels to assess its severity. For the EQ-5D-3L these are: '1' (no problems), '2' (moderate problems) and '3' (severe problems). With the five level version of the questionnaire, as proposed for the current study, the levels are: '1' (no problems), '2' (slight

problems), '3' (moderate problems), '4' (severe problems) and '5' (unable to / extreme problems) dependent upon the item. This equates to a combination of potentially 243 (=3⁵) and 3125 (=5⁵) health states from the three and five level questionnaires respectively.

Van Nispen *et al.* (2009b) used the EuroQol five-dimension, three-level (EQ-5D-3L) generic health status questionnaire with 296 visually impaired elderly patients. They observed that the patients in this study who had self-reported co-morbidities at baseline demonstrated a lower QoL than those who did not. Musculoskeletal conditions, chronic obstructive pulmonary disease / asthma, and stroke were the conditions that most predicted a subsequent decline in QoL, along with a higher logMAR visual acuity, although the exact value was not specified. The same group also used the LVQOL questionnaire with this dataset (van Nispen *et al.* 2007). The self-reported improvement in QoL scores for reading small print after five months led the authors to hypothesise that LVS improved aspects of functional vision-related aspects of QoL, rather than health-related QoL. Binns *et al.* (2012) also observed a trend of lack of sensitivity when general health-related QoL questionnaires are applied to the assessment of LVS.

Malkin *et al.* (2013) reported that the EQ-5D-3L was not a suitable outcome measure for LVS, stating that it was unresponsive as a measure of rehabilitation, and struggled to discriminate amongst patients exhibiting varying levels of visual impairment. However as it was a late addition to their study and only administered to 77 of 764 participants further work would be required to validate the results.

The current study aims to use both the LVQOL questionnaire and the extended five level EQ-5D-5L on all patients to examine whether the increased sensitivity of the five level response (c.f. Malkin *et al.* 2013) means that the EQ-5D general health questionnaire is more applicable to the assessment of LV related QoL. This is a combination that has not been used previously.

The EQ-5D questionnaire also contains a visual analogue scale (VAS) with which the patient rates their general health status on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state; EuroQol, 2014). De Boer *et al.* (2006) evaluated outcomes between two different types of LVS (optometric and multidisciplinary) with both the LVQOL and VCM1. The authors also used the VAS component of the EQ-5D to assess general health status, and corrected their analyses for this and other confounders. The current study will also use the VAS in combination with the EQ-5D-5L to allow greater insight into the additional health-related requirements of patients attending LVS.

1.5 Summary

Although LVS have been shown to improve clinical and functional outcomes for patients, evidence of their effect on vision and health-related QoL remains unclear. Access to a valid, reliable and reproducible questionnaire to aid the audit process for the benefit of future planning and provision is important when considering the potential impact of ARMD on LVS in years to come. This is of particularly relevance in Milton Keynes, where the elderly population is predicted to be the fastest increasing in the UK.

1.6 Aims

This study will use the established and validated LVQOL and EQ-5D-5L questionnaires in parallel to provide quantifiable assessment of LVS QoL outcomes for patients with ARMD attending the LV Clinic at MKUH. The aims of the study are to:

1. Evaluate LVS at MKUH and inform improvement of service delivery and efficiency.
2. Examine which patients suffering from ARMD are most likely to benefit from LVS in the future.
3. Determine whether or not the five level general health status EQ-5D questionnaire provides sufficient sensitivity to be used in isolation to evaluate LVS at MKUH and inform improvement in service delivery and efficiency.

1.7 Research Hypotheses

Hypothesis A for this study is:

H_{0(A)}: LVS at MKUH have no effect on the QoL of patients with ARMD.

Two alternative hypotheses are proposed:

H_{1(A)}: LVS at MKUH improve the QoL of patients with ARMD.

H_{2(A)}: LVS at MKUH decrease the QoL of patients with ARMD.

Hypothesis B for this study is:

H_{0(B)}: All patients with ARMD benefit equally from LVS.

One alternative hypothesis is proposed:

H_{1(B)}: It is possible to identify a subgroup of ARMD patients that benefit more from LVS than others.

Hypothesis C for this study is:

H_{0(C)}: The EQ-5D-5L general health status questionnaire has insufficient sensitivity to determine whether or not LVS at MKUH improves QoL in patients with ARMD.

One alternative hypothesis is proposed:

H_{1(C)}: The EQ-5D-5L general health status questionnaire has sufficient sensitivity to determine whether or not LVS at MKUH improves QoL in patients with ARMD.

1.8 Objectives

1. To design and conduct an experiment based on the LVQOL and EQ-5D-5L questionnaires to test hypotheses A, B and C in the LV Clinic at MKUH over a six month period.
2. To perform analysis using robust statistical techniques to test hypotheses A, B and C and to determine mechanisms by which LVS improve QoL where appropriate.
3. To provide recommendations to the hospital and wider audiences based on the findings of this study to improve the efficiency and effectiveness of LVS.
4. To make recommendations on the improvement of LVS at MKUH and in the wider NHS.
5. To evaluate the methodology and approach taken to provide recommendations for future work in this subject.

2 METHODOLOGY

2.1 Introduction

In order to achieve the objectives a questionnaire-based study was designed and carried out in the LV clinic at MKUH. The study was conducted on 40 patients diagnosed with ARMD in one or both eyes and attending the LV Clinic for assessment over a six month period. A six month period was selected to allow for two follow-up visits after the initial consultation.

2.2 Study Participants

2.2.1 Inclusion and exclusion criteria

Eligibility requirements for inclusion in the study were as follows:

1. Recent referral to, or current attendance at, the Optometrist-led LV clinic, MKUH.
2. Following the initial LV assessment, the patient was deemed to require three and six-month follow-up LV clinic reviews.
3. A diagnosis of ARMD (affecting at least one eye, regardless of subtype classification) had been made previously by an ophthalmologist.
4. Participants were aged 18 years or over.
5. Irreversible vision loss.

Exclusion criteria:

1. Patients that lacked the capacity to provide informed consent for themselves.
2. Participants had no other ocular co-morbidities, with the exception of lenticular opacities.

2.2.2 Recruitment

For all patients attending the LV clinic at MKUH on that particular day, the Chief Investigator (Louise James) read through any previous relevant eye clinic documentation in the hospital

records to determine patient suitability for participation in the study. Original / new referral letters to the LV clinic for each patient from local GPs (via community based optometrists), hospital ophthalmologists and the ECLO were also reviewed where available. Patients that had previously attended the clinic or another hospital LV clinic / provider (existing patients) were considered for the study, along with those who had never previously received LVS input (new patients).

Using the inclusion and exclusion criteria for the study, a decision was made as to whether any patients were suitable to participate, and these were noted by the Chief Investigator.

Following attendance at the LV clinic and on completion of an LV assessment (see Section 2.3.1), the Chief Investigator made a further assessment as to whether the patient would require both three and six-month follow-up LV clinic reviews. If these were considered necessary, the patient was deemed suitable for inclusion in the study.

Participants were then recruited through verbal invitation and presented with a verbal overview of the research and what participation in the study would involve (e.g. future attendance at LV clinics and questionnaire procedures). The Chief Investigator discussed the Patient Information Sheet (v2) and Consent Form (v2) (see Appendix 2.1) with the patient, who was then given a minimum 30 minute period for reflection. All invited patients decided that they would like to participate.

The minimum number of patients was determined using an a priori power analysis in G*Power (version 3.1.9.2, University of Düsseldorf) for a two-tailed paired Student t-test with a power of 80%, $\alpha=0.05$ and a medium effect size (Prajapati *et al.* 2010). The selection of the Student t-test was based on the normal distribution of LVQOL data in Wolffsohn and Cochrane (2000). This determined a minimum sample size of 34 patients. In total, 40 patients were recruited for the study between 5th March 2013 and 18th February 2014.

2.2.3 Informed consent

Prior to commencement of the study, and by way of a written consent form, patients were asked for their consent to use data collected from questionnaires. One copy of this consent form was given to the patient, and a second copy was kept securely by the Chief Investigator.

The Chief Investigator made it clear that:

1. Participation in the study was not necessary in order for the patient to continue to receive LVS at MKUH.
2. Consent to take part in the study was not compulsory.
3. There were to be no adverse consequences should consent not be granted.
4. Consent given at the beginning of the study was implied throughout the six month period that data was to be collected; however the participant was free to withdraw from the study at any stage without penalty.
5. The research involved collecting data by questionnaire, and included some questions of a sensitive nature as they related to QoL.
6. The research involved collecting data by questionnaire a maximum of three times over a six month period.
7. The Chief Investigator would be responsible for maintaining privacy and confidentiality throughout (and following) the study.
8. Only anonymous data would be published.

2.2.4 Privacy, confidentiality and data security

The Chief Investigator was responsible for maintaining privacy and confidentiality. All collected data from questionnaires were stored on a database, and information collected over the study period was added to this database. To maintain anonymity in the study, each participant was assigned a unique identification number between 001 and 040 on a consecutive basis. Patient names and / or hospital numbers were not included in the database.

Privacy and confidentiality was protected vigorously to the extent permissible by law. However, patients were made aware that privacy and / or confidentiality could not be guaranteed. All personal and collected data were stored securely and destroyed on study completion. Whilst participant identification numbers remained with the study data, there was no remaining link between identification numbers and personal details.

Published data do not require identification of patients or pseudonymisation - aggregated (statistical) anonymised data were used. Anonymised data were made available to Professor Stephen J. Anderson (Supervisor, Aston University) but non-anonymised data were not transferred externally from the Eye Clinic at MKUH.

2.2.5 Characteristics of study participants

Table 2.1 Demographic characteristics of study participants at baseline (n=40)

	All	Female	Male
Gender		n = 26 (65%)	n = 14 (35%)
Mean¹ Age (years)	81.4 ± 1.36	81.3 ± 1.75	81.4 ± 2.18
New Patients	n = 20	n = 14	n = 6
Existing Patients	n = 20	n = 12	n = 8
ARMD Sub-type²			
Geographic atrophy (GA)	n = 22	n = 14	n = 8
Exudative (Ex)	n = 10	n = 7	n = 3
Mixed	n = 8	n = 5	n = 3
ARMD Sub-type by eye			
GA both eyes	n = 19	n = 13	n = 6
Ex both eyes	n = 9	n = 6	n = 3
R/L: GA/Ex or Ex/GA	n = 8	n = 5	n = 3
Monocular GA	n = 3	n = 1	n = 2
Monocular Ex	n = 1	n = 1	n = 0
Living Status			
Lives alone	n = 20	n = 16	n = 4
Lives with spouse	n = 16	n = 7	n = 9
Lives with family (no spouse)	n = 4	n = 3	n = 1
Registration Status³			
Registered as SI	n = 13	n = 7	n = 6
Registered as SSI	n = 5	n = 3	n = 2
Not Registered	n = 22	n = 16	n = 6

Notes:

1. Mean ± standard error of the mean.

2. Where diagnosis was previously made by an ophthalmologist at MKUH and this information was obtained from the patient's hospital records.

3. Where registration as Severely Sight I (SSI) indicates: Group 1 – VA below 3/60; Group 2 – VA of 6/60 but below 3/60 with a very contracted field of vision; Group 3 – VA of 6/60 or above with a contracted field of vision, especially in the lower part of the field. Registration as Sight Impaired (SI) indicates: VA 3/60 to 6/60 with full field; or up to 6/24 with moderate contraction of the field, opacities in media or aphakia; or, 6/18 or even better if they have a gross defect, for example hemianopia, or if there is a marked contraction of the visual field. Adapted from the Certificate of Vision Impairment, Department of Health (2013).

2.3 Procedure

2.3.1 Low vision clinic assessment

Each participant received a 30 minute clinical LV assessment, carried out by the Chief Investigator. All techniques fell within the scope of normal professional practice and included the following (see also Appendix 1.1):

Comprehensive case history – to determine any general and / or specific problems that the patient was having with their vision, and the effect that these had upon their ability to perform everyday tasks. The patient's social situation, general health status and current level of support were identified, along with the level of adaptation to vision loss and expectations of the LV clinic. The date of the last full eye examination was noted, along with the type and age of any spectacle correction currently worn.

Assessment of distance visual acuity – an assessment of both monocular (OD and OS) and binocular distance visual acuities were obtained using the 'Bailey-Lovie Logarithmic Visual Acuity Chart 2000' (Sussex Vision, Rustington, UK). A standard chart illumination of 1206 ± 63.7 lux, and room illumination of 273 ± 17.5 lux (mean \pm standard error of five measurements using the Whitegoods LightMeter app on an iPhone 5S, www.whitegoods.com) was consistent throughout all initial and follow-up assessments, for all 40 study participants.

Due to the constraints of the clinic room, a 2 m (rather than the standard 4 m specified by the manufacturer) testing distance was used. To allow for this enforced alteration in testing distance, the addition of 0.3 log units was applied to each recorded measurement of both unaided and corrected distance visual acuities to ensure that the measured logMAR was accurately documented. By using this method, a range of acuity levels between logMAR 1.30 to 0.00 were obtained, equivalent to Snellen visual acuities of 3/60 and 6/6 respectively. This was extended to logMAR values of 1.80 for a Snellen visual acuity of 1/60 by movement of relative chart position.

If appropriate, standard notation of count fingers (CF), hand movements (HM; both at 0.6 m), perception of light (LP) and, no perception of light (NPL) were recorded; logMAR values of 2.00 and 3.00 were assigned to CF and HM respectively (Holladay, 2004). Monocular pinhole acuity was also recorded where visual acuity was found to be at a level equal to (or below) 0.20 logMAR.

Assessment of near visual acuity – assessment of monocular (OD and OS) and binocular near visual acuity (NVA) using the non-illuminated Times New Roman ‘N’ point notation chart (range between N5 to N48) with the patient wearing their current near correction (e.g. single vision, bifocal, multifocal). Working distance(s) were recorded for each patient, and a conversion to logMAR values made using the following formula:

$$y = \log_{10} \frac{x}{8w}$$

Where:

y is the near visual acuity in logMAR

x is the near visual acuity in N notation

w is the working distance in metres

Distance Refraction – retinoscopy and monocular subjective refraction were carried out for each patient.

Assessment of contrast sensitivity – was conducted with the optimum distance refractive correction in place at a testing distance of one metre, using the non-illuminated ‘Pelli-Robson Contrast Sensitivity Chart 2L’, copyright © 1988 by Denis G. Pelli (serial number: KB084).

Near refraction – where appropriate, a high reading addition ($\geq +4.00$ DS) was demonstrated at this stage, with any advantages (e.g. hands-free viewing) and disadvantages (e.g. close working distances) of this method of magnification explained to the patient.

To ensure that the patient was wearing the optimum correction for both their distance and near requirements, a verbal explanation of the best form(s) of spectacle correction was given. A new spectacle prescription was issued (where deemed appropriate) for the patient to present to their community dispensing optician. However, the limitation of visual improvement with the new spectacles was also discussed, where necessary, to manage the patient’s current and future expectations.

Optical low vision aid demonstration and training – trial LVAs were initially chosen based on the patient’s specific task requirements (e.g. size and contrast of print), level of visual acuity, patient motivation and handling ability. LVAs of different types (as appropriate for each task) were demonstrated, however the number of LVAs issued was limited to a maximum of three per patient as per clinic protocol (e.g. a stand magnifier for reading newsprint, a hand magnifier for reading packets in the kitchen and a foldaway magnifier for shopping).

A record was made of the LVAs trialled (and issued), the acuity level achieved, fluency of reading, type of spectacle correction worn (where relevant), and any other patient comments.

Distance optical LVAs (e.g. monoculars and binoculars) were demonstrated (and issued) as required. Note that no distance LVAs were issued in this study, so there were no data to analyse.

Guidance on how to achieve the optimum results with each magnifier was given verbally to the patient (and any family / carers present), and was also issued in large print written format. Explanation of the maintenance of LVAs was provided along with telephone details of the LV clinic in the event of any future problems. Patients were made aware that LVAs were loaned without cost on a long-term basis.

Lighting and non-optical low vision aids – limited advice on the most appropriate general and task lighting was issued as required. Techniques were discussed for improvement of contrast within the home, particularly if a reduced level of contrast sensitivity had been measured. For further help and advice with both improved lighting and contrast, a written referral was sent to the ECLO (see below).

Glare shields in various tints were demonstrated if the patient had previously indicated a problem with glare. One pair was loaned (if necessary) and the advantage of peaked hats / caps was discussed.

Demonstration of a limited range of large print items was carried out, along with both written and verbal information on how to purchase these and other items privately. If the patient was receptive to the concept of audio books and talking newspapers, written information was provided on both local and national schemes.

Other non-optical equipment (e.g. liquid level indicators and talking watches) were discussed, and details of where to trial / purchase these were issued. Reference was made to the advantages of eccentric viewing and steady eye strategy and if deemed appropriate, a referral made to the ECLO to arrange further training in these techniques.

Discussion of electronic LVAs (including e-readers, and portable / non-portable CCTVs) was provided along with information including estimates of the costs involved to purchase privately. Referral for demonstration of a range of CCTVs at the local resource centre was made via the ECLO.

Onward referral – if required, and with the patient’s consent, further referral was made to the ECLO within MKUH eye clinic through the completion of an RVI (Appendix 2.2). On receiving the RVI, the ECLO telephoned the patient to conduct an assessment of their needs and discuss further support processes. If deemed necessary, onward referral was made by the ECLO to the local Sensory Advice Resource Centre (SARC) allowing access to a wider range of rehabilitative services, advice and support. In cases whereby no further in-person support was needed, patients were provided with contact details for SARC (and / or other local and national support groups) in case of any future difficulties.

During the study, three (/40) patients were referred to the ECLO at the initial study visit (T0) and 14/40 patients had contact with the ECLO prior to the study. Five were awaiting home visits and 18 did not want to use the service during the study.

2.3.2 Questionnaires

On completion of the LV assessment and after informed consent had been given, the Chief Investigator conducted the two questionnaires (LVQOL and EQ-5D-5L) with the patient. For all participants, both questionnaires were interviewer-administered, with verbal responses recorded on paper forms. During this process, no feedback was given to the patient on their responses.

Low Vision Quality of Life (LVQOL) questionnaire:

The Low Vision Quality of Life (LVQOL) questionnaire (Wolffsohn and Cochrane, 2000) was used in this study (Appendix 2.3). Twenty-five consecutive questions on vision-specific QoL were asked within sections on ‘Distance Vision Mobility and Lighting’ (12 questions); ‘Adjustment’ (4 questions); ‘Reading and Fine Work’ (5 questions); and ‘Activities of Daily Living’ (4 questions). For each question, the patient was asked to provide a graded response on a numerical Likert scale related to the difficulty / problem with the specific task being assessed between ‘5’ (no problem due to their vision) and ‘1’ (great problem due to their vision). A response of ‘X’ was marked if the patient could no longer complete the task due to their visual impairment, and ‘N/A’ was recorded if they did not perform the task for non-visual reasons. If the patient made specific comments on any of the questions, these were recorded separately (see Patient Testimonials, Appendix 2.4).

The scores for each of the 25 questions were combined to provide a summed total questionnaire score for each patient with a minimum score of 0 and a maximum score of 125. It is assumed that the higher the total score, the higher the patient's QoL (Wolffsohn and Cochrane, 2000). Questions scored 'N/A' were given a midpoint score of 3, as recommended by Wolffsohn and Cochrane (2000), to prevent bias towards an artificially reduced QoL for those patients scoring multiple questions as not relevant to themselves. Questions scored as 'X' were given a score of zero.

EuroQol five-dimension, five-level (EQ-5D-5L) questionnaire:

The five-level version of the EuroQol five-dimension (EQ-5D-5L) generic health status questionnaire (Herdman *et al.* 2011) was used in this study (Appendix 2.5). For questions one 'Mobility', two 'Self-Care', and three 'Usual Activities', participants were asked to provide a graded response from five levels between '1' (no problem performing task) and '5' (unable to complete task). For questions four and five relating to level of 'Pain / Discomfort' and 'Anxiety and Depression' respectively, the response was scored between '1' (no pain or discomfort / not anxious or depressed) and '5' (extreme pain or discomfort / extremely anxious or depressed). Again, if the patient made any specific comments on any question, these were recorded separately (Patient Testimonials, Appendix 2.6).

For analysis, the summed score of the five questions was calculated with results between a lowest possible score of 5 and the highest of 25. Lower scores indicated a better health-related QoL.

Finally, a score was recorded for the patient's subjective assessment of their health at that particular time using the EuroQol visual analogue scale (EQ-VAS). This was given a value between '0' (worst health they could imagine) and '100' (best health they could imagine).

Follow-up appointment - the patient was given an appointment for a three month follow-up LV clinic review, and provided with details to enable them to contact the clinic by telephone if required in the meantime.

2.3.3 Three-month follow-up assessment

At the three-month follow-up visit, the Chief Investigator conducted an LV clinic review, this included:

History and symptoms – any new symptoms were noted, along with any new difficulties experienced with daily tasks. Patients were questioned as to how useful they had found the loaned LVAs, the tasks that they were used for, and any difficulties they faced with using them. If the patient had been referred to the ECLO following the first visit, the outcome of this was discussed and any new equipment provided / purchased was noted.

Distance / near visual acuity and contrast sensitivity – was reassessed.

Refraction – was not carried out at the three-month follow-up visit unless required.

Assessment of distance and near visual acuity with current low vision aids – assessment of the patients near acuity, fluency and handling technique with the current near optical LVAs. Demonstration of stronger / weaker or alternative types of aid was provided if necessary, along with further training and advice on handling techniques.

Further information on non-optical aids was issued if required. For those patients who had not previously been assessed by the ECLO but now needed this service, a referral was made.

Questionnaires: – the two questionnaires (LVQOL and EQ-5D-5L) were administered as before (see Section 2.3.2).

Follow-up appointment – the patient was given an appointment for the six-month follow-up low vision clinic review.

2.3.4 Six-month follow-up assessment

At the six-month follow-up visit, the Chief Investigator provided an LV clinic review as per the three-month follow-up described in Section 2.3.3. After completing both questionnaires at the six-month review, the patient was informed that they had completed all requirements for the study.

If no further appointments were required in the LV clinic, participants were then discharged from the clinic and given advice regarding the need for regular eye examination with their community optometrist. Patients were also advised to contact their own optometrist or GP should they develop any new symptoms, and on how to access LV clinic services in the future.

For those patients where a further routine appointment was required for the LVA and / or ophthalmology clinics, this was arranged.

2.3.5 Drop outs

One patient (023) was discharged from the LV clinic following the three-month follow-up assessment as they did not require a six-month assessment. In this case, the patient consented to the chief investigator collecting questionnaire data by telephone at the six-month time point.

Four other participants (009, 010, 011 and 020) attended for six-month LV clinic follow-up as planned but were seen by an optometrist other than the Chief Investigator as appointments had been rearranged previously. In these cases, the Chief Investigator obtained all questionnaire data by telephone.

Participant 036 completed the initial and three-month clinic visits and questionnaires but was unable to attend the six-month review, necessitating completion of the questionnaires by telephone.

Participant 038 attended the initial and six-month visit, but was unable to attend the three-month visit due to poor health and was unable to answer questionnaires by telephone during this period.

2.4 Ethics

The primary ethical issues raised by the scientific design of this protocol were randomization, psychological risks, testing vulnerable patients, statistical validity and data protection.

Although QoL questionnaires do not involve any physical risk to the patient, they do involve a risk of psychological harm due to the sensitive nature of some questions. This risk was minimised wherever possible and patients were able to leave the study at any time if they were experiencing any negative psychological reaction. There was also a risk of breaching

patient privacy and confidentiality in relation to the information contained within the questionnaires. This risk was minimised by seeking patient consent prior to participation to allow data to be analysed, along with the secure storage of collected data and anonymisation.

Patients were informed when consent was taken to expect no benefit from participating in this study. The results of this study may therefore only be beneficial to future patients attending for LVS.

To manage appropriately the ethical complexities inherent in this study, it was necessary to put the following additional protections of the research participants in place: informed continued consent, anonymisation and data security. By instituting these additional protections, the risks were appropriately minimised and a reasonable and ethically acceptable balance between risks and benefits was established.

Prior to the commencement of the study, ethical approval was obtained from Aston University Audiology / Optometry Research Ethics Committee on 13th January 2010. Approval was also gained from the NHS Cambridgeshire 3 Research Ethics Committee (now known as NRES Committee East of England - Norfolk) on 24th May 2011 (reference 11/H0306/1), along with the local ethics committee of MKUH on 24th June 2011 (Appendix 2.7).

2.5 Statistical Analysis

2.5.1 Testing for normal distribution of data

The first stage of the statistical analysis was to examine the frequency distribution of the sample data at each visit. Visits were designated as: the initial visit (T0), the three-month visit (T3) and the six-month visit (T6). The frequency distributions of the data were compared with the normal distribution using the Shapiro-Wilk Test ($p < 0.05$), appropriate for small sample sizes ($n = 40$).

Where data were normally distributed, parametric statistical methods were used. Where data were not normally distributed, attempts were made to transform the data using the square-root and logarithmic methods to enable a multifactorial analysis. Where these did not produce normal distributions through transformation, non-parametric statistical methods were used.

2.5.2 Determination of differences in visual acuity and questionnaire score among visits

Two types of omnibus test were used to determine whether statistically significant differences existed among sample visual acuity measures and questionnaire scores for each visit. For normally distributed data a repeated-measures analysis of variance (RMANOVA) test was used. RMANOVA considers the error variation of the comparisons among results for the same patients over the three time intervals simultaneously (i.e. it takes into account the error at T3 when comparing T0 to T6).

There are five assumptions of this test:

1. One dependent variable measured at the continuous (interval or ratio) level.
2. One within-patients factor (independent-variable) that comprises three or more categorical levels.
3. There should be no significant outliers in the within-patient factors.
4. The distribution of the dependent variable in the within-patient factors should be approximately normally distributed.
5. The variances of the differences between all combinations of levels of the within-patients factor must be equal (sphericity).

The questionnaires in this study use Likert-scales of one to five. The assumption is made that a score of four on this scale is twice as good (or bad) as a score of two. With this assumption, the aggregated score across a number of questions is routinely considered to be continuous in psychometric testing (Streiner *et al.* 2014). Therefore Assumption 1 is valid. It should be noted however that there is a maximum possible questionnaire score and therefore if 'improvement' is measured over time, the data will become skewed because patients cannot score more than the maximum (e.g. 125 for the LVQOL questionnaire).

Where significant differences among visits or interactions with patient categorisation effects existed ($p < 0.05$), post-hoc testing to determine differences between visit pairs (or patient categorisation effects) was carried out using the paired-sample Student t-test.

Where data were non-normal and it was not possible to transform the data to normal distributions by the square-root or logarithmic methods, the non-parametric Friedman's two-way analysis of variance by ranks test was used to detect differences in sample visual acuity or questionnaire score across the three visits.

Where significant differences were observed ($p < 0.05$), post-hoc comparison of samples between visit pairs was conducted using the Wilcoxon Signed Rank Test or the Paired-Samples Sign Test. The Wilcoxon Signed Rank Test is the non-parametric equivalent of

the Paired-sample Student t-Test for the determination of median difference between paired observations. This test does not require normal distribution of the data but has three assumptions:

1. One dependent variable measured at the continuous (interval or ratio) level.
2. One independent variable that comprises two categorical, related groups or matched pairs.
3. The distributions of difference between the two related groups should be symmetrical in shape.

The Paired-Samples Sign Test is a less statistically powerful test than the Wilcoxon Signed Rank Test and was used when the distribution of difference between the two related groups was not symmetrical (see Assumption 3 of the Wilcoxon Signed Rank Test above). This test has four assumptions:

1. One dependent variable measured at the continuous (interval or ratio) or ordinal level.
2. One independent variable that comprises two categorical, related groups or matched pairs.
3. The paired observations for each participant need to be independent, i.e. one patient cannot influence another patient's score.
4. The difference scores are from a continuous distribution.

A modification of the standard Paired-Samples Sign Test was necessary because there were a large number of neutral pairs in the analysis. These are patients whose visual acuity or questionnaire score does not increase (positive difference for LVQOL, negative difference for acuity and EQ-5D-5L) from visit to visit (particularly T3 to T6). The standard related-samples Sign Test ignores these neutral pairs and considers only the binomial positive or negative probability. Randles (2001) recommended the use of the more conservative Intermediate Preference Sign Test that weights the effect of neutrals using a factor of 1/3. This method was used where the proportion of neutrals was more than 10%.

2.5.3 Correlation analysis

Where data were normally distributed, the Pearson Correlation Test (r) was used to examine whether correlative relationships existed among different datasets. For data with a non-normal distribution, the Spearman Rank Correlation (r_s) was used.

2.5.4 Software used

Statistical analyses were conducted using SPSS version 21 (SPSS Inc, Chicago, Illinois), with the exception of the Intermediate Sign Test which was conducted using Microsoft Excel 2013 (Microsoft Corporation, Redmond, Washington).

3 RESULTS

3.1 Low Vision Assessments

3.1.1 Data characterisation

Patient habitual distance binocular visual acuity (DVA) was normally distributed at each visit (Figure 3.1; Shapiro-Wilk, $p=0.248$ to $p=0.287$, Table 3.1). Patient habitual monocular DVA was also normally distributed for the right and left eyes (Shapiro-Wilk, $p=0.389$ to $p=0.718$ for all visits).

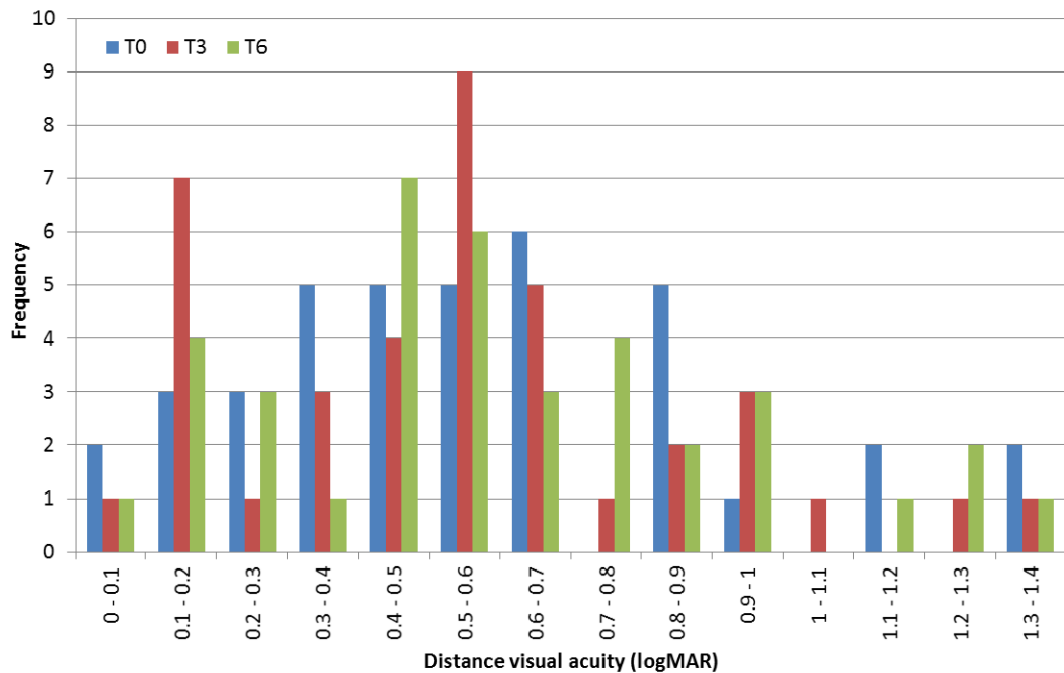


Figure 3.1 Frequency distribution of binocular distance visual acuity (DVA, logMAR) at the initial (T0, $n=39$), three-month (T3, $n=39$) and six-month (T6, $n=38$) visits.

The frequency distribution of binocular near visual acuity (NVA) was positively skewed and non-normal at each visit (Figure 3.2; Shapiro-Wilk, $p<0.05$, Table 3.1). A simple square-root transform rendered the data normally distributed for each visit. Patient monocular NVA was normally distributed for the right and left eyes (Shapiro-Wilk, $p=0.151$ to $p=0.980$ for all visits).

Optimum NVA in low vision patients is typically achieved using an LVA. The maximum NVA was determined for each patient using the LVA or LVAs with which they attended the appointment; this is referred to as NVA-LVA throughout this thesis. IN the situation where patients attended with multiple LVAs, the best acuity (lowest NVA-LVA) measurement was used for analysis. The NVA-LVA data were strongly positively skewed and non-normal

(Figure 3.3; Shapiro-Wilk, $p < 0.001$, Table 3.1). Neither a square-root or log transform of the data resulted in a normal distribution at any visit, principally because the majority of patients were achieving an optimum NVA-LVA of 0.19 logMAR when using their LVA. Monocular data were not recorded as LVAs tend to be used binocularly or with the patient's best eye.

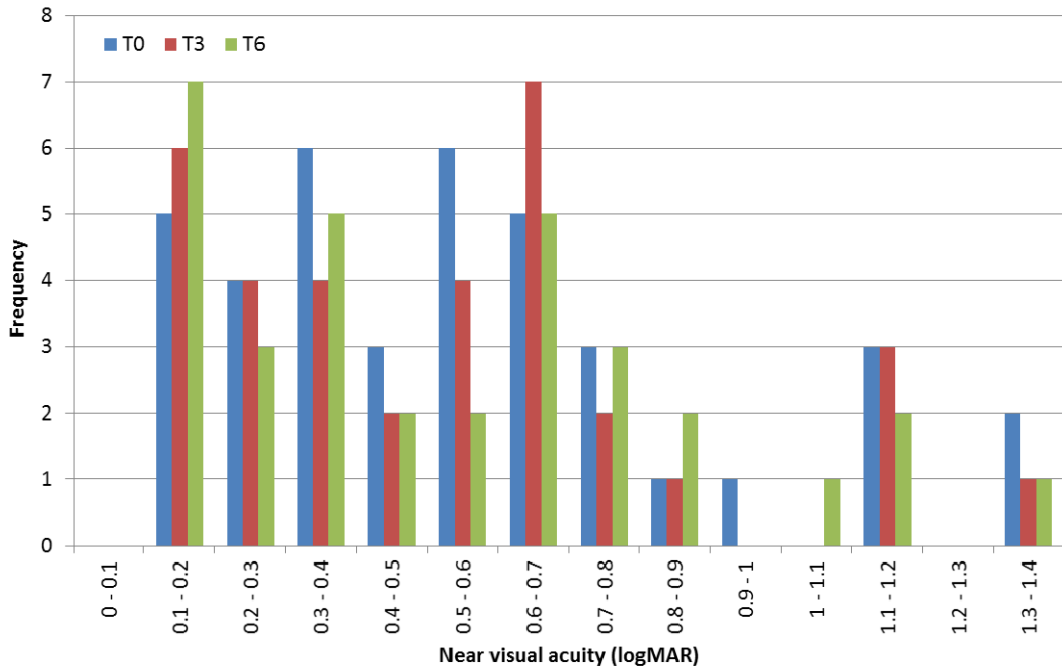


Figure 3.2 Frequency distribution of binocular near visual acuity (NVA, logMAR) at the initial (T0, $n=39$), three-month (T3, $n=34$) and six-month (T6, $n=33$) visits.

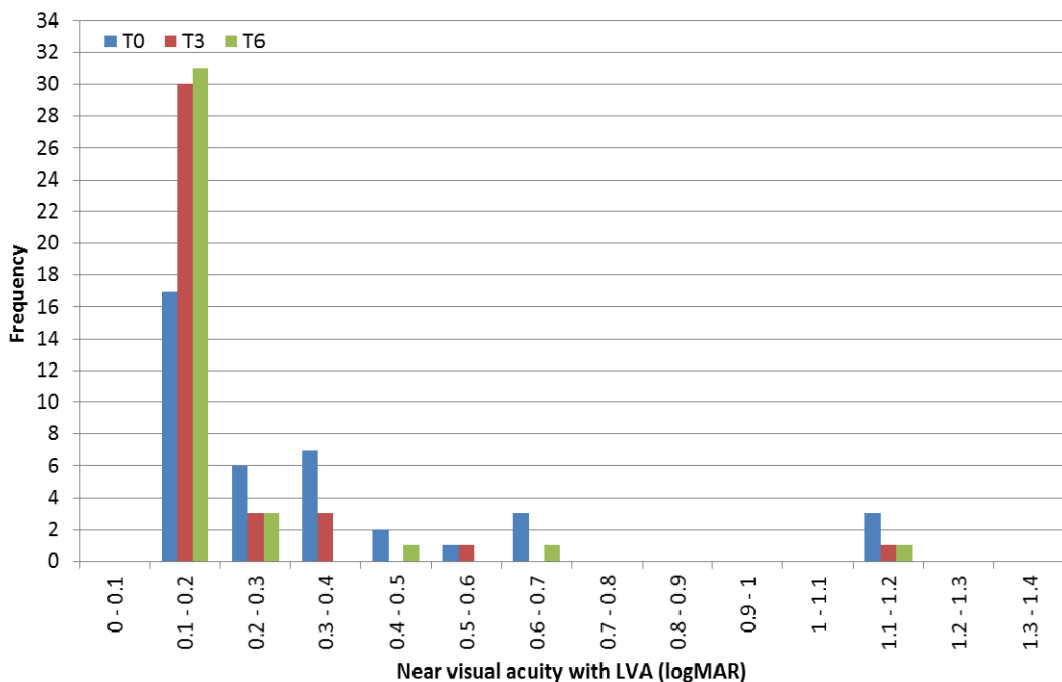


Figure 3.3 Frequency distribution of binocular near visual acuity with the patient's low vision aid (NVA-LVA, logMAR) at the initial (T0, $n=39$), three-month (T3, $n=38$) and six-month (T6, $n=37$) visits.

Table 3.1 Comparison of near visual acuity (logMAR) distribution to the normal distribution.

Visit	As measured		Square-Root Transform ¹		Logarithmic Transform ²	
	Skewness	Normal ³	Skewness	Normal ³	Skewness	Normal ³
Distance Visual Acuity						
T0	0.757	p=0.287				
T3	0.715	p=0.248		n/a		n/a
T6	0.577	p=0.273				
Near Visual Acuity						
T0	1.046	p=0.019	0.420	p=0.202		
T3	0.609	p=0.048	0.057	p=0.079		n/a
T6	0.897	p=0.015	0.387	p=0.080		
Near Visual Acuity with Low Vision Aid						
T0	2.210	p<0.001	1.656	p<0.001	1.114	p<0.001
T3	4.777	p<0.001	4.376	p<0.001	3.826	p<0.001
T6	4.611	p<0.001	4.302	p<0.001	3.996	p<0.001

Notes:

1. Square root transformation for positively skewed data.
2. Log₁₀ transformation for positively skewed data.
3. The Shapiro-Wilk test was used to determine whether the distribution of measured data was significantly different from the normal distribution (p<0.05).

3.1.2 Analysis of distance visual acuity

Mean presenting binocular distance visual acuity (DVA) is shown in Figure 3.4. A repeated-measures analysis of variance revealed that there was no significant change in DVA among the three visits (Greenhouse-Geisser correction, p=0.335). Monocularly, the same no significant change over time was observed (Greenhouse-Geisser correction, RE p=0.505, LE p=0.190).

Within the patient sample (n=40) there were 20 patients who were attending an LV clinic for the first time ('new patients') and 20 patients who had previously attended an LV clinic ('existing patients'). This sub categorisation of patients was included as a factor in a two-way RMANOVA. There was no significant interaction between the visit term and the classification of the patient as 'new' or 'existing' (p=0.388). This means that irrespective of whether or not the patient was new to the clinic, their binocular DVA did not improve or worsen significantly during the six-month experimental period. There was no significant interaction between the new and existing patient term for monocular DVA (either eye) in a two-way RMANOVA (RE p=0.877, LE p=0.749).

3.1.3 Analysis of near visual acuity

Mean presenting binocular near visual acuity is shown in Figure 3.4. RMANOVA of the square-root transformed data determined that there was no significant change in NVA among the three visits (Greenhouse-Geisser correction, $p=0.701$). As with distance acuity, there was no significant interaction between the visit term and the classification of the patient as 'new' or 'existing' ($p=0.116$).

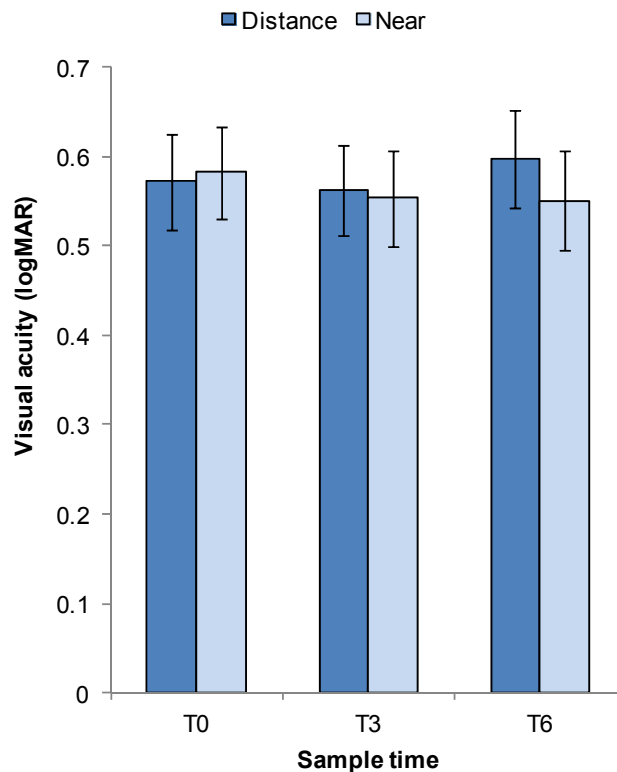


Figure 3.4 Mean presenting binocular visual acuity (for distance and near) at the initial (T0), three-month (T3) and six-month (T6) visits. Error bars represent the standard error of the mean.

Monocularly, the same no significant change over time was observed (Greenhouse-Geisser correction, RE $p=0.728$, LE $p=0.732$). There was no significant interaction between the new and existing patient term for either eye in a two-way RMANOVA (RE $p=0.798$, LE $p=0.263$).

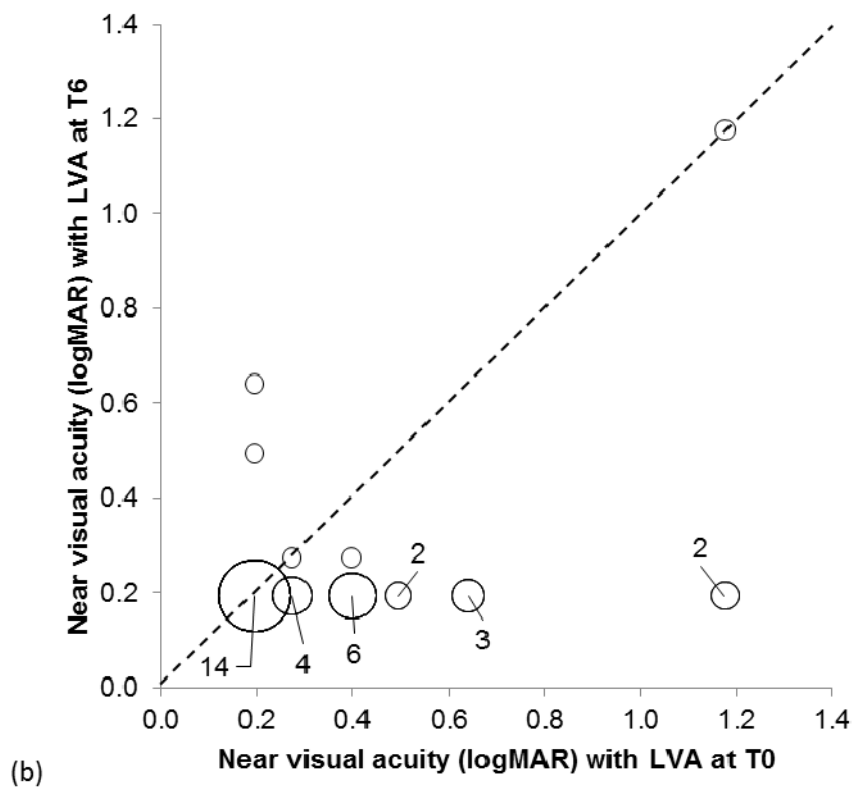
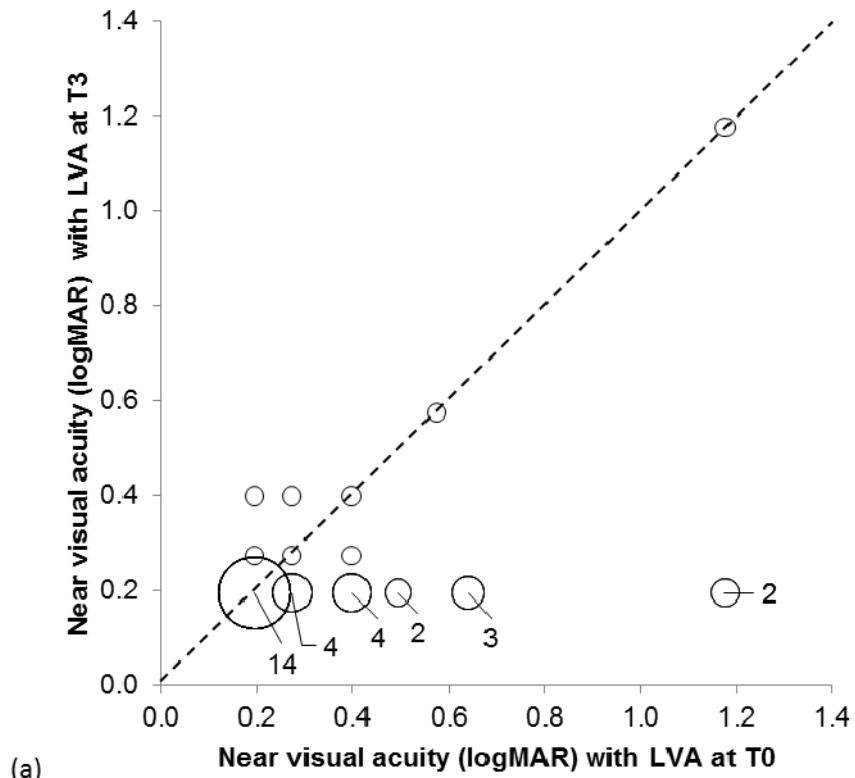


Figure 3.5 Comparison of binocular near visual acuity with a low vision aid (NVA-LVA, logMAR) for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with visual acuities at the centre of the marker, which are also labelled (markers with no label represent single-patient acuity measurements). The dashed line represents the line of equal acuity measurements at each visit (i.e. the 'line of no effect').

3.1.4 Analysis of near visual acuity using a low vision aid

Figure 3.5a shows that just under half of the 37 patients had the same NVA-LVA at T0 and T3 (18/37 patients on the line of no effect), a few deteriorated slightly (three patients above the line) but some improved dramatically (16 patients below the line). Figure 3.5b shows that between T0 and T6 more patients were below the line of no effect (18/36) than on (16/36), or above (2/36); this indicates a greater improvement between T0 and T6 than between T0 and T3. Measurement of NVA-LVA at T0 was prior to any improvements made during the clinic and therefore represents the best NVA-LVA influencing the patient's QoL prior to assessment by questionnaire. These data were not normally distributed (Shapiro-Wilk $p < 0.001$, Table 3.1) and therefore non-parametric statistical methods were used for analysis. Median (\pm interquartile range) NVA-LVA increased from 0.27 ± 0.20 logMAR at T0 to 0.19 ± 0.00 logMAR at T3 and T6. The Friedman's two-way ANOVA by ranks test demonstrated that there was a significant difference in NVA-LVA among visits ($p < 0.001$).

The related-samples Sign Test was used post-hoc to determine whether there was a significant difference in the median differences in NVA-LVA between sample pairs at T0, T3 and T6 (i.e. T0-T3, T3-T6 and T0-T6). Table 3.2 shows that the number of neutral pairs (NVA-LVA acuities that do not change from T0 to T3, or from T0 to T6, or T3 to T6) is a high proportion of the data for all three comparisons. The Intermediate Sign Test showed that there was a statistically significant median decrease of 0.08 logMAR between T0 and T6 ($p = 0.011$), but no significant difference in T0-T3 or T3-T6.

Table 3.2 Number of positive, negative and neutral differences in near visual acuity with low vision aid, between visit pairs. Positive differences are an increase in logMAR (i.e. a decline in acuity) between two visits; negative differences are a decrease in logMAR (i.e. an improvement in acuity) between two visits; and neutral differences are ties (i.e zero change in acuity).

Difference	Comparison between visit pairs		
	T0-T3	T3-T6	T0-T6
Positive	3	2	2
Negative	16	6	18
Neutral (ties)	18	27	16
Total	37	35	36

Table 3.3 Number of positive, negative and neutral differences in near visual acuity with low vision aid, between visit pairs for existing and new patients. Positive differences are an increase in logMAR (i.e. a decline in acuity) between two visits; negative differences are a decrease in logMAR (i.e. an improvement in acuity) between two visits; and neutral differences are ties (i.e zero change in acuity).

Difference	Comparison between visit pairs		
	T0-T3	T3-T6	T0-T6
	Existing Patients		
Positive	2	2	2
Negative	3	3	5
Neutral (ties)	12	13	12
Total	17	18	19
	New Patients		
Positive	1	0	0
Negative	13	3	13
Neutral (ties)	6	14	4
Total	20	17	17

The analysis was repeated using subsets of the data based on whether the patient was new or existing (Table 3.3; Figure 3.6). Median (\pm interquartile range) NVA-LVA for existing patients was 0.19 logMAR at T0 (\pm 0.08 logMAR), T3 (\pm 0.00 logMAR) and T6 (\pm 0.02 logMAR). Figure 3.6 shows that the range in NVA-LVA was smaller for existing patients than new patients, reflecting the increased use of magnifiers among the existing patient group prior to T0. For new patients, median NVA-LVA increased from 0.40 \pm 0.32 logMAR at T0 to 0.19 logMAR at T3 (\pm 0.02 logMAR) and T6 (\pm 0.00 logMAR). A Friedman's two-way ANOVA by ranks test revealed that there were no significant differences among the NVA-LVA results for existing patients at the three visits (T0 to T6; $p=0.368$). For new patients, there was a significant (Intermediate Sign Test) median decrease of 0.10 logMAR between T0 and T3 ($p=0.005$) and 0.20 logMAR between T0 and T6 ($p=0.001$). Intervention by LVS between T0 and T3 resulted in an improvement in NVA-LVA in new patients.

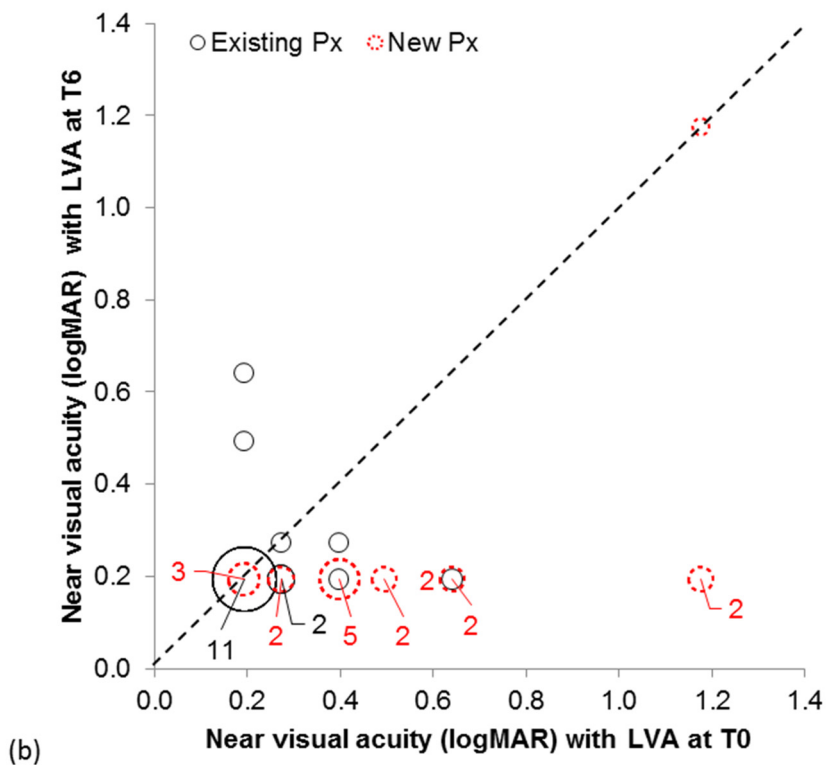
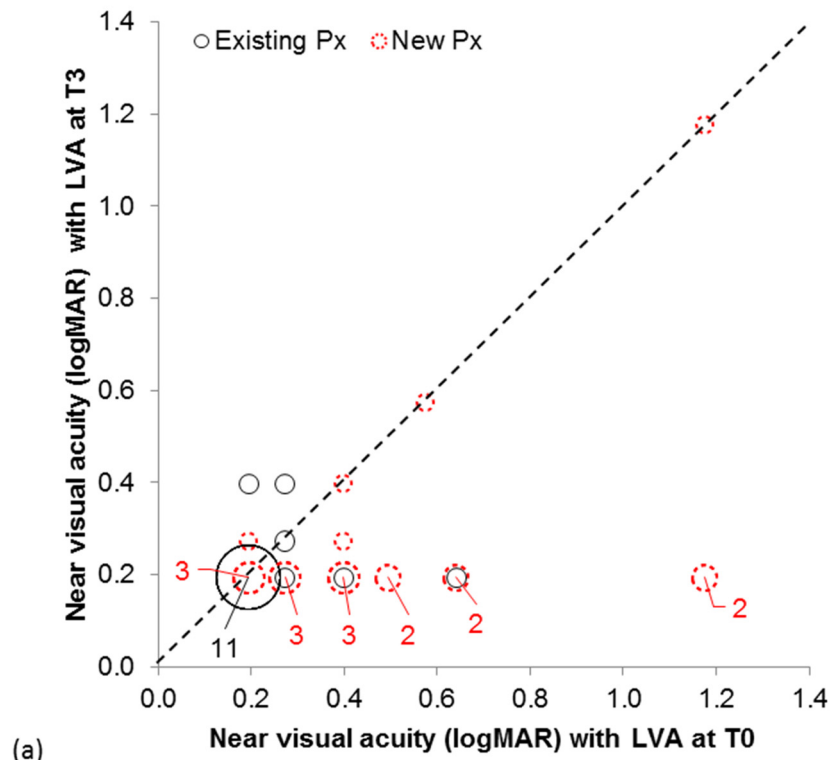


Figure 3.6 Comparison of binocular near visual acuity with a low vision aid (NVA-LVA) in logMAR for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker colour differentiates between existing patients (black, solid) and new patients (red, dashed). The marker area is proportional to the number of patients with visual acuities at the centre of the marker, which are also labelled (markers with no label represent single-patient acuity measurements). The black dashed line represents the line of equal acuity measurements at each visit (i.e. the 'line of no effect').

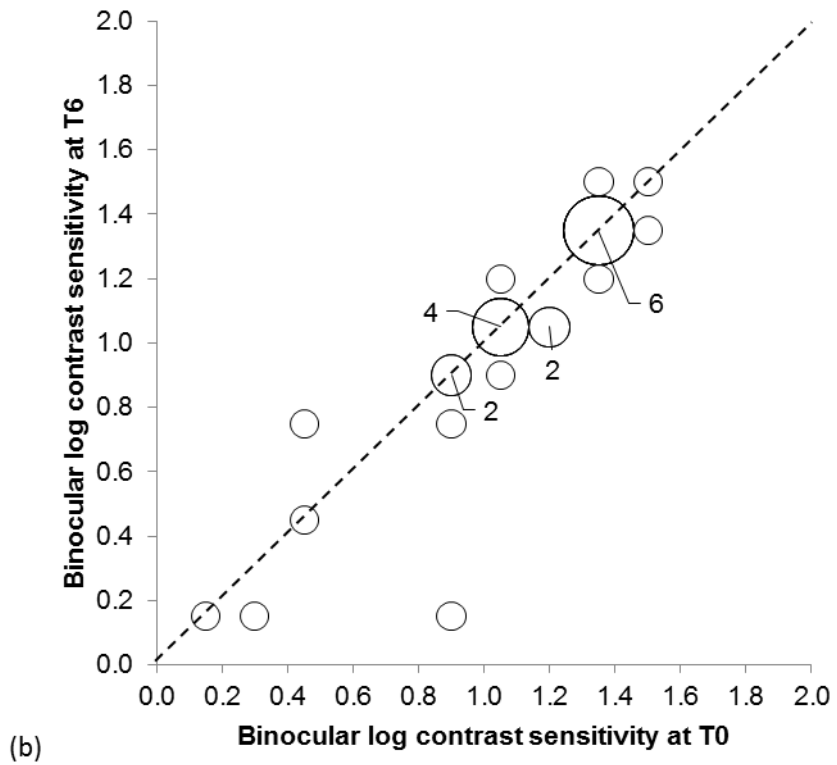
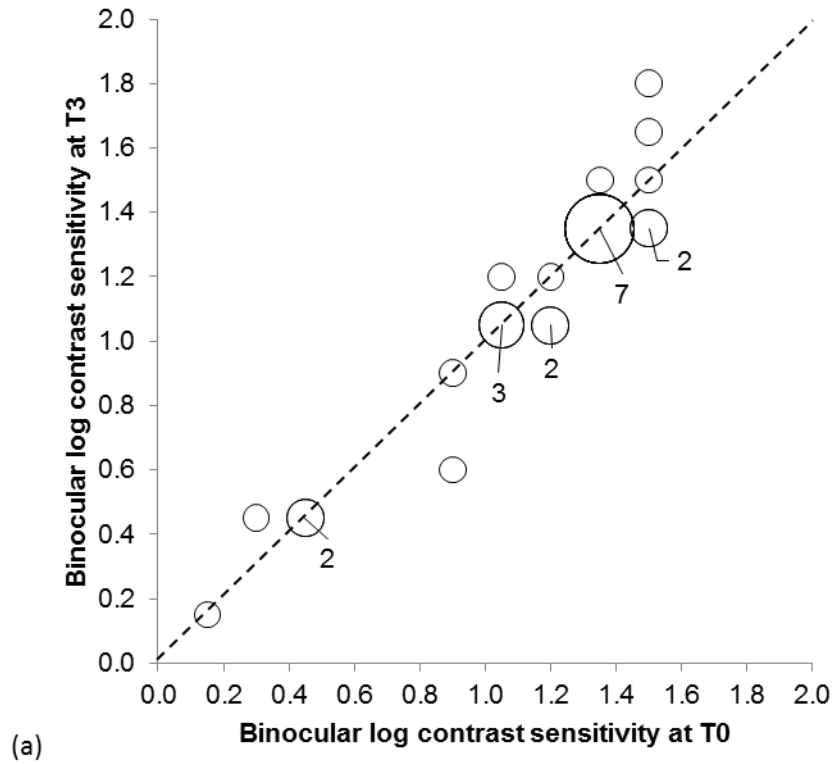


Figure 3.7 Comparison of binocular log contrast sensitivity for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with contrast sensitivity at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal measurements at each visit (i.e. the 'line of no effect').

3.1.5 Contrast sensitivity

Binocular distance contrast sensitivity was negatively skewed and not normally distributed for any visit (Shapiro-Wilk, $p=0.004$ to $p=0.014$). Figure 3.7 shows that the majority of patients are close to the line of no effect, i.e. patients with a high contrast sensitivity at T0, maintain a high contrast sensitivity at T3 and T6 (and vice-versa). Median (\pm interquartile range) log contrast sensitivity was 1.20 ± 0.30 at T0 and T3, and reduced to 1.05 ± 0.45 at T6. A related-samples Friedman's two-way ANOVA by ranks test revealed that there were no significant differences among the contrast sensitivity results for all three visits (T0 to T6; $p=0.216$).

There was no correlation between contrast sensitivity and DVA, NVA, or NVA-LVA visual acuity at the first (T0) and second (T3) visits (Spearman Rank Correlation, $p>0.05$ in all cases). At the six-month visit (T6), however, there were small but significant negative correlations between contrast sensitivity and both DVA ($r_s=-0.437$, $p=0.011$) and NVA-LVA ($r_s=-0.444$, $p=0.012$). The negative correlations observed at T6 are intuitive: as contrast sensitivity increases the visual acuity improves (logMAR decreases). Lord *et al.* (1991) found that in patients with a mean age of 83 years (similar to the 81.4 mean age for this study), both high and low contrast measures of visual acuity were correlated to Melbourne Edge Test contrast sensitivity measurements.

3.2 Low Vision Quality of Life Questionnaire

3.2.1 Data characterisation

At the initial visit (T0), the total LVQOL questionnaire score was normally distributed (Figure 3.8; Shapiro-Wilk, $p=0.102$, Table 3.4). At subsequent visits (T3 & T6), the total LVQOL score was not normally distributed (Shapiro-Wilk, $p>0.05$) and was negatively skewed (Figure 3.8, Table 3.4), which is indicative of an improvement in QoL. As it was not possible to transform the data (Table 3.4) non-parametric testing methods were employed.

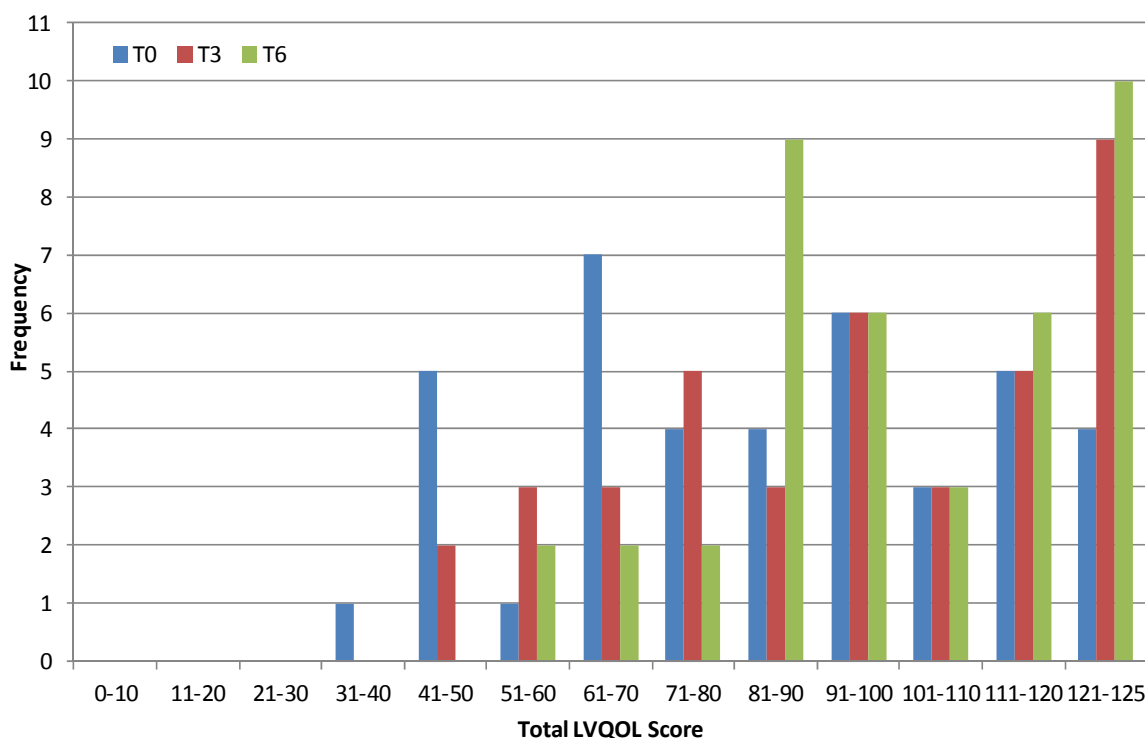


Figure 3.8 Frequency distribution of total Low Vision Quality of Life (LVQOL) score at the initial (T0), three-month (T3) and six-month (T6) visits.

Table 3.4 Comparison of total Low Vision Quality of Life (LVQOL) questionnaire score distribution to the normal distribution.

Visit	As measured		Square-Root Transform ¹		Logarithmic Transform ²	
	Skewness	Normal ³	Skewness	Normal ³	Skewness	Normal ³
T0	-0.121	p=0.102	-0.558	p=0.045	-1.542	p<0.0005
T3	-0.405	p=0.013	-0.185	p=0.024	-0.381	p<0.0005
T6	-0.417	p=0.018	-0.261	p=0.018	-0.952	p<0.0005

Notes:

1. Reflect and square root transformation for negatively skewed data.
2. Reflect and log₁₀ transformation for negatively skewed data.
3. The Shapiro-Wilk test was used to determine whether the distribution of measured data was significantly different from the normal distribution (p<0.05).

3.2.2 Analysis of total (overall) score

There was an increase in total (/125) LVQOL score for 26 of the 39 study patients between T0 and T3 (Figure 3.9a), with a reduced score for 10 patients and no change in score for three patients. This increased to 31 out of 40 patients with an increased total LVQOL score between T0 and T6 (Figure 3.9b), with a reduced score for eight patients and no change for one patient.

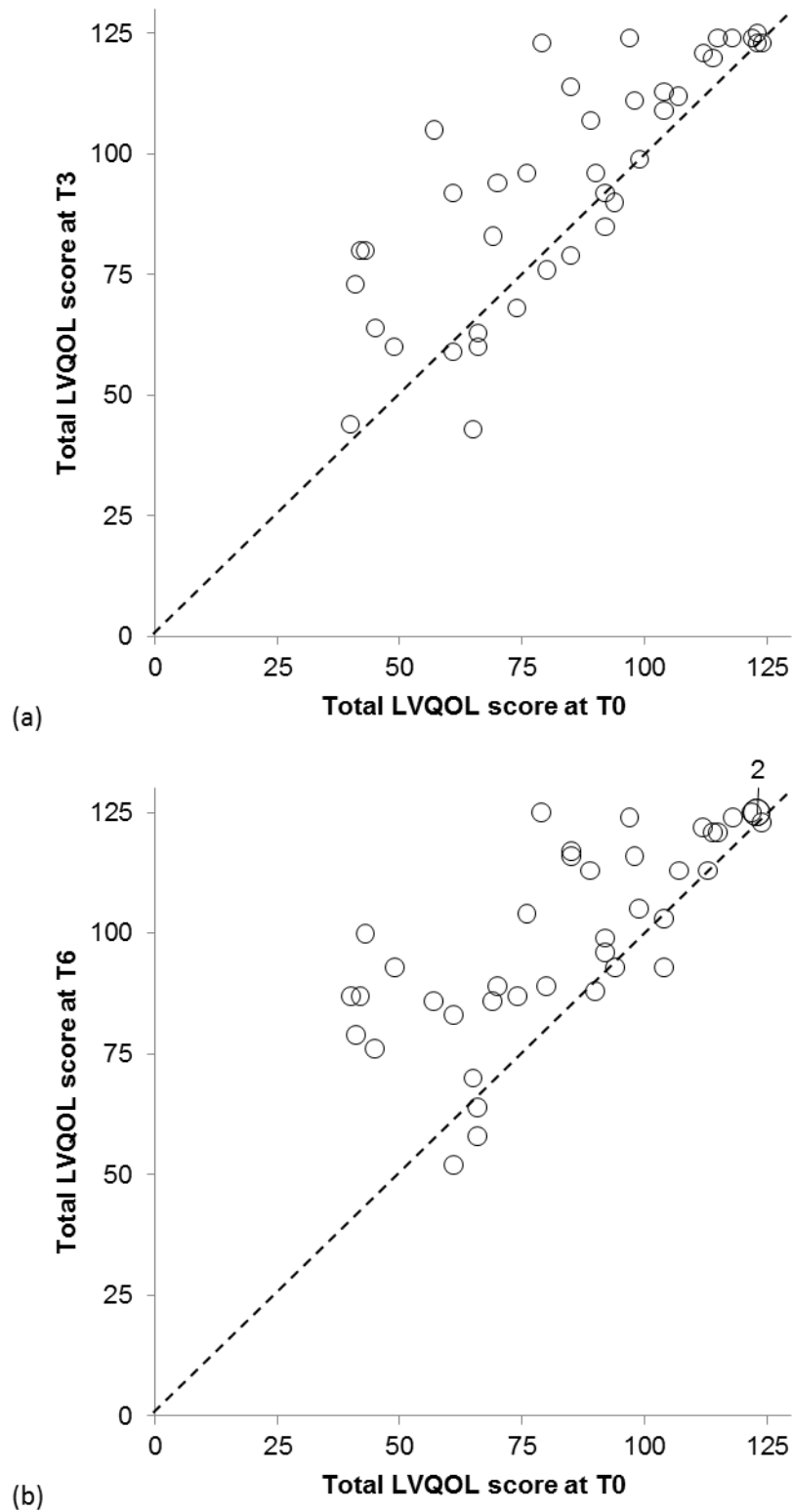


Figure 3.9 Comparison of total Low Vision Quality of Life (LVQOL) questionnaire scores for each patient between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with total LVQOL score at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal scores at each visit (i.e. the 'line of no effect').

The individual data points in each panel show the results for individual participants, while the diagonal line in each panel is the 'line of no effect' (i.e. equal score for both visits). Note that the data lie predominantly above the diagonal in Figure 3.9a and Figure 3.9b, indicating that individual patient scores increase from T0 to T3 and from T0 to T6.

Friedman's two-way ANOVA by ranks revealed a significant difference in the distribution of LVQOL data among visits T0, T3 and T6 ($p < 0.001$). Initially, the Related-Samples Wilcoxon Signed Rank Test was used to determine whether the median total LVQOL score was significantly different between paired samples at T0-T3, T3-T6 and T0-T6. Post-hoc examination of the differences between pairs revealed that these differences were not symmetrical and therefore Assumption 3 of the Wilcoxon Signed Rank Test (see Section 2.5.2) was not valid and the Paired-Samples Sign Test was used.

Median (\pm interquartile range) total LVQOL score increased from T0 (87.0 ± 39.0) to T3 (96.0 ± 44.0), a significant median increase of 6.0 ($p = 0.012$). Between T3 and T6, median (\pm interquartile range) total LVQOL score increased from 96.0 ± 44.0 to 99.5 ± 34.0 , with a significant median increase of 2.0 ($p = 0.007$). There was an increase in total LVQOL score for 26 patients, a decrease for nine patients and no change for four patients. There was no significant change in distance and near visual acuity (either with or without LVAs) during this same period.

The cumulative effect of interventions at T0 and other factors between T0 and T6 caused median (\pm interquartile range) total LVQOL score to increase from T0 (87.0 ± 39.0) to T6 (99.5 ± 34.0), a significant median increase of 8.0 ($p < 0.001$).

3.2.3 Comparison of existing and new patient scores

An effect of whether or not the patient is new to the clinic has already been observed in the visual acuity data (Section 3.1.4), and this factor was explored further in the LVQOL data. A mixed RMANOVA model was used to examine whether or not LVQOL scores for new patients were significantly different from those for existing patients. The assumptions of the two-way RMANOVA model were tested and were valid in all but one case (existing patients at T3; Shapiro-Wilk, $p = 0.041$).

While there was a significant interaction between the new / existing patient grouping and time (T0, T3, T6) on total LVQOL score ($p = 0.001$; Table 3.5), post-hoc analyses using the

Student t-test determined that there was no statistically significant difference in total LVQOL score between new and existing patients at T0 ($p=0.103$), T3 ($p=0.363$) and T6 ($p=0.923$).

For existing patients, there was a significant difference in total LVQOL scores between T0 and T3 ($p=0.031$) and between T0 and T6 ($p=0.006$), but not between T3 and T6 ($p=0.251$). For new patients, a significant difference was observed between T0 and T3 ($p=0.003$), T3 and T6 ($p=0.048$) and T0 and T6 ($p<0.001$).

There was a significant increase in mean total LVQOL score (6.8) for existing patients over the first three months but no significant difference after that. In new patients, a significant increase in mean total LVQOL score (13.9) occurred after three months, followed by a further significant increase of 8.2 between T3 and T6 (Table 3.5).

Table 3.5 Summary of mean (\pm standard deviation) total Low Vision Quality of Life (LVQOL) questionnaire score for existing and new patients at each visit (T0, T3, T6).

LVQOL score	Maximum Possible Score	Initial visit (T0)		Three-month visit (T3)		Six-month visit (T6)	
		Existing	New	Existing	New	Existing	New
<i>n</i>		20	20	19	20	20	20
Total	125	90.3 \pm 22.96 ^a	75.4 \pm 26.16 ^a	97.1 \pm 23.29 ^b	89.9 \pm 25.78 ^b	99.4 \pm 21.50 ^b	98.1 \pm 19.34 ^v

Note: superscript letters indicate significantly different sample means as determined by the Student t-test ($p<0.05$). Because there was no significant difference in total LVQOL score between new and existing patients at T0, T3 or T6 ($p\geq 0.05$), comparisons should not be made between groups with Latin and Greek alphabets.

3.2.4 The impact of living alone

Mean total LVQOL score at any particular visit (T0, T3, T6) for patients living alone ($n=20$) was normally distributed (Shapiro-Wilk, $p>0.05$) and was not significantly different from patients living with a partner / family ($n=19$; RMANOVA $p=0.999$, Table 3.6). The distributions of both the T3 and T6 LVQOL scores for patients not living alone were non-normal (Shapiro-Wilk, $p=0.010$ and $p=0.043$ respectively). The reflect and square-root transform was applied but the outcome of the RMANOVA was similar; there was no significant interaction between patients living alone or patients living with a partner / family ($p=0.571$). In brief, whether or not the patient lived alone was not significant in determining total LVQOL score at any visit.

Table 3.6 Summary of mean (\pm standard error) total Low Vision Quality of Life (LVQOL) questionnaire score for patients that live alone and not alone at each visit (T0, T3, T6).

LVQOL score	Maximum Possible Score	Initial visit (T0)		Three-month visit (T3)		Six-month visit (T6)	
		Alone	Not Alone	Alone	Not Alone	Alone	Not Alone
<i>n</i>		20	20	19	20	20	20
Total	125	82.5 \pm 5.86	85.4 \pm 6.01	92.9 \pm 5.59	95.8 \pm 5.73	98.1 \pm 4.60	100.8 \pm 4.72

3.2.5 Analysis of scores by questionnaire section

The LVQOL questionnaire can be split into four sections which relate to different aspects of a patient's life as follows:

- Section A – Distance Vision, Mobility and Lighting (12 questions, maximum score 60)
- Section B – Adjustment (4 questions, maximum score 20)
- Section C – Reading and Fine Work (5 questions, maximum score 25)
- Section D – Activities of Daily Living (4 questions, maximum score 20)

Table 3.7 and Figure 3.10 to Figure 3.13 show that as per the total LVQOL score, the distribution of scores in each section, at each visit, was non-normal (Shapiro-Wilk, $p < 0.05$; except for Section A at T0, $p = 0.112$) and negatively skewed (except for Section C at T0).

Table 3.7 Comparison of Low Vision Quality of Life (LVQOL) section score distribution to the normal distribution.

Visit	Section	Shapiro-Wilk	Skewness
T0	A	$p = 0.112$	-0.286
	B	$p = 0.002$	-0.577
	C	$p = 0.019$	0.118
	D	$p = 0.004$	-0.237
T3	A	$p = 0.006$	-0.256
	B	$p < 0.001$	-1.290
	C	$p = 0.001$	-0.706
	D	$p = 0.003$	-0.424
T6	A	$p = 0.006$	-0.405
	B	$p < 0.001$	-1.261
	C	$p < 0.001$	-1.166
	D	$p = 0.001$	-0.681

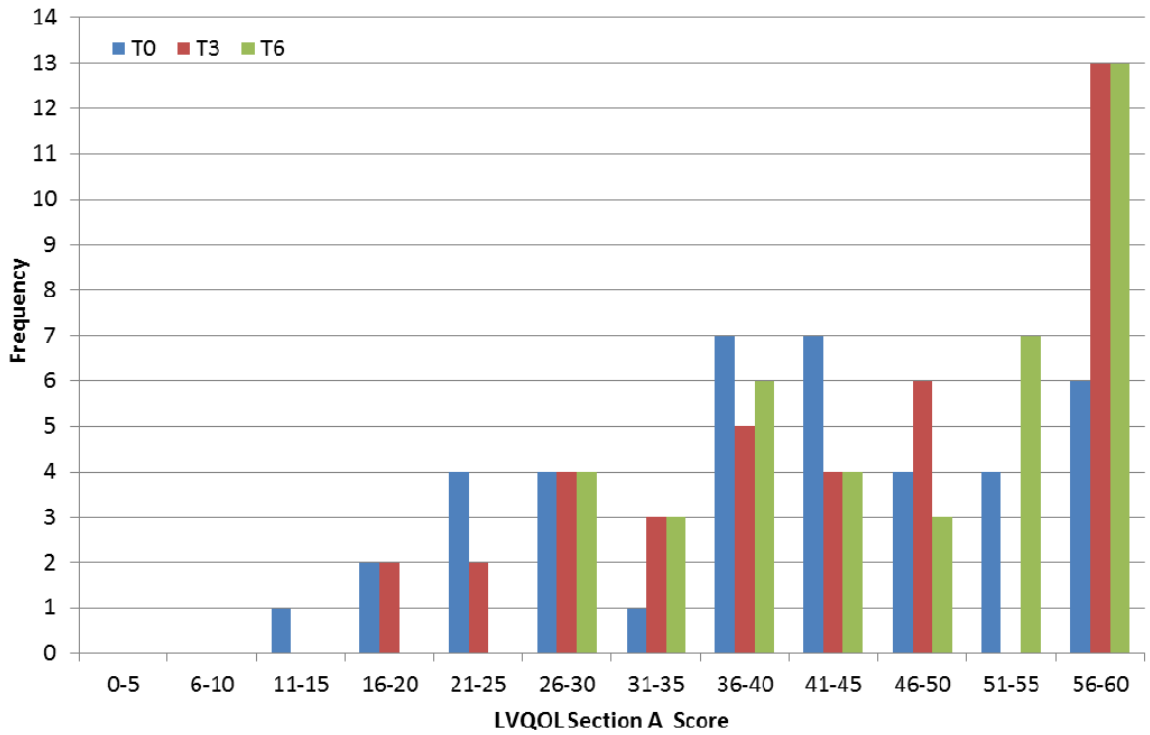


Figure 3.10 Frequency distribution of Low Vision Quality of Life (LVQOL) score for Section A at the initial (T0), three-month (T3) and six-month (T6) visits.

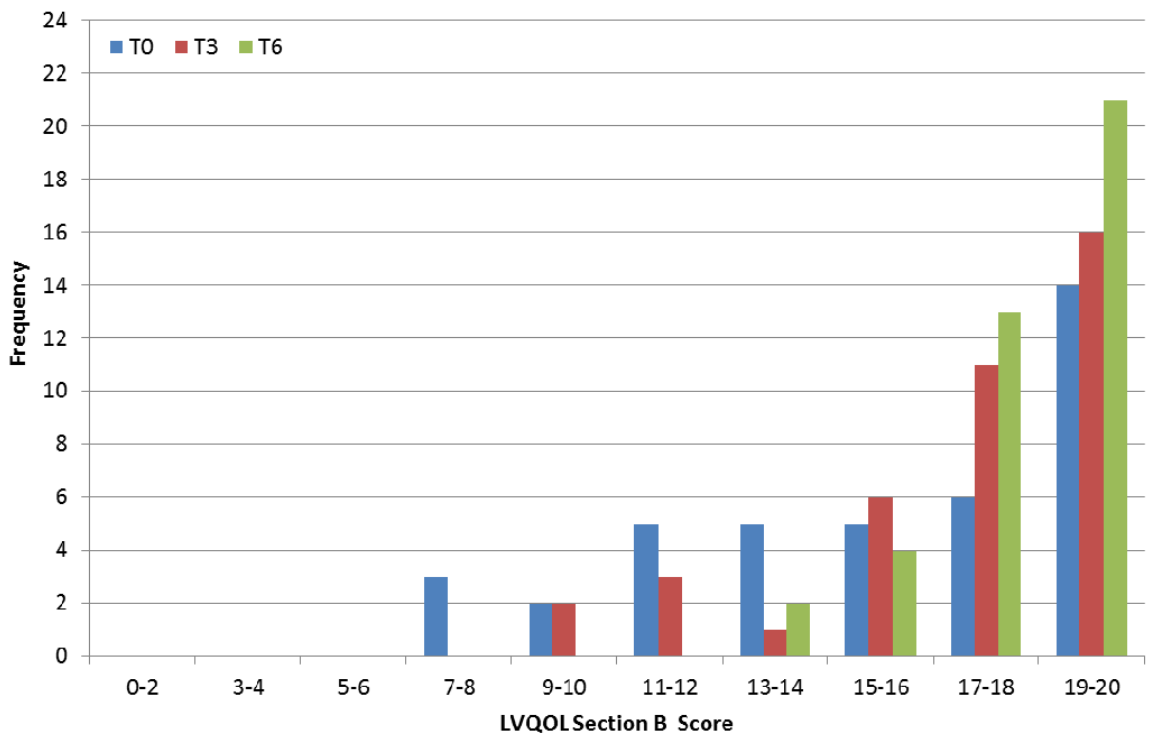


Figure 3.11 Frequency distribution of Low Vision Quality of Life (LVQOL) score for Section B at the initial (T0), three-month (T3) and six-month (T6) visits.

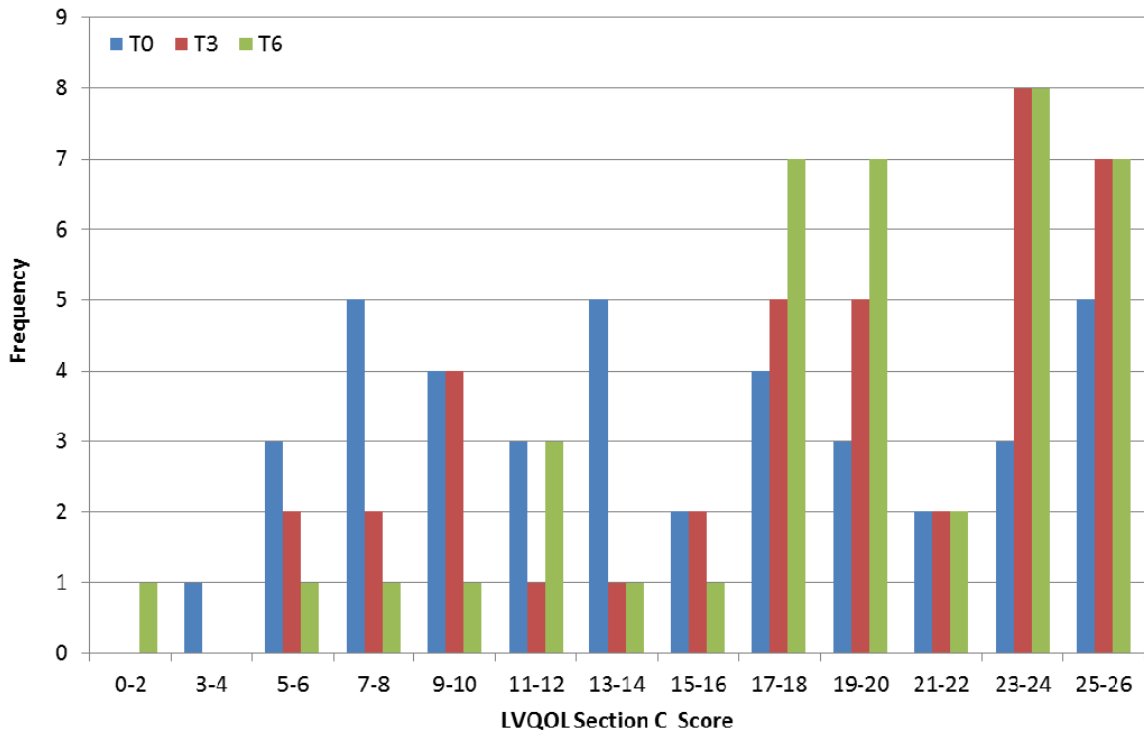


Figure 3.12 Frequency distribution of Low Vision Quality of Life (LVQOL) score for Section C at the initial (T0), three-month (T3) and six-month (T6) visits.

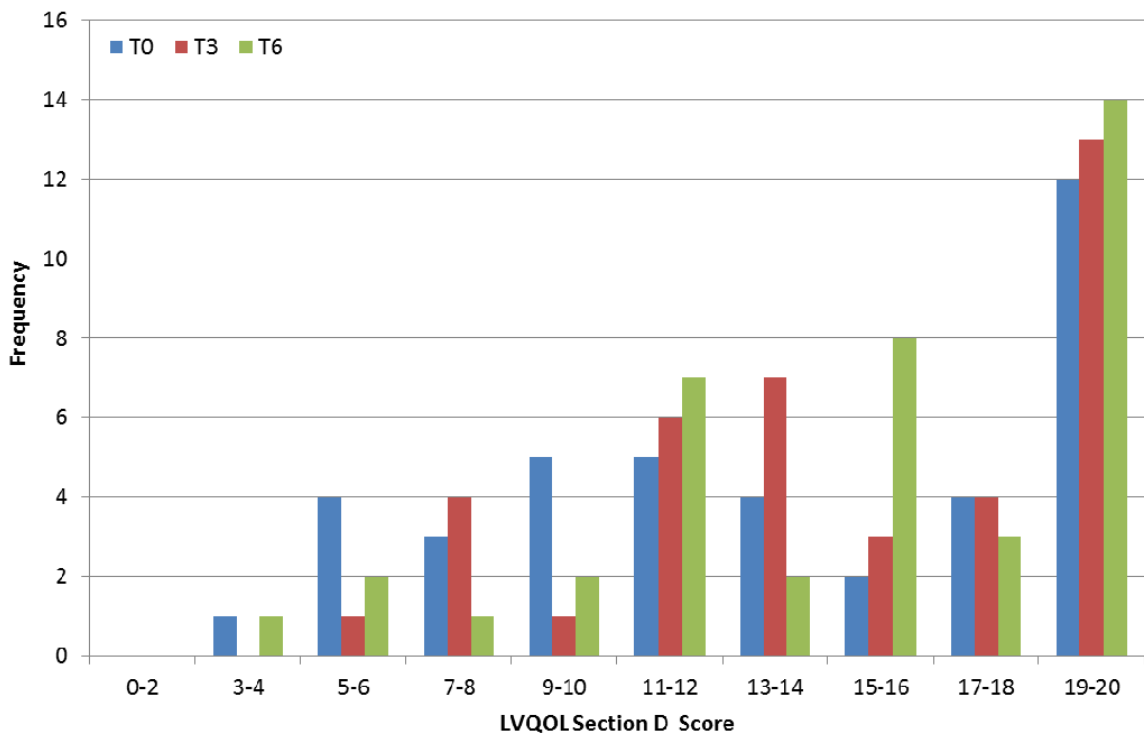


Figure 3.13 Frequency distribution of Low Vision Quality of Life (LVQOL) score for Section D at the initial (T0), three-month (T3) and six-month (T6) visits.

Table 3.8 shows the median (\pm interquartile range) LVQOL score for each section (A to D) and the total score at T0, T3 and T6. A Friedman's two-way ANOVA by ranks test determined that there were significant differences in LVQOL scores among the three visits in each section (A-C: $p < 0.001$, D: $p = 0.049$). The Intermediate Sign Test was used post-hoc to determine significant median differences in LVQOL score between visit pairs within each section (Table 3.9).

Table 3.8 Summary of median (\pm interquartile range) Low Vision Quality of Life (LVQOL) questionnaire score for each section (A – distance vision, mobility and lighting, B – adjustment, C – reading and fine work and D – activities of daily living) and in total at each visit (T0, T3, T6).

Section	Maximum Possible Score	Initial visit (T0)	Three-month visit (T3)	Six-month visit (T6)
<i>n</i>		40	39	40
A	60	42.0 \pm 21.0 ^a	45.0 \pm 23.0 ^b	48.0 \pm 19.0 ^c
B	20	16.0 \pm 7.0 ^a	18.0 \pm 4.0 ^b	19.0 \pm 2.0 ^c
C	25	14.0 \pm 12.0 ^a	19.0 \pm 10.0 ^b	19.0 \pm 7.0 ^b
D	20	14.0 \pm 10.0 ^a	15.0 \pm 8.0 ^a	16.0 \pm 8.0 ^a
Total	125	85.0 \pm 39.0 ^a	96.0 \pm 44.0 ^b	99.0 \pm 34.0 ^c

Note: superscript letters indicate where there is a significant ($p < 0.05$) median increase or decrease between LVQOL score among visits (T0, T3, T6) within each category as determined by the Intermediate Sign Test (Randles, 2001). Comparisons among section scores are not valid in this analysis, i.e. a median denoted *a*, in Section A should not be compared with a median denoted *b* in Section C.

Table 3.9 Intermediate Sign Test probability values when comparing between the initial visit (T0), the three-month visit (T3) and the six-month visit (T6).

Section	All Patients			Existing Patients			New Patients		
	T0-T3	T3-T6	T0-T6	T0-T3	T3-T6	T0-T6	T0-T3	T3-T6	T0-T6
A	0.002	0.008	<0.001	0.194	0.048	0.008	0.001	0.043	<0.001
B	0.062	0.038	0.001	0.537	0.153	0.059	0.016	0.069	0.004
C	0.006	0.568	<0.001	0.128	0.402	0.043	0.008	0.685	0.001
D	0.094	0.851	0.116	0.270	0.856	0.500	0.104	0.655	0.050

Figure 3.14 shows individual patient LVQOL section A scores at T0 plotted against LVQOL section A scores at T3 (a) and T6 (b). Note that in panel (a) results are clustered around the line of no effect, while in panel (b) the data are predominantly above the line of no effect indicating that there is a greater improvement in Section A scores between T0 and T6 than between T0 and T3. A similar pattern is observed in Section B (Figure 3.15). In both sections A and B (Table 3.8), median scores increased significantly at each visit (Intermediate Sign Test, $p < 0.05$).

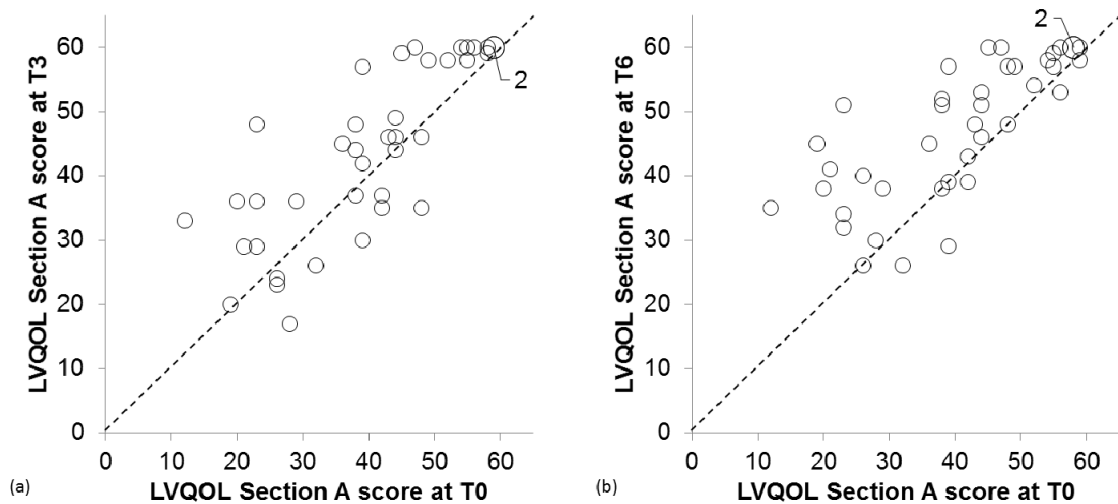


Figure 3.14 Comparison of Low Vision Quality of Life (LVQOL) score in Section A (distance vision, mobility and lighting) for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with scores at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal score at each visit (i.e. the 'line of no effect').

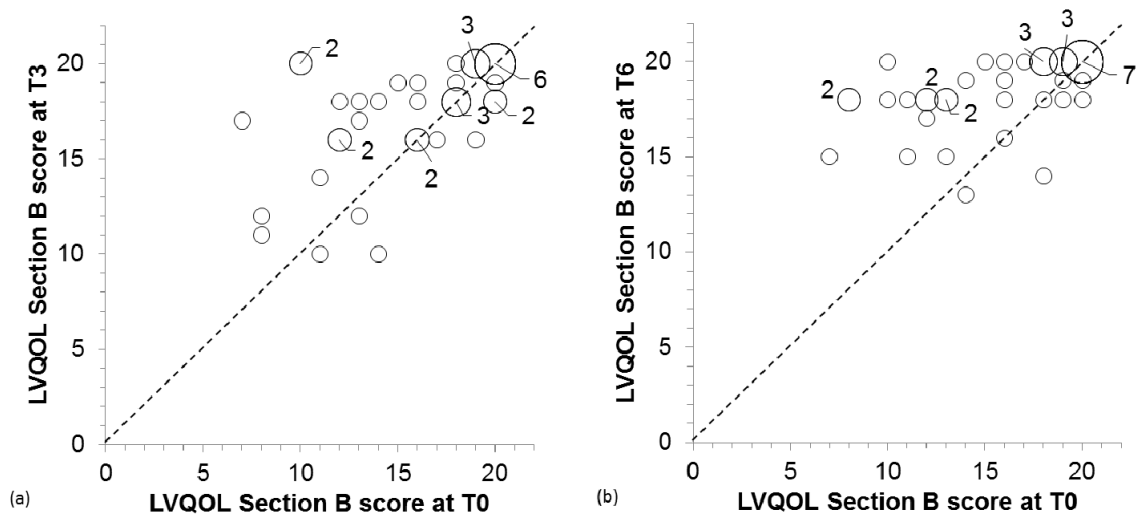


Figure 3.15 Comparison of Low Vision Quality of Life (LVQOL) score in Section B (adjustment) for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with scores at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal score at each visit (i.e. the 'line of no effect').

Figure 3.16 shows that in Section C, individual patient LVQOL scores are greater at T3 than T0 (panel a) but that scores do not appear to move further above the line of no effect at T6 (panel b). In Section C (Figure 3.16, Table 3.8, Table 3.9), there was a significant increase in median LVQOL score between T0 and T3 ($p=0.006$) but no further significant difference between visit T3 and T6 ($p=0.568$). In Section D (Figure 3.17, Table 3.8, Table 3.9), there

was no significant difference in median score among the three visits ($p \geq 0.05$) and this is shown in Figure 3.17 where data are distributed either side of the line of no effect.

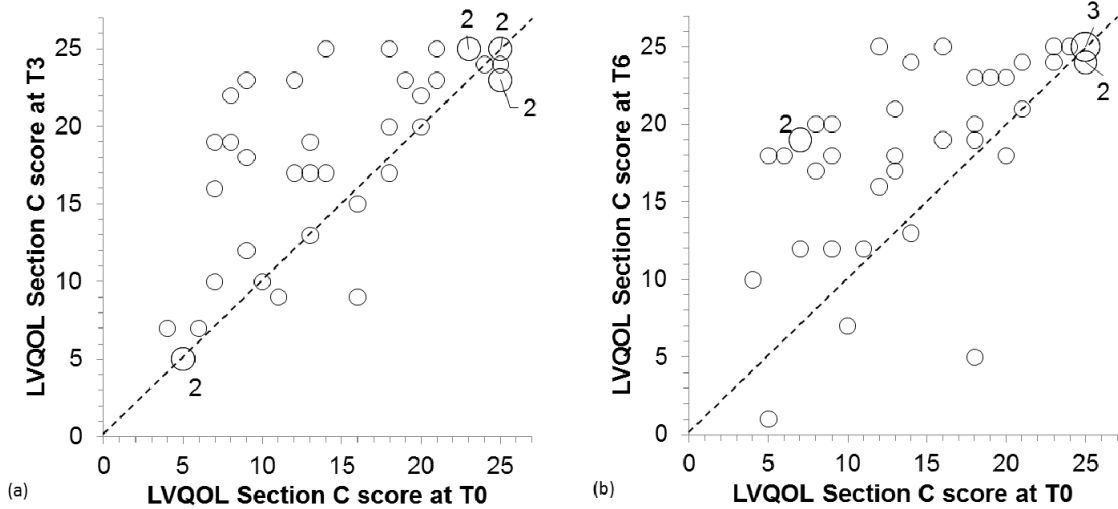


Figure 3.16 Comparison of Low Vision Quality of Life (LVQOL) score in Section C (reading and fine work) for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with scores at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal score at each visit (i.e. the 'line of no effect').

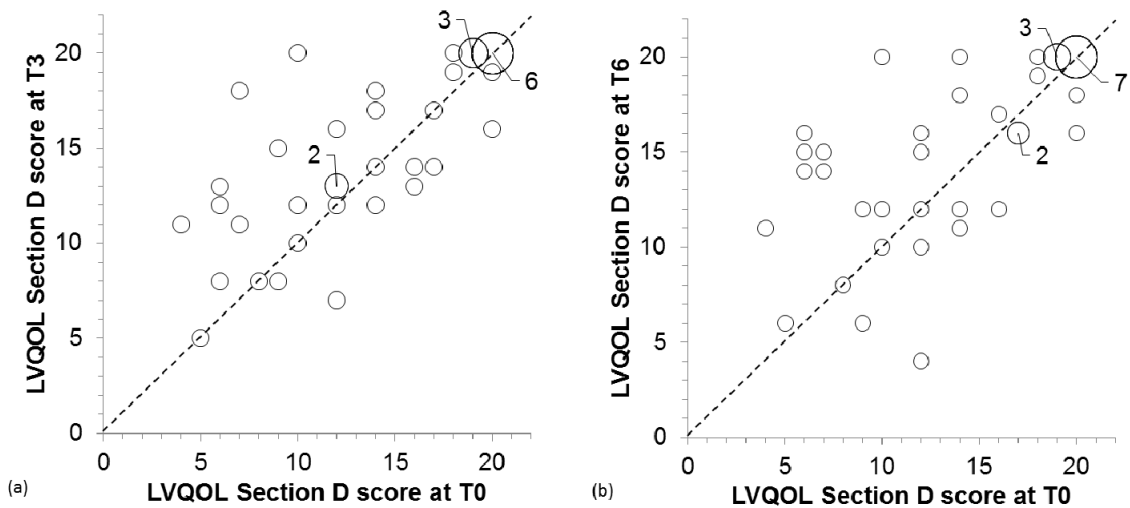


Figure 3.17 Comparison of Low Vision Quality of Life (LVQOL) score in Section D (activities of daily living) for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with scores at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal score at each visit (i.e. the 'line of no effect').

3.3 EuroQol Five-Dimension, Five-Level (EQ-5D-5L) Questionnaire

3.3.1 *Data characterisation*

Figure 3.18 shows that the total EuroQol five-dimension, five-level (EQ-5D-5L) score was positively skewed and non-normally distributed at T0, T3 and T6 (Figure 3.18, Table 3.10), indicating a bias towards lower scores (greater general-health related QoL).

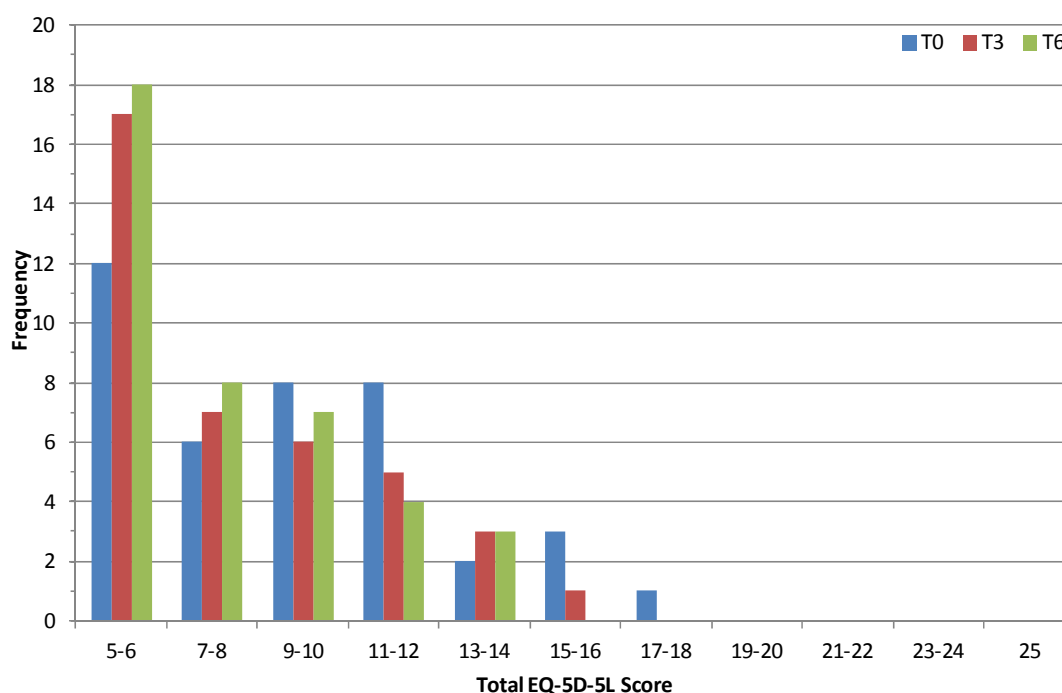


Figure 3.18 Frequency distribution of total EuroQol five-dimension, five-level (EQ-5D-5L) score at the initial (T0), three-month (T3) and six-month (T6) visits.

Table 3.10 Comparison of total EuroQol five-dimension, five-level (EQ-5D-5L) score distribution to the normal distribution.

Visit	As measured		Square-Root Transform ¹		Logarithmic Transform ²	
	Skewness	Normal ³	Skewness	Normal ³	Skewness	Normal ³
T0	0.346	p=0.013	0.103	p=0.015	-0.120	p=0.009
T3	0.722	p<0.001	0.526	p=0.001	0.343	p=0.001
T6	0.711	p<0.001	0.508	p=0.001	0.319	p=0.001

Notes:

1. Square root transformation for positively skewed data.
2. Log₁₀ transformation for positively skewed data.
3. The Shapiro-Wilk test was used to determine whether the distribution of measured data was significantly different from the normal distribution (p<0.05).

3.3.2 Analysis of total (overall) score

There was a decrease (improvement) in total (minimum 5 to maximum 25) EQ-5D-5L score for 18 of the 40 study patients between T0 and T3 (Figure 3.19a), and for 23 of the 40 patients between T0 and T6 (Figure 3.19b).

Median (\pm interquartile range) total EQ-5D-5L score decreased from T0 (9 ± 6) to T3 (7 ± 5). Of the 39 patients analysed, there was a decrease in EQ-5D-5L score at T3 for 18 patients, an increase for six patients, however 15 (37.5%) patients showed no change in score. The Intermediate Sign Test revealed that the median difference between scores at T0 and T3 was zero and not significant ($p=0.084$). A similar effect was observed between T3 and T6 where median EQ-5D-5L score increased from 7 ± 5 to 8 ± 4 (15 patients reduced their score, 8 patients increased their score and there were 16 ties), but there was not a significant median difference ($p=0.369$). Median EQ-5D-5L score decreased from T0 (9 ± 6) to T6 (8 ± 4), (23 decreased score, 5 increased score and 12 tied), a median difference that was significant (Intermediate Sign Test, $p=0.005$).

Analysis investigated whether there was a correlation between total LVQOL score and total EQ-5D-5L score. Figure 3.20 shows that generally as LVQOL score increased, EQ-5D-5L score decreased but there was significant variation about this trend. Over all three visits the Spearman's Rank Correlation coefficient between total LVQOL score and total EQ-5D-5L score (Figure 3.20) was $r_s=-0.476$, $p<0.001$. Correlation coefficients at each visit were: $r_s=-0.563$, $p<0.001$ (T0); $r_s=-0.496$, $p=0.001$ (T3); and $r_s = -0.312$, $p=0.050$ (T6).

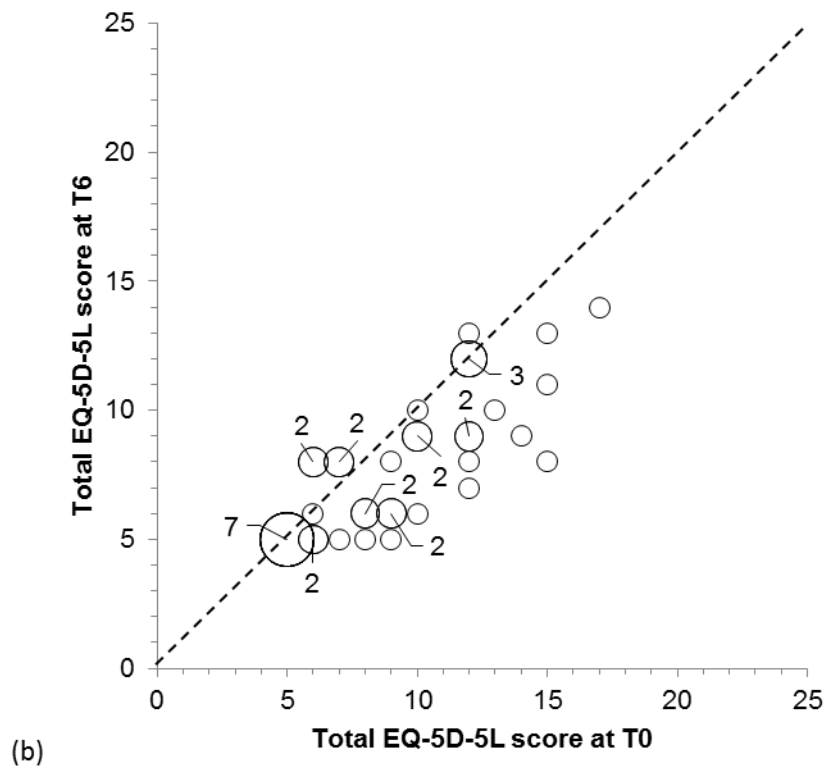
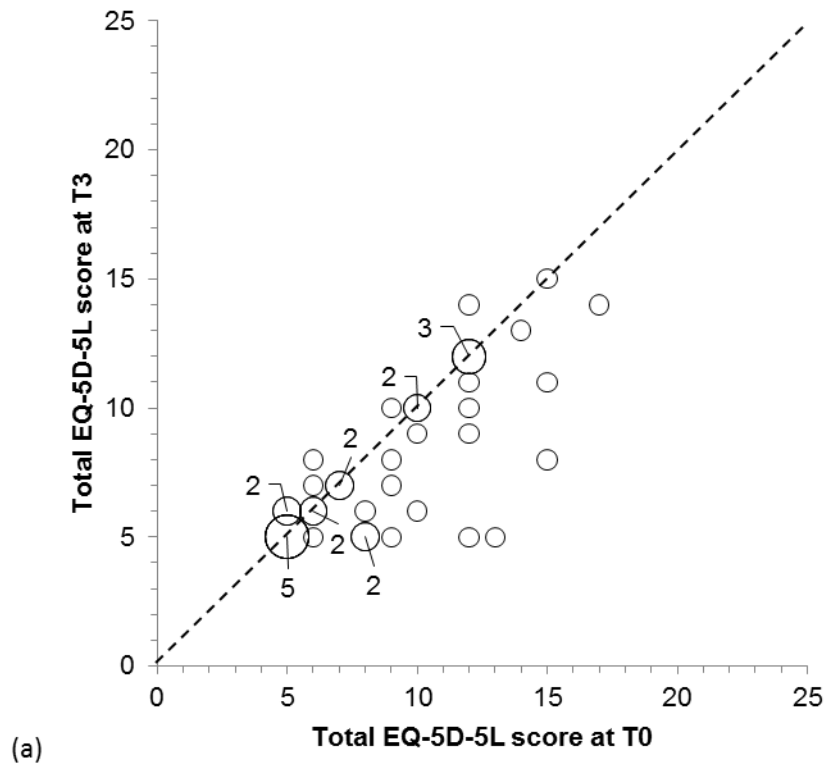


Figure 3.19 Comparison of total EuroQol five-dimension, five-level (EQ-5D-5L) score for each patient, between: (a) the initial (T0) and three-month (T3) visits; (b) the initial (T0) and the six-month (T6) visits. The marker area is proportional to the number of patients with scores at the centre of the marker, which are also labelled (markers with no label represent single-patient measurements). The dashed line represents the line of equal score at each visit (i.e. the 'line of no effect').

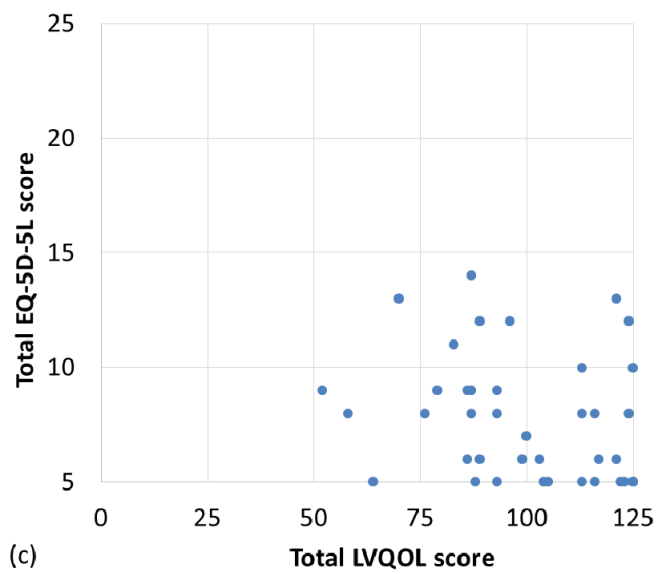
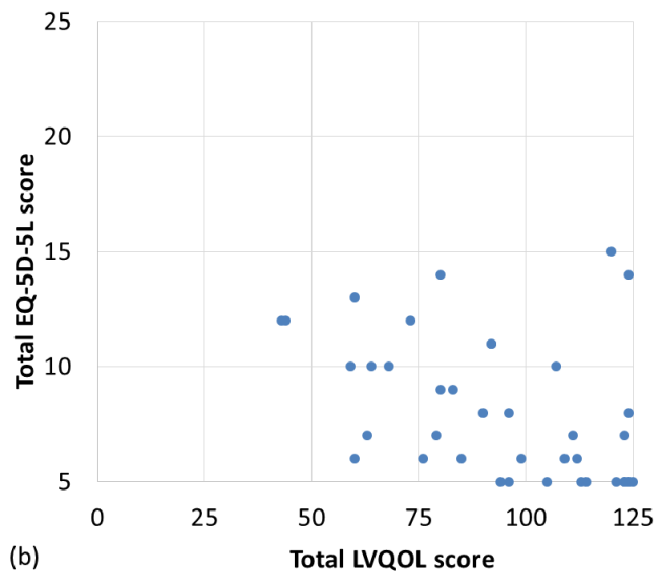
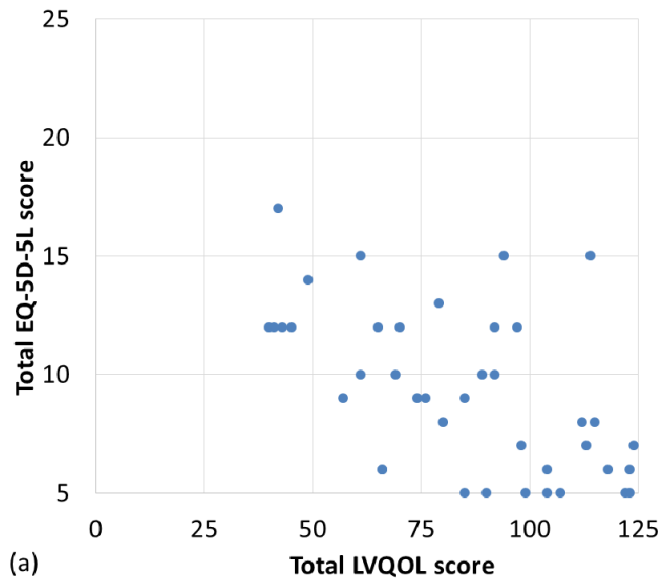


Figure 3.20 Plot of total Low Vision Quality of Life (LVQOL) score (/125) against total EuroQol five-dimension, five-level (EQ-5D-5L) general health-related quality of life score (/25) at the (a) initial (T0), (b) three-month (T3) and (c) six-month (T6) visits.

3.3.3 EuroQol visual analogue scale (EQ-VAS)

The distributions of the EQ-VAS scores (Figure 3.21) were non-normal (Shapiro-Wilk, $p < 0.05$), negatively skewed at each visit and were not significantly different among visits (Friedman's two-way ANOVA by ranks, $p = 0.662$).

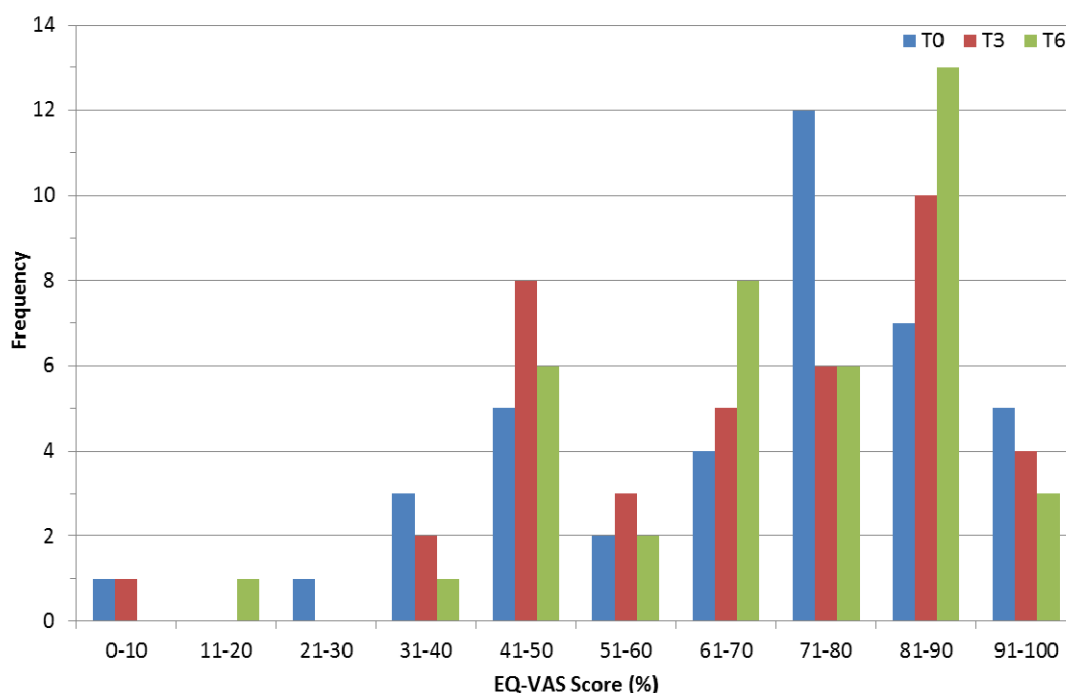


Figure 3.21 Frequency distribution of the EuroQol visual analogue scale (EQ-VAS) score at the initial (T0), three-month (T3) and six-month (T6) visits.

3.4 Relationship Between Visual Acuity and Quality of Life Questionnaire Scores

Examination of the Spearman Correlation coefficients in Table 3.11 reveals that there was no significant correlation between total EQ-5D-5L score and any measure of visual acuity using the Spearman Rank Correlation method, whether overall or at a particular visit. This is evident in the wide spread of data shown in the various panels in the right-hand column of Figure 3.22 which shows the relationship between each of the three measurements of acuity (DVA, NVA, NVA-LVA) and the QoL questionnaire scores (LVQOL, EQ-5D-5L).

Total LVQOL score was negatively correlated with measures of visual acuity (Table 3.11). Correlation coefficients increased from NVA-LVA ($r_s = -0.456$, $p < 0.01$), to NVA ($r_s = -0.549$, $p < 0.01$), to DVA ($r_s = -0.599$, $p < 0.01$). For each measure of acuity, correlation coefficients increased with each visit, except for NVA-LVA where there was no significant correlation at T6 (Table 3.11).

Table 3.11 Spearman's rank correlation coefficients (r_s) for total Low Vision Quality of Life (LVQOL) and total EuroQol five-dimension five-level (EQ-5D-5L) scores against distance visual acuity (DVA), near visual acuity (NVA) and near visual acuity with low vision aid (NVA-LVA). Significant correlations are denoted as significant at the $p < 0.01$ level (**) and at the $p < 0.05$ level (*).

Visit	Spearman's Rank Correlation Coefficient (r_s)		
	DVA	NVA	NVA-LVA
		LVQOL	
T0	-0.571**(1)	-0.500**	-0.487**
T3	-0.608**	-0.522**	-0.381*
T6	-0.743**	-0.643**	-0.298
All	-0.599**	-0.549**	-0.456**
		EQ-5D-5L	
T0	0.113	<0.001	0.187
T3	0.154	0.046	0.007
T6	0.156	-0.059	-0.004
All	0.133	-0.001	0.130

Notes:

1. Pearson correlation coefficient as these two datasets are normally distributed (Shapiro-Wilk test, $p > 0.05$).

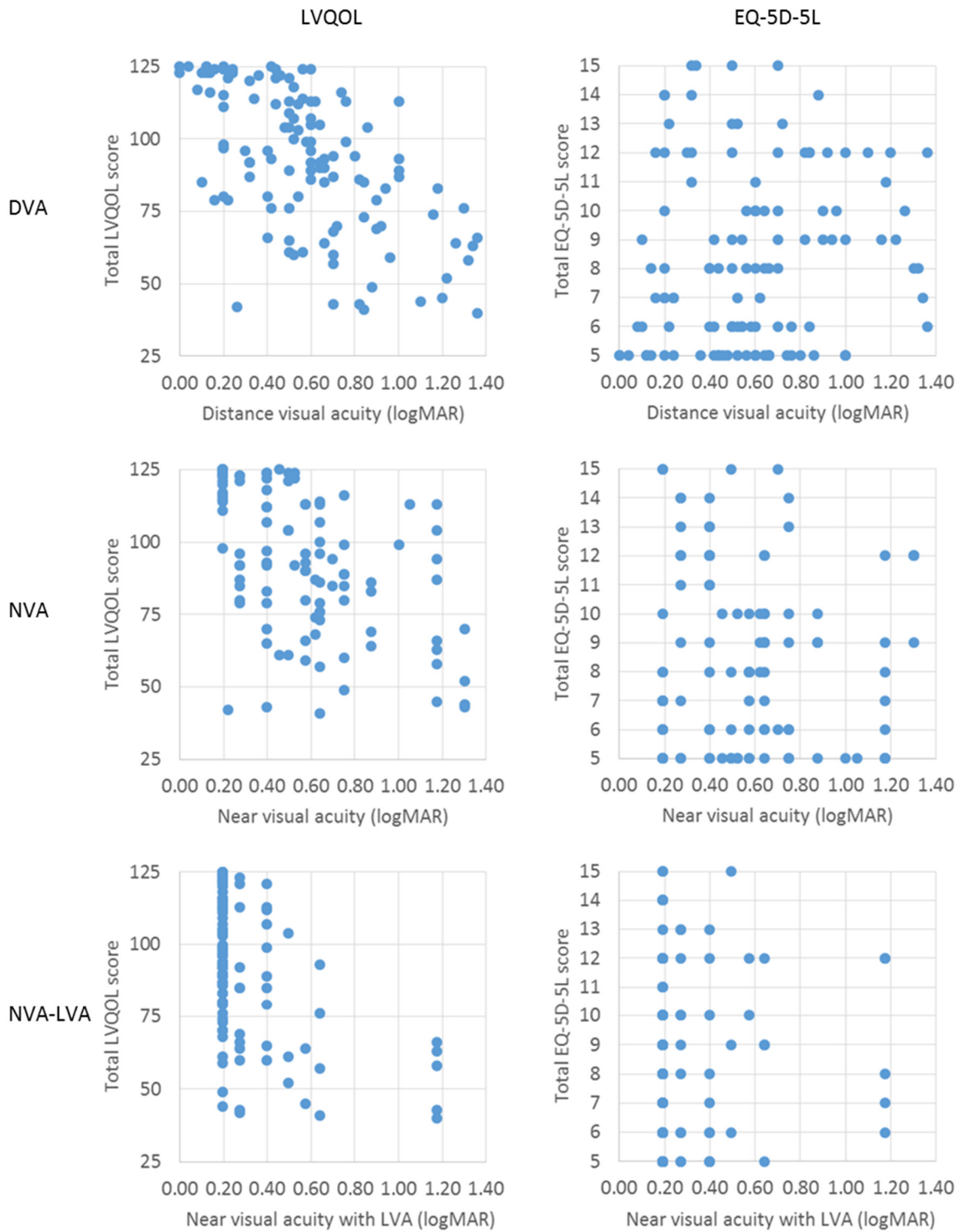


Figure 3.22 Total Low Vision Quality of Life (LVQOL) score (left) and total EuroQol five-dimension, five-level (EQ-5D-5L) score (right) in relation to distance visual acuity (DVA, top), near visual acuity (NVA, middle) and near visual acuity with low vision aid (NVA-LVA bottom).

4 DISCUSSION

4.1 Discussion of Results

4.1.1 Low vision services and quality of life

Over a six-month study period, intervention by LVS through the LV Clinic at MKUH had a significant positive impact upon patient reported quality of life (QoL). The median (\pm interquartile range) total LVQOL score increased from 87.0 ± 39.0 at the initial (T0) visit to 96.0 ± 44.0 at the three-month (T3) visit ($p=0.012$), and again to 99.5 ± 34.0 at the six-month (T6) visit ($p=0.007$). On this basis the null hypothesis $\{H_{0(A)}: \text{LVS at MKUH have no effect on the QoL of patients with ARMD}\}$ is rejected and the alternative hypothesis $\{H_{1(A)}: \text{LVS at MKUH improve the QoL of patients with ARMD}\}$ is accepted.

Potential mechanisms for this improvement in QoL are an improvement in visual acuity and / or the impact of rehabilitation, as these are the two principal outcomes from LVS. A third mechanism is an improvement in wider general health QoL that is related to improvement in co-morbidities, and this is discussed further in Section 4.2. The use of LVAs provided by the LV clinic significantly improved NVA, although for the complete dataset ($n=40$) this improvement was only significant over the six month period (T0 to T6, $p=0.011$). Differences between the initial and three-month visits (T0 to T3), and three and six-month visits (T3 to T6) were not significant due to the large numbers of neutral pairs where visual acuity remained stable.

Whilst there was a significant increase in median LVQOL score between T3 and T6 ($p=0.007$), there was no significant change in DVA, NVA or NVA-LVA during the same period. Therefore the improvement in LVQOL score between T3 and T6 could be a function of the rehabilitation mechanism, providing that an improvement in general health-related QoL can be excluded.

The increase in LVQOL score between T0 and T3 is in contrast to Wolffsohn *et al.* (2000), who assessed patients with a range of conditions causing LV and found a reduction (although not significant) in QoL scores after three months. Note that Wolffsohn and Cochrane (2000) reported a mean (\pm SD) total LVQOL score of 60.8 ± 27.8 prior to attendance at an LV clinic for the first time and 68.5 ± 28.0 post-attendance (time period not reported, $n=278$). These scores are significantly lower than those obtained here. ARMD-specific mean totals in Wolffsohn *et al.* (2000) were $65.1 (\pm 23.1)$ pre- and 71.7 ± 22.8 post-rehabilitation. De Boer *et al.* (2006) also published LVQOL scores comparing pre- and post-attendance at LV clinics. However their data were transformed and they did not provide

sufficient information to enable conversion back to the 0-125 total score range used in this study.

The current study comprised patients exhibiting different classifications and stages (early or late) of ARMD, in either one or both eyes. These different forms of the disease did not impact significantly upon visual acuity (DVA / NVA, binocularly or monocularly) or contrast sensitivity measurements over the six-month period. This may be a reflection of the greater number of study patients with geographic atrophy (GA), the slower progressing form of the disease (Sunness, 1999). Binocularly or monocularly, there were 22 patients with GA only and 10 patients with exudative ARMD only (Table 2.1). It was not possible to determine a significant difference in QoL scores between patients with GA and exudative ARMD because of this imbalance in sub-sample size. As highlighted by Bennion *et al.* (2012), research that separated the QoL of patients with different types, stages and treatability of ARMD would be beneficial. This also applies to the length of time that a patient has been living with ARMD prior to intervention and the rate of vision loss. To analyse these factors fully would require a larger study(ies), with an equal number of patients recruited to each sub-type, time to intervention and rate of vision loss.

Analysis of scores within each of the four sections of the LVQOL questionnaire revealed that there were significant differences in median score among the three visits in Section A (distance vision, mobility and lighting), Section B (adjustment), and Section C (reading and fine work). The median total LVQOL questionnaire scores for Section A increased significantly between T0 and T3 ($p=0.002$), and between T3 and T6 ($p=0.008$; Table 3.9). As the 12 questions within this section refer to issues surrounding glare, mobility and distance vision, rather than near vision, they are less likely to be influenced by LVA provision and more likely to be influenced by advice and / or equipment given during the LV clinic assessment (e.g. provision of glare shields, advice on repositioning the television). The impact of rehabilitation from external services such as SARC would also be expected to improve patient QoL in these areas, particularly if a patient was to receive mobility training and therefore regain greater independence outside of the home. This is illustrated by patient testimonials, see Appendix 2.4, but for example:

‘I’ve not been out on my own since October 2013’ (reported April 2014).

‘I go out with my husband – always’.

‘I never go out alone’.

It is difficult to attribute the continued increase in score for Section A purely to LV assessment or rehabilitative services; it is likely to be due to a combination of both.

Section B of the LVQOL questionnaire considered the impact of a patient's adjustment to their visual loss. The median total LVQOL questionnaire scores for this section increased significantly between T0 and T6 ($p=0.001$) and between T3 and T6 ($p=0.038$), but not between T0 and T3 ($p=0.062$; Table 3.9). As three of the four questions relate to patient frustration, unhappiness and restriction in visiting friends and family, a number of factors could be involved in the observed increase in score. LV clinic assessment allows patients the chance to discuss (for perhaps the first time) with a professional, their feelings towards the loss of vision though ARMD. Although patients will have received the diagnosis in a previous visit to the consultant or specialist doctor, this may have been unexpected and by the time the patient attends for LV assessment they may have many (as yet unanswered) questions. Discussion of the eye condition, reassurance, and referral to the ECLO for further emotional support may therefore help the patient adapt to living with their sight loss but this adaptation could take longer than three months for some patients. Furthermore, the time between diagnosis and initial LV clinic assessment is of importance, particularly for new patients. This could not be evaluated in the current study as new patients attended for the initial visit at various time points following diagnosis, and may have previously attended multiple doctor's clinics beforehand. Other factors such as poor general health or loss of a partner may also impact on the patient's ability to adapt to their loss of vision, for example see patient testimonials in Appendix 2.4, such as:

'Hearing impairment makes it harder'.

'My hearing is also an issue'.

The five questions in Section C (reading and fine work) related to areas that require good near visual acuity (e.g. reading letters and mail, reading labels). Therefore the observation that the median total Section C score increased significantly between T0 (14) to T3 (19) ($p=0.006$; Table 3.9) is likely to reflect the issuing of LVA(s) at the initial visit to assist these tasks and the significant improvement in NVA-LVA observed during the same period. This increase in acuity between T0 and T3 was the largest proportional increase (20%) between two visits over three months for any section. Wolffsohn and Cochrane (2000) also observed the most improved scores within this section of the LVQOL questionnaire. Together, the results from both studies indicate that reading skills / fine work is one area whereby significant improvements can be made to patient QoL and daily living skills (e.g. reading prices when shopping and maintaining correspondence), from attendance at the LV clinic. For example see patient testimonials in Appendix 2.4, such as:

'I have no problems if I use a magnifier'.

'With magnifier it is better'.

'The magnifier has made a huge impact on my vision'.

There was no change in score between the three (19) and six-month (19) visits ($p=0.568$; Table 3.9). By visit two (T3), the majority of patients had adapted well to the use of LVA(s), achieving their maximum possible NVA-LVA and therefore no further impact could be made on QoL scores at the third visit (T6).

Section D (activities of daily living) scores did not change significantly over time ($p\geq 0.05$; Table 3.9) and questions in this section do not appear to be sensitive to the effects of LV clinic input. There is a greater variation in Section D scores among patients: interquartile range among visits is between 8 and 10, *c.f.* Section B (which also has four questions) with interquartile ranges of 2 to 7 (Table 3.8, Figure 3.15 & Figure 3.17). One reason for these observations is that only one of the four questions (reading your own hand writing) is assisted by the provision of LVA(s). While advice is issued to make the remaining three tasks easier (finding out the time, writing, and everyday activities), no specific equipment is provided by the clinic to complete these activities. In the author's experience, although advice may be issued on where to purchase large numeric / digital talking watches and clocks to assist with determining the time, this has often not been followed when questioned at the next clinic visit. The question relating to household chores is broad and covers a wide range of tasks. When asked this question, some patients reported that family came in to do specific tasks (e.g. ironing), whilst others employed a cleaner / gardener. Within the LV clinic, limited advice is given to address any particular problem mentioned by the patient, however access to rehabilitation services is an important factor in improving QoL in this area. A rehabilitation assessment within the patient's home is more likely to focus on specific problems, whilst equipment can also be provided or recommended.

4.1.2 Is it possible to identify a subgroup or subgroups of patients with age-related macular degeneration that benefit more from low vision services than others?

Analysis of the total sample of patients is potentially misleading. New patients had a greater increase in mean quality of life score between T0 and T3 (14.5, $p=0.003$) than existing patients (6.8, $p=0.031$; Table 3.5). Mean total LVQOL scores for new patients are 12.7 and 23.3 greater than those in the Wolffsohn and Cochrane (2000) study at T0 and T3, respectively. The difference between new and existing patient scores in this study was related to a significant improvement in QoL from the initial prescription of LVAs to new patients, which resulted in an improvement in NVA from 0.40 ± 0.32 logMAR at T0 to 0.19 ± 0.02 logMAR at T3 ($p=0.005$). In the author's experience, most new patients attend for

the first time with either no form of LVA, or an LVA that is sub-optimal (e.g. one that had been inherited from a family member). Existing patients were already benefitting from optimised LVA provision and this was illustrated with no significant change in NVA-LVA among T0, T3 and T6 for this subgroup.

New patients had a significant increase in total LVQOL score from T0 to T3 and from T3 to T6. Existing patients did exhibit significant increases in LVQOL score between T0 and T3 ($p=0.031$), and T0 and T6 ($p=0.006$) but not between T3 and T6 ($p=0.251$). The initial (T0-T3) increase in QoL score for existing patients cannot be attributed to the improvement in NVA-LVA mechanism discussed above; i.e. significant increases in LVQOL score between T0 and T3 are likely explained by different mechanisms for new patients than for existing patients. Of the 20 existing patients, for 15 patients T0 was only their second visit to the LV Clinic. Therefore for 15/20 existing patients, the increase between T0 and T3 is equivalent to the increase observed between T3 and T6 for new patients. Patients are exhibiting an increase in QoL for the first six months but at periods greater than this, there is no statistical evidence for an improvement in QoL in this study. On an individual patient basis however, this will depend on the rate of disease progression. The implications of these findings on clinic follow-up times are discussed further in Section 4.1.3.

Patient recruitment in this study was not specifically designed to achieve an equal distribution of new and existing patients. Further studies could standardise for the length of time a patient has spent within LVS, particularly if these studies were carried out over a longer period and / or multiple hospitals.

Although existing patients presented with a higher QoL score at T0 compared with new patients, there was no statistically significant difference in LVQOL score between the two groups. Patients who have already attended clinic should have optimised LVAs but are living with a debilitating untreatable disease and might have been doing so for a long time. Existing patients might not be achieving optimal use from LVAs provided previously, which requires correction of technique, a change in LVA type or strength, or motivational support. Other factors could be a change in emotional support (e.g. from the death of a partner, and / or changes in living circumstances and support networks since the previous LVS intervention).

Whether or not the patient lived alone did not have an impact on total LVQOL score at any of the three visits. This was unexpected based on the author's subjective experience of working within the LV clinic. Prior to the study it would have been expected that patients living alone would have a lower QoL in comparison to those living with somebody else who

could support them. It could be that although a patient lives alone, they may have excellent support from friends, family and neighbours. At each clinic visit, clarification of the level of current support is obtained, along with any changes to previous visits. This is important as it allows the clinician to be aware of occasions when signposting to other support services may be beneficial.

The null hypothesis B for this study was:

$H_{0(B)}$: *All patients with ARMD benefit equally from LVS.*

This hypothesis can be rejected and two alternative hypotheses are proposed:

$H_{1(B)}$: *New patients' quality of life improves as the result of the prescription of optimised LVAs (or the optimisation of LVA prescription) over the initial six months.*

$H_{2(B)}$: *Patients that live alone do not have a reduced quality of life compared with patients living with a partner or wider family because of the support received in LVS and / or the wider community / friendship circle.*

4.1.3 Does inclusion of the EuroQol five-dimension five-level questionnaire improve the assessment of quality of life in low vision patients?

It is well documented that patients who access LVS (particularly the elderly) are often living with health-related co-morbidities (van Nispen *et al.* 2009b) that can affect QoL (Parrish, 1996). The EQ-5D-5L questionnaire was included in this study to assess whether patient co-morbidities confound low vision-specific assessment of QoL in patients with ARMD. The direct link between improvement in near visual acuity with LVAs and the initial improvement in LVQOL between T0 and T3 has been established above. Change in EQ-5D-5L score did not follow this pattern and only decreased significantly between T0 and T6 ($p=0.005$). This longer term decrease indicates a significant improvement in general health-related QoL over the period of the study. The question is whether the improvement in EQ-5D-5L assessment of general health-related QoL is a function of the improvement in low vision QoL determined by the LVQOL, whether this is coincidental, or whether the EQ-5D-5L is insensitive to changes in general health-related quality of life. It was not possible to test the

latter within the scope of this study but the validation work reported in the literature (Janssen *et al.* 2013) would rule this out.

Table 4.1 Number (and percentage of number of patients questioned) of ties in each time comparison for the Low Vision Quality of Life (LVQOL) and the EuroQol five-dimension, five-level (EQ-5D-5L) questionnaires.

Questionnaire	T0-T3 (/39)	T3-T6 (/39)	T0-T6 (/40)
LVQOL	3 (8%)	4 (10%)	1 (3%)
EQ-5D-5L	15 (38%)	16 (41%)	12 (30%)

There is a larger proportion of ties observed in comparisons of the EQ-5D-5L score over time than with the LVQOL score (Table 4.1). This is in part because the EQ-5D-5L score only ranges from five to 25, giving 20 possible total scores, compared to the 125 with the LVQOL. It could be assumed that co-morbidities are deteriorating / improving to a lesser extent over the same time period; whereas there are direct, measureable improvements in visual acuity and vision-related QoL. It should be noted that to test this assumption would require specialist assessment of change in co-morbidities across a range of specialities and hospital departments.

It is unlikely that the improvement in LV related QoL is being damped by a deterioration in general health QoL, but it is not possible to determine whether or not improvement in vision-related QoL is causing any improvement in general health QoL. Results from this study demonstrated a significant (but weak) correlation between the two questionnaires when all the data from the three visits are considered ($p < 0.001$). This weak correlation is observed at the initial ($p < 0.001$) and three-month ($p = 0.001$) visits, but is not evident after six months ($p = 0.050$). The weak correlation between the two questionnaires used in this study also indicates that general health-related QoL has only a limited effect on total LVQOL score and vice-versa. In previous studies, Wolffsohn *et al.* (2014) included the EQ-5D (level not stated) in the development of their functional ability Quality of Vision (faVIQ) questionnaire and found no correlation ($p = 0.476$).

It is not possible to determine a causal relationship between vision-specific QoL and general health-related QoL in this study. The mean age of patients was 81.4 years, and therefore these patients will be at increased risk of other chronic conditions (e.g. diabetes, stroke and arthritis which may all cumulatively influence QoL). This may occur through changes in motivation, memory and handling of LVAs (Wolffsohn and Karas, 2004). At the same time intervention by LVS, although shown to improve LVQOL score, will not simultaneously improve these conditions. For example, attendance at the LV clinic will not improve a patient's arthritis or diabetes but will hopefully - from the provision of LVAs - improve vision

and a general feeling of well-being. In the case of arthritis, handling of the LVA may also be an issue and exacerbate the condition if an unsuitable aid is prescribed, and so on an individual patient basis the assessment and understanding of patient specific co-morbidities and their impact on QoL is important for individual QoL outcomes. It is not possible to isolate the effect of these co-morbidities using the EQ-5D-5L questionnaire alone. Other specific questionnaires such as the Stroke-Specific Quality of Life Scale (Williams *et al.* 1999) would need to be used, however due to the complex nature of co-morbidities in the elderly, many different questionnaires would be required and therefore this would not be practical in the LV clinic setting. The EQ-5D-5L questionnaire does include a question on depression and the levels of depression in visually impaired patients has been reported as comparable to those of patients with other chronic conditions such as stroke, cancer and diabetes (Tabrett and Latham, 2009). Depression is not addressed directly in the LVQOL and so there is a particular role for a depression-specific questionnaire.

The questionnaire assessment method could also be a confounding factor. It is not known how well patients with low vision can discriminate vision- and health-related QoL when being asked questions in the LV clinic setting. In other words, does discussion of the impact of their low vision at the same time as administering the EQ-5D-5L have a bearing on their perception of their health-related QoL?

This study demonstrates that the EQ-5D-5L is not sensitive enough to be used as a standalone questionnaire within the LV clinic in the assessment of patient QoL over a six month period, and therefore would not be useful (on its own) in the process of planning future LVS. For this reason, the null hypothesis $H_{0(C)}$ is not rejected.

$H_{0(C)}$: The EQ-5D-5L general-health questionnaire has insufficient sensitivity to determine whether or not LVS at MKUH improves QoL in ARMD patients.

Furthermore, this study has shown that, without a detailed analysis of the complex co-morbidities of a patient sample with a mean age of 81.4 years, the inclusion of the EQ-5D-5L questionnaire does not contribute to the assessment of QoL in the LVS context over a six-month period. This is in agreement with Binns *et al.* (2012), who concluded that in a high proportion of studies undergoing review, rehabilitation by LVS had no impact on health-related QoL. Whether or not the EQ-5D-5L would contribute to a longer term study (e.g. over five years) has not been assessed.

4.2 The Improvement of Low Vision Services within the Hospital Eye Service

4.2.1 Direct implications for the optimisation of low vision service delivery at Milton Keynes University Hospital and the wider Hospital Eye Service

Milton Keynes has the fastest growing and fastest ageing population in the country (Snelson, 2012). Because ARMD is a function of ageing, the predicted 45% increase of the over 65 years age group between 2012 and 2020 living within Milton Keynes (Snelson, 2012) is set to burden ophthalmology services within the hospital. Therefore efficient and effective delivery of LVS at MKUH is essential.

This following findings of this study have implications for the delivery of LVS at MKUH:

- Evidence that provision of LVAs improves NVA and that this in turn improves patient QoL in the first three months provides justification for LVS delivery and support for the methods used, but also highlights the importance of dispensing LVAs correctly.
- Improvement in QoL is greatest three months after prescription of LVAs but QoL increases significantly up to six months and this appears to be a function of rehabilitation and adaptation. This has the potential to optimise the timing of patient appointments.

The LVS service is improving patient quality of life but currently patient attendance following the initial visit can be on a three monthly frequency, although this is dependent upon the clinician and requirements of the patient. This study shows that this 'three monthly visit' approach is valid for the first two follow-up visits at three and six months but there is an indication that the follow-up frequency could be reduced to six months following this (i.e. patients are seen at 0, 3, 6, 12, 18, 24 months and so on). This would create additional capacity within the LV clinic, which will be essential for seeing greater patient numbers in the future.

4.2.2 Using the questionnaires in routine clinical decision making

The LVQOL questionnaire was used to evaluate specific research hypotheses, and detailed analysis of the data by section indicates that the questionnaire could be used as a pre-screening tool to help tailor LV services. Whether or not this would provide information that cannot be obtained through standard optometric discussions with patients is questionable, but it would provide systematic collection of information and a decision making process could be built based on patient response to questions. For example, if a patient gave a

score of 1 (great problem) on question number 17 (reading large print) an LVA could be issued to help, whereas a score of 5 (no problem) would indicate that such input would not be needed.

Use of the LVQOL in clinical decision making is particularly valuable in the assessment of whether or not a patient would benefit from additional rehabilitation services such as consultation with an Eye Clinic Liaison Officer (ECLO). Specific examples of this can be found in each section (e.g. a number of questions from Section A relate to mobility - the ability to see steps or curbs, getting around safely outdoors, and crossing a road with traffic). Patients who respond with concerns in these areas could then be referred for further mobility training. In these examples (and others) the LVQOL would serve to highlight specific patient concerns that require further referral / intervention, concerns that might otherwise not have been evident. However, the LVQOL does not include questions which would routinely be asked as part of the LV clinic assessment at MKUH. For example, although in Section D there is a question relating to everyday activities (household chores), this is non-specific and would not elicit information such as the patient's ability to safely prepare hot food and drinks, one aspect which is routinely questioned by the author. Although the LVQOL does not (and cannot) comprehensively cover a full range of patient abilities and concerns, its use (or that of an alternative questionnaire) may help to standardise LV clinic protocols among colleagues working within MKUH.

The LVQOL questionnaire is 25 questions long and takes approximately five to seven minutes to answer in the clinic context. With clinic time under increasing pressure, the questionnaire could be provided to the patient for completion prior to the LV clinic appointment. Another strategy would be to reduce the number of questions for use in a pre-screening context. Van Nispen *et al.* (2007) carried out analysis of the psychometric properties of the LVQOL using item response theory analysis to assess QoL prior to and following LVS. They concluded that the 'reading and fine work' subsection should be split into 'reading small print' and 'visual (motor) skills', reducing the number of items overall to 23. Items number 5 ('problems reading street signs') and 25 ('problems in performing everyday activities') were removed due to low factor pattern coefficients and confusing interpretation of factors. A later study (van Nispen *et al.* 2011) concluded that a further reduction to 21 questions was appropriate to remove differential item functioning and further improve the validity of results. In this study the authors omitted items '1' ("your vision in general") and '24' (problems using tools).

The reduction of the 25-item questionnaire to a 21-item version was achieved in this study by deletion of questions 1, 5, 24 and 25. Table 4.2 shows that the headline comparison of

total LVQOL score for all patients between visits was similar using the 25 and 21 questions versions. This indicates that the 21 question version would have provided similar results and could be used in future studies.

Table 4.2 Comparison of related-samples Sign Test results for the full 25 question Low Vision Quality of Life questionnaire and the reduced 21 question version (van Nispen et al. 2011).

Number of questions	T0 vs T3		T3 vs T6		T0 vs T6	
	25	21	25	21	25	21
Positive	26	30	26	24	31	30
Negative	10	9	9	11	8	8
Ties	3	0	4	4	1	2
p	0.012	0.001	0.007	0.043	<0.001	0.001

4.2.3 Audit and evaluation

As well as testing hypotheses in a controlled research context, the study is effectively a six month audit of the performance of LV services for ARMD patients at MKUH. The LVQOL has been shown to be a useful tool for audit of LV services in the context of ARMD, and a similar methodology could be used for assessing it as an audit tool for other diseases causing low vision such as glaucoma and diabetes. This audit could be extended over a longer time period and it would be of value to compare data with other causes of low vision to see whether LVS could be optimised further.

Nationally, low vision is an expanding problem due to the ageing population and the increased prevalence of untreatable sight loss (Binns *et al.* 2012). Through the provision of LVS, patients are supported to enable them to live as independently as possible. However there is obviously a financial cost involved. Binns *et al.* (2012) concluded that there was a lack of evidence to clarify what constitutes an effective (and cost-effective) service. Evidence-based information regarding both the effectiveness and efficiency of services is fundamental in a time of financial constraint for continued allocation of resources within the NHS. Ongoing evaluation of LVS is therefore essential to enable future service provision.

Although the current study was carried out in only one hospital clinic, it would be beneficial to be able to recommend a method of service evaluation utilising QoL questionnaires that could be used nationally. Naturally, the different locations of hospital LV clinics in the UK would be subject to the effects of different demographics (e.g. eye conditions, age, gender and race). Regardless, consistency of evaluation methods among different service

providers (hospitals) is important. This would ensure that any different measures of outcome among providers related to the differences between the various approaches to LVS, rather than differences due to the method of evaluation.

Binns *et al.* (2012) proposed that the use of such a broad range of QoL questionnaires in the evaluation of LVS was a disadvantage because variation among questionnaires can mask treatment effects (such as QoL outcomes from different LVS models). It would therefore be beneficial to reach a conclusion on the most suitable vision-related QoL questionnaire to use, and whether or not this should be supplemented by a health-related QoL measure. The current study does not provide the answers to this question, however, it does contribute new data to the knowledge base on the LVQOL to support this assessment.

The benefit of an NHS-wide evaluation of services would be the identification of best practice in a range of contexts, allowing identification of the most effective (and cost-effective) model of LVS. This could then be shared amongst service providers to improve knowledge and understanding of these services for the future. The wider optometric community would also benefit as optometrists would be able to use this knowledge to make clinical decisions, particularly when deciding which patients to refer into the service. Once it is evident which method or approach to LVS provision is most effective, wider questions could be asked such as how to optimise the service for use in different circumstances. Ultimately this evaluation would need to determine how the service needs to adapt going forward to ensure provision for a greatly increased number of service users in the future.

A centrally funded study would be required with data collected at multiple LV clinic providers (hospitals). The use of a QoL questionnaire(s) such as the LVQOL for this multi-centre study would be critical to ensure that quantifiable results are obtained, rather than purely subjective assessment. Questionnaire(s) and implementation methods would need to be standardised throughout to reduce bias. The broad number of current approaches to low vision within hospital optometry in the UK includes a range of different rehabilitation services and multidisciplinary approaches comprising a wide range of health care professionals and levels of attachment to social services (CO-RCO, 2013; Ryan, 2014). The proposed study would be designed to include a representation from as many of these systems as possible, to inform debate as to the effectiveness of these different approaches. Of course, there may not be one single approach that is suited to all areas of the UK. However, evaluation will lead to knowledge of what works well, where, and how services (and resources) can be tailored and integrated to meet the specific requirements of patients served by hospitals based in different demographic areas.

Results could then be disseminated through the Hospital Optometrists Annual Conference and Head of Department meetings to ensure that all practitioners working within LV clinics are following the same guidelines. From study results, a number of key questions for UK hospital departments offering LVS would then need consideration. For example, does the current approach to LVS offered meet best practice to ensure effectiveness? If not, how could each provider improve their service based on recommendations from the study? Once any changes were implicated, further evaluation of the new model of provision would be required to ensure these changes had improved outcomes. Ultimately, an assessment would need to be made of the benefit of investment in this research.

The College of Optometrists together with the Royal College of Ophthalmologists have provided recommendations on the evaluation of LVS (CO-RCO, 2013). One of the objectives contained within this report focuses on the use of QoL questionnaires to assess the role of LVS. Suggested QoL questionnaires include the Manchester Low Vision Questionnaire (MLVQ), the Vision-Related Quality of Life Questionnaire, the Mass of Activity Inventory (MAI; modified version) and the National Eye Institute Visual Function Questionnaire (NEI-VFQ).

4.2.4 Provision of rehabilitation services within low vision services

It has been demonstrated above that improvement in QoL is not simply a function of improvement in NVA, and that rehabilitation provided within LVS may also contribute to improved QoL. For those patients attending the LV clinic, the ability to refer to the ECLO on the same day for rehabilitation advice enables a greater proportion of optometric time to be spent on clinical assessment and demonstrating LVAs, with the ECLO focussing on adaptations at home and emotional support. The ECLO was not present in the clinic on any of the days that this study took place. However three (/40) patients were referred to the ECLO at Visit 1 (T0) whilst 14 patients had contact with the ECLO prior to the study. In this study several patients had no rehabilitative support, others received telephone ECLO support only, while a small number had access to a home visit and telephone support. To determine the impact of ECLO services objectively would require a study designed with an LVS + ECLO, vs LVS - ECLO factor as per Reeves *et al.* (2004) and de Boer *et al.* (2006). However, to withhold rehabilitative support could be considered unethical.

4.3 Evaluation and Further Development of This Study

Research hypotheses regarding the impact of LVS on QoL in ARMD patients was assessed at MKUH.

Limitations of the study, largely dictated by the time and resources available, include:

1. Sample size.
2. Variable history within the LV Clinic before T0.
3. Time limited to six months.
4. No control group (as a result of ethical constraints), and no randomisation.
5. Impact of direct implementation method.
6. Limited to ARMD.
7. Limited to one vision-specific and one general health questionnaire.
8. Limited to one hospital / LV clinic model.

Sample size and variable prior history in the LV clinic before T0

A total of 40 patients were recruited, resulting in an 18 month study period. This sample size exceeded the minimum required for the experimental protocol (34 patients; see Section 2.2.2). A larger sample, however, may have allowed subdividing the participant group into new and existing patients. This may be beneficial because it would add more power to the analysis of the difference in QoL outcomes between new and existing patients.

Stage (of disease) and time since diagnosis are also important factors that should be included in the selection of patients for future studies. This is because it is hypothesised that the stage and rate of disease progression will be significant factors in determining the QoL benefit of LVS.

Time limitations

Results indicated that the QoL benefit of attendance at LV clinic appointments appears to decrease over time, but over a greater time period than six months (indicated by examining existing patients). This needs to be tested over a 24 or even 36 month period. This is because the rate of disease progression in ARMD patients occurs on a longer time frequency than six months.

Other confounders include co-morbidities and ARMD subtype and these should be explored further in future studies.

No control group and no randomisation

To have had a control group that did not receive LVS despite their ARMD and the problems with visual acuity that this causes was not done for ethical reasons. De Boer *et al.* (2006) recommended the use of a 'waiting list group' as a control; this would not have been practical at MKUH due to the management of waiting lists, although it may be an option for a future study.

Limited to ARMD

ARMD is one of many conditions that cause low vision. It would be of interest to determine whether patients attending the LV clinic with other ocular diseases benefit equally from the LV clinic. For example, a comparison between patients with glaucoma and patients with ARMD would test the hypothesis that loss of peripheral vision has less impact on QoL than the loss of central vision, and that LVS (provision of LVAs and rehabilitation) has different impacts on the QoL of the two groups. This was explored by Evans *et al.* (2009) who reported that although QoL was affected to a similar level in patients with either glaucoma or ARMD, general and mental health were a greater problem for those with glaucoma, whilst physical function was more restricted for those with ARMD.

Questionnaire selection and implementation method

Further evaluation of LVS within MKUH could include a comparison of two vision-related QoL questionnaires e.g. the LVQOL and the functional ability Quality of Vision (faVIQ) questionnaire (Wolffsohn *et al.* 2014). The latter has recently been shown to be a sensitive tool for the measurement of QoL in patients with visual impairment and employs more recently developed statistical techniques, thought to be more robust. In a future study, patients could be randomly assigned to one of two groups – one receiving the LVQOL (as per the current study), and the other receiving the faVIQ. Providing each group received the same method of administration, over the same time period, with the same controls on disease and patient history in the LVS, the effect of bias from these factors should be minimised.

Some of the differences observed between the Wolffsohn and Cochrane (2000) study and this study could be due to implementation method. This study used in-person implementation, while Wolffsohn and Cochrane (2000) used postal implementation for self-

completion. Wolffsohn *et al.* (2000) observed that postal implementation resulted in a lower QoL score compared with in-person interviews due to a lack of interaction with the ophthalmic practitioner. This is one explanation for the larger LVQOL scores observed in the present study. Patients completing the questionnaire with the optometrist may give a better impression of how they are managing, therefore artificially increasing QoL scores.

The large differences in total LVQOL scores observed between the current study and those of Wolffsohn and Cochrane (2000) may not be attributable to implementation method alone. A further study is required to test the effect of implementation method on QoL scores, whereby low vision patients would be randomised into two groups – one group receiving the questionnaire in large print format by post for self-completion, the other attending the LV clinic to complete the questionnaire with the optometrist.

Study was limited to one hospital / LV clinic model

The study was conducted in one hospital using a single model of LVS delivery. It is reasonable to extend the findings of this study to similar LVS models at similarly sized hospitals. However other models of LVS delivery exist and these would need to be examined in further studies to determine whether the findings of this study are applicable to other LV clinics.

5 MAJOR FINDINGS AND CONCLUSIONS

1. Over a six month period, low vision aids significantly improved near visual acuity ($p=0.011$). Over this same period, no significant difference was recorded in binocular distance visual acuity ($p=0.335$), near visual acuity without low vision aids ($p=0.701$) or, binocular distance contrast sensitivity ($p=0.216$).
2. There was no significant change in near visual acuity with low vision aids over the six-month study period for patients who had previously attended a low vision clinic (existing patients; $p=0.368$). For patients who were new to the clinic, the maximum improvement in near acuity with low vision aids occurred within the first three months following intervention ($p=0.005$).
3. Median total Low Vision Quality of Life (LVQOL) score increased between the initial (T0) and the three-month (T3) visits ($p=0.012$), and again between the three and six-month (T6) visits ($p=0.007$). Because there was no significant change in visual acuity measures (including near acuity with low vision aids) between the second and third visits, the improvement in LVQOL score within this period is likely related to factors other than vision (e.g. rehabilitation / adaptation).
4. There was no significant difference in the mean total LVQOL questionnaire score between new and existing patients at all three visits: T0 ($p=0.103$), T3 ($p=0.363$) and T6 ($p=0.923$). In existing patients, there was a significant increase in mean total LVQOL score (8.6) between T0 and T3 ($p=0.031$), but no further increase between T3 and T6 ($p=0.251$). In new patients, a significant increase in score (13.9) occurred between T0 and T3 ($p=0.003$) and between T3 and T6 ($p=0.048$). These results provide evidence to suggest that intervention by low vision services for new patients increases their quality of life following the initial appointment.
5. Mean total LVQOL questionnaire scores at any of the three visits was not significantly different for patients living alone compared with those living with a partner / family ($p=0.571$).
6. Analysis of scores within each of the four sections of the LVQOL questionnaire revealed that there were significant differences in median score between the three visits for Sections A (distance vision, mobility and lighting), B (adjustment) and C (reading and fine work). In Section A, the median total LVQOL score increased significantly between T0 and T3 ($p=0.002$), and between T3 and T6 ($p=0.008$). It is difficult to attribute the continued increase in score for this section purely to low vision clinic assessment or rehabilitative

services: the increased score is likely to be due to a combination of both. The significant increase in Section C score between T0 and T3 ($p=0.006$) is assumed to reflect the significant improvement in near acuity with low vision aids during that period. Adaptation to the use of low vision aids by the second visit is a likely explanation for no change in score between the three and six-month visits ($p=0.568$). Section D (activities of daily living) scores did not change significantly over the three visits ($p\geq 0.05$), and these questions do not appear to be sensitive to the effects of low vision clinic input.

7. The EuroQol five-dimension, five-level (EQ-5D-5L) questionnaire scores decreased significantly between T0 and T6 ($p=0.005$) indicating a significant improvement in general health-related quality of life over the period of the study. A further multi-disciplinary assessment of co-morbidities would be needed to determine whether or not the improvement in vision-related quality of life was linked to these findings.

8. The EQ-5D-5L questionnaire is not sensitive enough to be used as a standalone questionnaire within the low vision clinic in the assessment of patient quality of life over a six month period.

9. The findings of this study can be used to improve the efficiency of low vision service delivery at Milton Keynes University Hospital by initially seeing new patients on a three-month frequency but increasing this to a six-month frequency after the first three visits (i.e. after the initial, three-month and six-month visits). This is a more resource efficient approach.

6 REFERENCES

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APPENDICES

Appendix 1.1

Protocol for low vision assessment for a new patient attending Milton Keynes University Hospital low vision clinic

1. Comprehensive case history – to determine any general and / or specific problems that the patient is having with their vision, and the effect that this has upon their ability to perform everyday tasks. The patient's social situation and current level of support should be identified.
2. Assessment of visual function – measurement of distance and near visual acuity for each eye (including pinhole) and binocularly, providing an initial assessment of the limitations of vision. Assessment of contrast sensitivity to indicate whether further advice on contrast and lighting is required.
3. Refraction – to ensure that the patient is wearing the optimum spectacle correction for both distance and near. Discussion on the best form(s) of spectacle correction. Demonstration of high reading addition spectacle prescription (where appropriate).
4. Optical LVA demonstration and training – choice of LVA based on the specific task (e.g. size and contrast of print), patient's level of visual acuity, patient motivation and handling ability. Demonstration of more than one type of LVA for separate tasks, and guidance on how to achieve the optimum results from each. Explanation of the provision of LVAs on free-of-charge loan, how to change batteries, and LV clinic contact details in case of any problems.
5. Lighting and non-optical low vision aids – advice on appropriate lighting and improvement of contrast, provision of glare shields. Discussion of electronic LVAs, how to obtain a demonstration, and estimates of the costs involved to purchase privately. Demonstration of large print, advice on audio books and talking newspapers, along with other products that can be purchased privately. Eccentric viewing and steady eye strategy training.
6. Referral to other services – with informed consent from the patient, a 'Referral of Vision Impairment' (RVI) is completed to enable access to social services for assessment and support. Provision of information on other local and national (voluntary) support groups.
7. Arrangements for follow-up LV assessment or discharge.

Appendix 2.1

Patient Information Sheet v2

PATIENT INFORMATION SHEET

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 30 minutes.

Talk to others about the study if you wish.

Research workers, school and subject area responsible:

Mrs Louise James

*Milton Keynes Hospital NHS Foundation Trust
and School of Life & Health Sciences, Vision Sciences, Aston
University*

Professor Stephen J. Anderson

School of Life & Health Sciences, Vision Sciences, Aston University

Project Title:

Evaluation of Low Vision Services on Quality of Life

Invitation:

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the purpose of the study?

The purpose of this study is to determine the impact of low vision rehabilitation on the quality of life of patients with macular disease. The results of this study will be analysed to determine which patients benefit from the rehabilitation process, thereby providing useful information as to which patients are most likely to benefit from visual rehabilitation in the future.

Why have I been chosen?

You have been chosen because you have been diagnosed with macular disease and are currently attending the Low Vision clinic at Milton Keynes General Hospital. A minimum of 34 participants will be asked to take part.

What will happen to me if I take part?

By volunteering to participate in this study you will be required to answer questions on your experiences of living with macular disease and how this impacts upon your quality of life. This will involve completing two short questionnaires after your initial Low Vision Assessment in the Low Vision clinic at Milton Keynes General Hospital.

When you return for your 3 and 6 month Low Vision Review appointments you will be asked to complete the questionnaires again. You will be asked to complete the questionnaires up to three times in a period of six months.

It will be necessary for NHS staff in the Low Vision Clinic to access your medical records as part of this research.

Are there any potential risks in taking part in the study?

There are no physical risks from taking part in this study. Any risk of breaching privacy and confidentiality in relation to data collected from the questionnaire will be minimised by seeking your consent prior to participation to allow data to be analysed. It may be necessary to breach your confidentiality if your health and safety or that of another is at risk.

Questions about your lifestyle will be asked, and you may consider these to be an intrusion. We shall take every step to ensure that the risk of causing offence will be minimised.

Do I have to take part?

It is up to you to decide to join the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

Expenses and payment:

There are no expenses or payments for participation in this study.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised (if it is applicable to your research).

We shall collect your response to the questionnaires on paper records. These will not carry your name, hospital number, NHS number or any information that can be used to identify you, outside of the Low Vision Clinic at Milton Keynes Hospital. Instead we shall mark each questionnaire response with a unique number.

We shall keep a list of unique identification numbers securely in the clinic offices throughout the period of research. On completion of the research we shall securely destroy this list and only anonymous data

will be used in our analysis and in our discussions with research staff at Aston University.

All questionnaire responses will therefore be anonymised and will be stored securely. Only staff in the Low Vision Clinic at Milton Keynes Hospital will have access to identifiable records.

Data from the questionnaire responses will be used in statistical analysis that will help inform how we deliver Low Vision services in the NHS.

Anonymised questionnaire responses will be retained for a minimum period of five years in the School of Health and Life Sciences at Aston University and will then be disposed of securely.

Please note that privacy and confidentiality will be protected vigorously to the extent permissible by law. We cannot, however, guarantee privacy or confidentiality.

What will happen to the results of the research study?

We aim to publish the results of this study in appropriate medical research journals. However, there will be no reference to any individual's results in any publication. Published research will be available to all participants – to receive your copy, please contact Louise James at Milton Keynes General Hospital.

Who is organising and funding the research?

The Chief Investigator is Mrs Louise James working under the supervision of Professor Stephen J. Anderson at The School of Life & Health Sciences, Aston University. This research study is organised in conjunction with Aston University. This research is not funded.

Indemnity

This research is covered by the Aston University Indemnity Insurance provided by Zurich Municipal under policy number NHE-02CA02-0013.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by Cambridgeshire 3 Research Ethics Committee.

The research has also been reviewed by the Aston University's Ethics Committee.

Who do I contact if something goes wrong or I need further information?

Please feel free to contact Mrs Louise James (jameslc@aston.ac.uk, 01908 660033 x 5403)

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

If you have any concerns about the way in which this study has been carried out, then you may contact the Secretary of the Aston University Research Ethics Committee by email j.g.walter@aston.ac.uk or telephone 0121 204 4665

PATIENT CONSENT FORM

Evaluation of Low Vision Services on Quality of Life

Name of Chief Investigator: Mrs Louise James

Patient Identification number for this study: _____

Please initial boxes

1	I confirm that I have read and understand the information sheet dated 1 May 2011 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	<input type="checkbox"/>
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	<input type="checkbox"/>

3	I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	<input type="checkbox"/>
4	I agree to take part in the above study.	<input type="checkbox"/>

Name of Patient _____ Date _____ Signature _____

Name of Person _____ Date _____ Signature _____

taking consent

When completed: 1 for participant; 1 for researcher site file.

Appendix 2.2

Milton Keynes University Hospital Referral of Vision Impairment (RVI) Form

Milton Keynes Optometry Department
Low Vision Summary

Tel no.....

Patient Label

Registered: SVI/Blind
VI/ Partially sighted
Not Yet

DateNew/Old Requested Rehab. Revisit Yes / No
Reason.....

Eye condition(s).....
.....

Best V A: Dist R..... L..... Bin.....With/without glasses

Near R..... L..... Bin.....With/without glasses
Working distance.....cms.

LVAs issued : Distance Yes / No
Type :-

: Near Yes / No
Type :-

Hospital Follow-up arranged:-

This form contains confidential information for use by the
Rehabilitation Officers working with the person concerned. I have
explained what it contains and to whom it will be sent.

Optometrist Signature..... Print name.....
Patient Name

I am happy for this information to be sent to my Rehabilitation
Officer

Appendix 2.3

Low Vision Quality of Life Questionnaire

THE LOW VISION QUALITY-OF-LIFE QUESTIONNAIRE

Distance Vision, Mobility and Lighting

How much of a problem do you have:

	none		moderate		great		
With your vision in general	5	4	3	2	1	x	n/a
With your eyes getting tired (e.g. only being able to do a task for a short period of time)	5	4	3	2	1	x	n/a
With your vision at night inside the house	5	4	3	2	1	x	n/a
Getting the right amount of light to be able to see	5	4	3	2	1	x	n/a
With glare (e.g. dazzled by car lights or the sun)	5	4	3	2	1	x	n/a
Seeing street signs	5	4	3	2	1	x	n/a

Seeing the television (appreciating the pictures)	5	4	3	2	1	x	n/a
Seeing moving objects (e.g. cars on the road)	5	4	3	2	1	x	n/a
With judging depth or distance of items (e.g. reaching for a glass)	5	4	3	2	1	x	n/a
Seeing steps or curbs	5	4	3	2	1	x	n/a
Getting around outdoors (e.g. on uneven pavements) because of your vision	5	4	3	2	1	x	n/a
Crossing a road with traffic because of your vision	5	4	3	2	1	x	n/a

Adjustment

Because of your vision are you:

	no	moderately	greatly				
Unhappy at your situation in life	5	4	3	2	1	x	n/a
Frustrated at not being able to do certain tasks	5	4	3	2	1	x	n/a
Restricted in visiting friends or family	5	4	3	2	1	x	n/a

	well				poorly	not explained
How well has your eye condition been explained to you	5	4	3	2	1	x

Reading and Fine Work

With your reading aids / glasses, if used, how much of a problem do you have:

	none		moderate		great		
Reading large print (e.g. newspaper headlines)	5	4	3	2	1	x	n/a
Reading newspaper text and books	5	4	3	2	1	x	n/a
Reading labels (e.g. on medicine bottles)	5	4	3	2	1	x	n/a
Reading your letters and mail	5	4	3	2	1	x	n/a
Having problems using tools (e.g. threading a needle or cutting)	5	4	3	2	1	x	n/a

Activities of Daily Living

With your reading aids / glasses, if used, how much of a problem do you have:

	none		moderate		great		
Finding out the time for yourself	5	4	3	2	1	x	n/a
Writing (e.g. cheques or cards)	5	4	3	2	1	x	n/a
Reading your own hand writing	5	4	3	2	1	x	n/a
With your everyday activities (e.g. household chores)	5	4	3	2	1	x	n/a

Appendix 2.4

Patient Testimonials (Low Vision Quality of Life Questionnaire)

Underlined text represents interpretation by Chief Investigator. T0 is the initial visit, T3 is the three-month follow-up and T6 is the six-month follow-up. Three digit number is patient identifier code. Numbers in brackets indicate LVQOL response score (1-5, x, n/a).

Section A: Distance Vision, Mobility and Lighting

How much problem do you have:

Q1: With your vision in general

001 (T6) – “I can’t see faces now” (3)

011 (T3) – “better with my new glasses” (4). Gave a score of (2) at (T0) and issued prescription for new spectacles on this occasion.

015 (T0) – “problems with bus numbers” (1)

015 (T3) – “slightly improved” (3)

020 (T6) – “I have large support from family” (5). Patient lives with family

021 (T3) – “seems worse” (1). Patient scored (4) at (T0)

023 (T6) – “people need to be closer before I recognise them now” (3). Scored (4) at (T3).

025 (T6) – “It goes dark sometimes” (3)

029 (T0) – “In a crowd I find faces a problem” (4)

Q2: With your eyes getting tired (e.g. only being able to do a task for a short period of time)

007 (T3) – “my magnifier has helped with this” (3). Gave a score of (1) at (T0).

009 (T0) – “with television especially” (2)

022 (T0) – “at the end of the day they feel gritty” (1)

024 (T6) – “evenings mainly” (4)

025 (T0) – “after 20 to 30 minutes reading” (3)

028 (T0) – “in the evenings” (4)

035 (T3) – “I am aware of it – moderately” (3)

038 (T0) – “depends upon the task” (4)

038 (T6) – “evenings with television – but otherwise no” (4)

Q3: With your vision at night inside the house

012 (T3) – “I have a torch to help” (3)

015 (T0) – “a change in light levels is especially a problem” (1)

015 (T3) – “I use glare shields” (4)

015 (T6) – “dusk outside is more of a problem” (5)

- 024 (T0) – “I’m better in the dark” (5)
024 (T3) – “I see better in the dark” (5)
034 (T6) – “I can’t see the clock on my microwave” (2)
039 (T0) – “I use a torch” (2)

Q4: Getting the right amount of light to be able to see

- 016 (T0) – “I need a new lamp” (3)
017 (T3) – “especially in winter” (1)

Q5: With glare (e.g. dazzled by car lights or the sun)

- 003 (T6) – “eyes watery”
007 (T6) – “even when I wear my own dark sunglasses” (1)
035 (T3) – “especially going from dark to light” (2)

Q6: Seeing street signs

- 027 (T0) – “I don’t need to” (1)
035 (T0) – “I need to be close” (2)

Q7: Seeing the television (appreciating the pictures)

- 001 (T6) – “not faces” (3)
006 (T6) – “I can watch for a maximum of 2 hours only” (3)
007 (T6) – “but I wear tinted glasses” (5)
012 (T3) – “ok if a big screen” (4)
015 (T0) – “I can only listen” (1)
015 (T6) – “better” (4). Patient had new spectacles made after (T3), scored (3) at (T3).
018 (T3) – “they are hazy” (3)
019 (T6) – “it’s worse on HD [high definition]” (5)
023 (T6) – “I can’t see faces and recognise actors that I know” (1)
024 (T6) – “I sit close to it” (2)
025 (T6) – “I need to get very close” (2)
026 (T6) – “It irritates me due to the distortion” (1)
029 (T0) – “I have gone a bit nearer” (5)
033 (T3) – “slight problem with text on the television, yellow on black is better” (4)
034 (T6) – “I have a large screen” (3)
035 (T6) – “I am sitting closer” (4)
037 (T0) – “It’s foggy” (3)
038 (T0) – “I have a large screen but text is a problem” (4)
039 (T0) – “faces difficult” (3)

Q8: Seeing moving objects (e.g. cars on the road)

- 003 (T6) – “I listen” (3)
- 018 (T3) – “I’m careful” (2)
- 024 (T6) – “daylight is worse than evenings” (2)
- 027 (T0) – “especially dark cars” (1)

Q9: With judging depth or distance of items (e.g. reaching for a glass)

- 016 (T0) – “pouring liquids a problem” (4)
- 017 (T6) – “reaching tablets from the side in the kitchen” (4)
- 023 (T6) – “I have broken a glass before as I’ve misjudged” (4)
- 024 (T3) – “I feel for things” (1)
- 024 (T6) – “I smashed a glass – I feel for things” (1)
- 025 (T0) – “problems with pouring and miss the cup when I pour tea” (1)
- 026 (T0) – “I miss when pouring water” (1)

Q10: Seeing steps or curbs

- 006 (T6) – “I use my stick to help me feel” (3)
- 008 (T6) – “steps particularly” (3)
- 015 (T0) – “recently” (3)
- 017 (T0) – “I don’t go out alone” (1)
- 018 (T3) – “I use my scooter generally” (2)
- 025 (T0) – “I do fall down curbs” (1)
- 025 (T6) – “I tripped down the curb two to three weeks ago” (1)
- 035 (T3) – “I am very careful” (5)

Q11: Getting around outdoors (e.g. on uneven pavements) because of your vision

- 006 (T0) – “I need my trolley to help me” (3)
- 024 (T6) – “I stagger now” (1)
- 034 (T0) – “I have a white cane now” (2)
- 038 (T0) – “I go out with my husband – always” (5)

Q12: Crossing a road with traffic because of your vision

- 001 (T6) – “I almost stepped out in front of a car last week” (1)
- 002 (T6) – “getting worse” (1)
- 006 (T6) – “I can manage on my own” (3)
- 012 (T3) – “only if I know where I am” (3)
- 012 (T6) – “I choose quiet times to cross” (4)
- 014 (T3) – “I never go out alone” (4)
- 014 (T6) – “I choose not to cross on my own” (3).

- 015 (T3) – “Ok if cars are coming from the left, not from the right” (2)
- 017 (T6) – “I only cross side streets” (2)
- 019 (T0) – “but my mobility is poor” (5)
- 023 (T6) – “I need to be extremely careful now” (1)
- 024 (T6) – “Usually I would hold onto my wife’s wheelchair, I would not cross on my own” (1)
- 025 (T6) – “I need to be careful crossing the road, I get blank patches as cars are coming towards me” (1)
- 026 (T0) – “I’m always accompanied” (1)
- 026 (T6) – “I’ve not been out on my own since October 2013” (x). Reported April 2014.
- 027 (T0) – “I wouldn’t go out on my own” (1)
- 035 (T0) – “I am becoming more careful” (3)
- 038 (T0) – “I am always with my husband” (5)

Section B: Adjustment

Because of your vision are you:

Q13: Unhappy at your situation in life

- 031 (T6) – “I have to get on with it as I live alone – that’s the way it is” (5)
- 034 (T6) – “I try not to get depressed – I don’t want to go on tablets” (4)

Q14: Frustrated at not being able to do certain tasks

- 004 (T6) – “my hearing is also an issue” (4)
- 007 (T3) – “sewing - my eyes get sore if I try to sew for any length of time” (4)
- 015 (T0) – “driving” (1)
- 016 (T0) – “reading especially” (4)
- 017 (T6) – “knitting – I have bags of wool upstairs I can’t use” (3)
- 021 (T0) – “hearing impairment makes it harder” (3)
- 023 (T6) – “Yes, I am, but I don’t let it get at me” (5)
- 025 (T0) – “I don’t get frustrated, there’s no point” (5)
- 025 (T6) – “I feel it is what I expect at my age, there’s no point getting frustrated or angry” (5)
- 036 (T3) – “frustration over not being able to drive – my wife drives” (4)

Q15: Restricted in visiting friends or family

- 014 (T3) – “I have people visit now” (5)
- 015 (T3) – “by not driving” (2)
- 016 (T0) – “my daughter lives five minutes away but I don’t like to rely on her too much and try to manage on my own as much as I can” (5)
- 020 (T0) – “live with family” (5)
- 025 (T0) – “I live with my son” (5)

034 (T6) – “I need to have a taxi door to door so I tend to phone friends rather than visit” (3)

036 (T3) – “my wife drives” (5)

Q16: How well has your eye condition been explained to you

Section C: Reading and Fine Work

With your reading aids / glasses, if used, how much of a problem do you have:

Q17: Reading large print (e.g. newspaper headlines)

026 (T3) – “for a short time it’s ok” (5)

Q18: Reading newspaper text and books

003 (T3) – “I just don’t bother to read” (n/a)

005 (T0) – “I don’t read the newspaper anymore” (x)

018 (T3) – “I know I can read this (N6 - with bifocals and no magnifier) but I still feel this is very poor near vision” (3)

021 (T0) – “I have no problems if I use a magnifier” (5)

024 (T3) – “My wife reads the newspaper to me” (1)

025 (T6) – “but not reading for very long” (5)

029 (T3) – “my Kindle is great” (5)

033 (T0) – “I hold them closer if need be” (5)

034 (T6) – “I have Sound News”

039 (T3) – “I dislike using magnifiers”

Q19: Reading labels (e.g. on medicine bottles)

013 (T6) – “even with the magnifier I struggle” (3)

016 (T0) – “I can’t shop on my own, my daughter has to be there” (1)

016 (T6) – “with magnifier it’s better” (4). Patient attended at (T0) with her own magnifier (reading N12) and was loaned new LVAs (reading N5).

018 (T6) - “with good light” (5)

019 (T6) – “when they are very small print” (4)

029 (T0) – “slight problems” (4)

035 (T0) – “cooking instructions are difficult” (3)

Q20: Reading your letters and mail

004 (T0) – “I’ve stopped because of my vision” (x)

006 (T6) – “my son reads them for me due to my vision” (x)

008 (T3) – “I have a lot of large print” (3)

012 (T3) – “it depends how complex they are” (4)

014 (T0) – “I have large print” (4)

- 014 (T6) – “I don’t bother though” (x)
- 020 (T0) – “family help” (3)
- 024 (T6) – “I’m doing less reading than I was three months ago. My wife reads everything to me now – even my letters” (x). Scored (1) at (T3) and (T0).
- 025 (T6) – “small print is difficult, my son reads it to me” (4)
- 026 (T6) – “I have large print bank statements” (3)
- 028 (T3) – “my wife generally does it” (5)
- 030 (T3) – “the magnifier has made a huge impact on my vision” (5). Scored (4) at (T0).
- 032 (T0) – “my husband reads them” (1)

Q21: Having problems using tools (e.g. threading a needle or cutting)

- 006 (T0) – “I’ve stopped sewing due to my vision” (x)
- 007 (T3) – “my magnifier helps” (5)
- 012 (T6) – “needles – I can’t manage to thread them now” (1)
- 018 (T6) – “I need good lighting” (5)
- 021 (T3) – “missing cross stitch – I can’t do it and can’t thread a needle” (2)
- 021 (T6) – “needles” (x)
- 023 (T0) – “hands free magnifier helps” (1)
- 023 (T6) – “I still do a little bit of sewing but it’s much more difficult – I have tried a needle threader but it didn’t help much” (2)
- 025 (T3) – “needles – son does it” (1)
- 025 (T6) – “I love sewing, it’s a shame – I do small bits of sewing but my son threads all the needles now, he leaves two or three already threaded for me before he goes to work” (x)
- 026 (T3) – “scissors” (4)
- 026 (T6) – “I can’t thread needles” (1)
- 027 (T0) – “I can knit with light wool, not coloured. I attend a (knitting) group in the sheltered accommodation” (1)
- 029 (T0) – “I’m managing to use my sewing machine – I get there in the end” (5)
- 031 (T3) – “I cannot find the hole when threading needles” (3)
- 038 (T0) – “threading needles” (1)

Section D: Activities of Daily Living

With your reading aids / glasses, if used, how much of a problem do you have:

Q22: Finding out the time for yourself

- 016 (T0) – “I guess” (3)
- 017 (T6) – “but I’m guessing” (3)
- 018 (T0) – “my mobile has yellow on blue – large print” (5)
- 034 (T6) – “I am just about seeing my watch” (2)

Q23: Writing (e.g. cheques or cards)

- 005 (T3) – “I don’t write due to my vision” (x)
006 (T6) – “I write very little” (2)
008 (T3) – “I have stopped sending cards etc due to problems writing addresses, I’ve told people I will phone them instead” (3)
012 (T6) – “I only write my shopping list - I have a pad with lines” (3)
013 (T6) – “I have help with writing” (x)
017 (T6) – “my husband does all my writing” (x)
023 (T6) – “I forget to write big” (1)
024 (T3) – “I manage signing forms only” (2)
024 (T6) – “I can’t even sign a cheque” (x)
025 (T3) – “Letters – I don’t write anymore as I’m untidy” (4)
025 (T6) – “all wavy” (3)
026 (T6) – “I am managing what I need to” (3)
028 (T3) – “little bits” (5)
037 (T0) – “It’s guesswork” (1)

Q24: Reading your own hand writing

- 002 (T6) – “I don’t check what I write anymore” (3)
006 (T6) – “I write large” (5)
025 (T0) – “It’s terrible” (1)
025 (T6) – “I don’t read any letters/cards that I’ve written anymore” (3)

Q25: With your everyday activities (e.g. household chores)

- 006 (T6) - “I have a cleaner every two weeks” (3)
012 (T6) – “I do break glasses and lose things” (3)
013 (T6) – “my daughter helps” (3)
015 (T0) – “I have a son (aged 10), my wife may have to move back in?” (1)
015 (T6) – “cooking ok and washing ok” (3). Patient had a home visit from ECLO following (T0). Scored (3) at (T3).
016 (T0) – “My daughter helps as I live alone. My housework is not as good as it used to be and this matters to me a lot, I am independent and stubborn and I like to manage on my own” (3)
017 (T6) – “I help with the cooking, but it’s mainly done by my husband. My daughter does the cleaning” (3)
018 (T0) – “I have a cleaner” (3)
020 (T0) – “cooking is very difficult” (1)
024 (T3) – “I can only do little bits” (2)
024 (T6) – “I still Hoover and make the bed” (5)

- 025 (T0) – “I love baking but can’t see the numbers on the scales anymore – but I still do it” (3)
- 026 (T3) – “shopping a problem” (1)
- 026 (T6) – “managing – I have a cleaner”
- 027 (T0) – “I have a cleaner” (3)
- 028 (T3) – “but limited due to a back problem” (5)
- 034 (T0) – “I have a shopper to help me” (1)
- 034 (T6) – “I cannot take my blood every morning as I can’t see, I am waiting for help with this” (2)
- 036 (T0) – “packet instructions difficult” (4)
- 039 (T0) – “my husband cooks, I Hoover” (2)
- 039 (T3) – “my husband is disabled but has to do all the cooking, the only way I know if the stove is on is if I wave my hand over it” (1)

EQ-5D-5L HEALTH QUESTIONNAIRE

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

- I have no problems in walking about
- I have slight problems in walking about
- I have moderate problems in walking about
- I have severe problems in walking about
- I am unable to walk about

SELF-CARE

- I have no problems washing or dressing myself
- I have slight problems washing or dressing myself
- I have moderate problems washing or dressing myself
- I have severe problems washing or dressing myself
- I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

- I have no problems doing my usual activities
- I have slight problems doing my usual activities
- I have moderate problems doing my usual activities

I have severe problems doing my usual activities

I am unable to do my usual activities

PAIN / DISCOMFORT

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extreme pain or discomfort

ANXIETY / DEPRESSION

I am not anxious or depressed

I am slightly anxious or depressed

I am moderately anxious or depressed

I am severely anxious or depressed

I am extremely anxious or depressed

We would like to know how good your health is TODAY.

Where '0' describes the worst health you can imagine and '100' describes the best health you can imagine.

Write the number between 0 and 100 that describes your health today in the box below:

Appendix 2.6

Patient Testimonials (EuroQol Five-Dimension Five-Level Questionnaire)

Underlined text represents interpretation by Chief Investigator. T0 is the initial visit, T3 is the three-month follow-up and T6 is the six-month follow-up. Three digit number is patient identifier code. Numbers in brackets indicate EQ-5D-5L response score (1-5).

Patient Testimonials – EQ-5D-5L Questionnaire

Mobility

012 (T3) – “getting more unsure now” (3 – moderate problems in walking about)

014 (T6) – “I have a stick and have somebody with me all the time – I would not go out alone” (2 – slight problems in walking about)

015 (T3) – “dependent upon lighting” (2)

020 (T0) – “I’m getting a scooter at the weekend” (4 – severe problems in walking about)

020 (T3) – “now I have my scooter” (1 – no problems in walking about)

025 (T0) – “main problem is vision” (2)

Self-Care

009 (T0) – “my husband helps me every day” (3 – moderate problems washing or dressing myself)

012 (T3) – “mixing up colours is a problem – blues and blacks” (3)

012 (T6) – “choosing colours is difficult, I have torches to help, and a carer” (3)

013 (T3) – “I am having problems with the bath, occupational therapy are helping with this – they visit next week” (2 – slight problems washing or dressing myself)

014 (T3) – “I have help with the bath” (2)

015 (T0) – “If nobody is there I put on the wrong combinations of colours” (2)

019 (T0) – “due to mobility” (4 – severe problems washing or dressing myself)

019 (T3) – “I have a carer to put my shoes and socks on” (3)

019 (T6) – “carer helps” (3)

039 (T3) – “I cannot do my hair and make-up” (3)

Usual Activities (e.g. work, study, homework, family or leisure activities)

015 (T3) – “my son (aged 10) helps” (2 – slight problems doing my usual activities)

016 (T0) – “pouring liquid” (2)

018 (T0) – “I have a cleaner” (3 – moderate problems)

019 (T3) - “I have a cleaner” (3)

019 (T6) – “I do little bits only in one go” (3)

035 (T3) – “cooking – I use the magnifier for recipes” (2)

039 (T6) – “my husband helps” (2)

Pain / Discomfort

001 (T6) – “Arthritis – can be severely painful sometimes” (4 – severe pain or discomfort)

Anxiety / Depression

010 (T0) – “my sister went into hospital yesterday” (2 – slightly anxious or depressed)

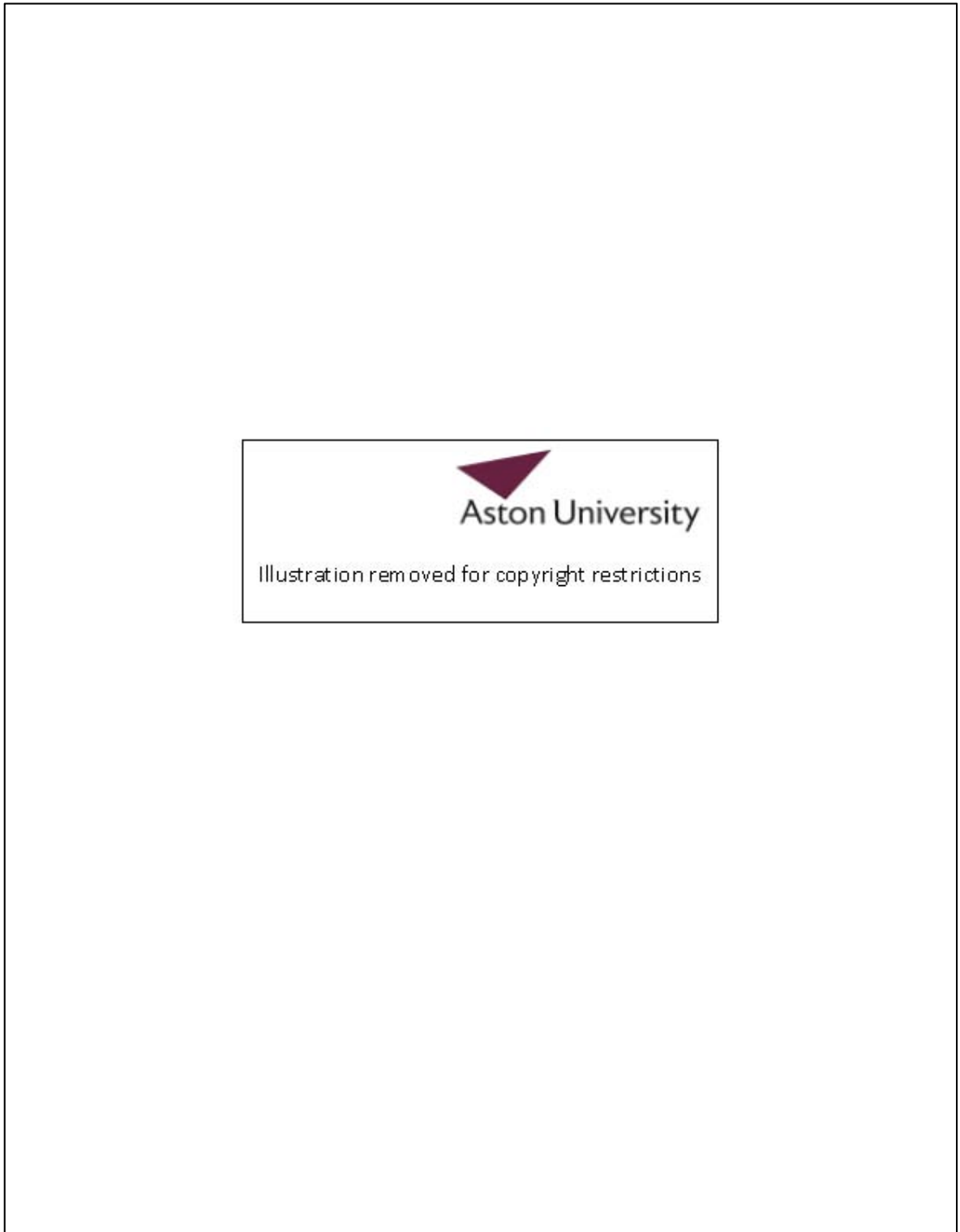
012 (T3) – “getting worse” (3 – moderately anxious or depressed). Scored (3) at (T0).

EQ-VAS

026 (T3) – “50 – depends upon my company. Today ok as my daughter is present but would be lower if I were on my own”. Patient scored 50 on all three visits.

Appendix 2.7

Aston University Ethics Approval





For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

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

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of insurance or indemnity: Certificate from Zurich Municipal		07 July 2010
Investigator CV: Louise James		
Other: Academic Supervisor CV: Professor Stephen J Anderson		
Participant Consent Form	2	01 May 2011
Participant Information Sheet	2	01 May 2011
Protocol	2	01 May 2011
Questionnaire: LVQOL		
Questionnaire: GDS-15		
Questionnaire: EQ-5D		
REC application: Submission Code 42787/181153/1/854		
Referees or other scientific critique report: Letter from AOREC confirming approval		13 January 2011
Response to Request for Further Information		01 May 2011

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

This Research Ethics Committee is an advisory committee to East of England Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England



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Milton Keynes University Hospital Ethics Approval

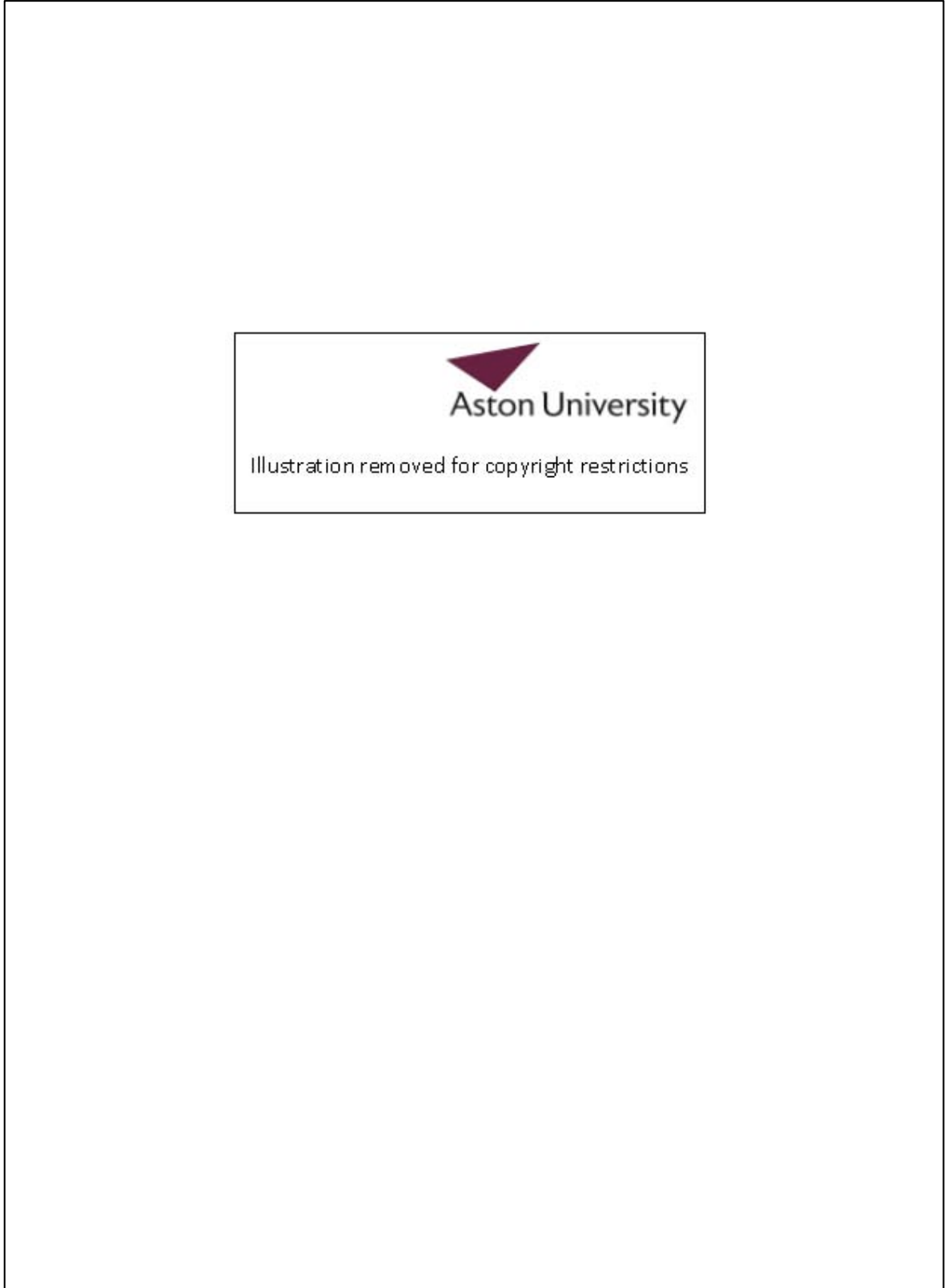




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